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Manuscripts and editorial correspondence should be addressed to

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Szent István Kórház, Urológia
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CHANGING DIAGNOSTIC AND THERAPEUTIC APPROACHES TO THE 'OGILVIE SYNDROME'

Á. Hrívó and I. Besznyák

Department of Surgery, National Institute of Oncology, H-1122 Budapest, Ráth Gy. u. 7–9, Hungary

The only thing that has remained unchanged about the genuinely described 'Ogilvie syndrome' is its name. Recently it was considered to be an acute colonic pseudoobstruction, a clinical entity mimicking the mechanic ileus of the distal large intestine, without organic obstruction. It is almost always secondary to other disases. Not all details of the pathogenesis are known, but it has become clear that the direct factor leading to the disturbance of the motility is a vegetative imbalance. X-ray findings are highly characteristic and critical in the planning of treatment. The danger for the patients is the progression of the state or the long duration of the process. Conservative treatment is suitable only for early cases, without complications. In case of failure non-invasive endoscopic or endoscopically assisted minimally invasive procedures may be mandatory. These methods have seen rapid advance in recent years. Uncertain diagnoses or complications call for open surgery. Cecostomy is the solution of choice anyway. The mortality is high in this group of elderly polymorbid patients. Authors compase six of their cases with data collected from the literature.

Introduction

Perhaps the only thing that has remained unchanged about the 'Ogilvie syndrome', since it was first described by Sir William Heneage Ogilvie in 1948, is its name [1]. Ogilvie reported the history of two patients with tumours in the dorsal subdiaphragmatic region and with a history of subacute or chronic disorder of the gastrointestinal passage.

In recent years, the name has been used to refer to an acute disorder or intestinal motility resulting in the physical and radiological finding of an acute ileus of the large bowel, but without any organic obstruction of that. It is a dynamic disorder mimicking a mechanical one, therefore "acute pseudoobstruction of the colon" (hereafter: APC) might be the most appropriate characterization of the patient's state.

It is not the primary process, but rather the ensuing complications, that endanger the patients. The process lasts several days and may be constant, progressive or even recurrent, and may lead either to splitting or rupture of the proximal colon – generally the cecum – or to wall tension which results in its perforation, in turn causing necrosis.

In the last few decades a hypothesis of the pathomechanism has gained acceptance.

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The radiomorphology seems to be crucial in the assessment of the prognosis. This has been thoroughly analysed elsewhere [2].

The physical basics of the dilation and rupture have been studied and described in connection with the pathoanatomy [3], and alternative ways of treatment have been worked out.

The number of cases reported in the literature is up to a thousand, although each group of surgeons or other specialists reports on only a few cases [4]. There is a rate of perforation of up to 15%, and when occurring, mortalitz could rise to 40%.

Less than twenty cases have been reported in Hungary since the 1960s, but the actual number must be much higher.

Patient and Methods

In the last ten years there have been six undisputed diagnoses of Ogilvie syndrome. The characteristic data are summarised in Table 1. One of them is detailed in the followings:

A 63-year-old male was referred to our department with verified cancer in the LUL of the lung. The patient was an alcohol addict and otherwise a poor risk candidate for COLB. He underwent lung resection. In the first few postoperative days a mild hypoxaemia was detected. Bronchus-toilette, oxygen-therapy and physiotherapy were administered. Pleural drains were removed on the third day. Psychic and neurologic signs of alcohol withdrawal were seen and medically treated. A marked intestinal gas collection was observed from the third postoperative day, which was found to increase continuously. Moderate intestinal sounds were heard. Following surgery stools were evacuated at all, in spite of the medical treatment. The pseudoobstruction was conservatively treated. A very mild and diffuse tenderness appeared on the sixth day, without physical symptoms of peritonitis. The intestinal movements were assumed to become normalised, however, in spite of the changing state, the daily routine chest X-ray revealed a very delicate gas collection under the right diaphragm. Urgent laparotomy was performed. Extreme, gaseous cecum dilation was found, which was accompanied by moderate dilation of the ascendant and transverse colon. There were short tears alongside the teniae of the cecum. One of them showed a very fine leakage of gases and stool with initial peritonitis around it. A cecostomy was formed at the site of the leakage. An eventful postoperative period followed and six weeks later the stoma was closed.

Discussion

Though the syndrome has been known for forty-seven years, there is hardly any mention of it in recent handbooks of gastroenterology, and occasionally it is merely regarded as a transient disturbance of bowel motility.

According to the literature, APC is clustered in the fifth or sixth decades. The youngest patient found was 15 and the syndrome is common in the elderly (see our cases). There is an even distribution between sexes.

The pathogenetic factors of the syndrome have been clarified. According to Ogilvie, the tumours around the crura of the diaphragm interrupt the sympathetic and parasympthetic innervation of the abdominal viscera and the sacral parasympathetic innervation starts to dominate the former balance. In this opinion the impact results in a spasm of the distal large intestine, creating a pseudoobstruction, or rather a dynamic obstruction.

Today, our idea is just the opposite. The parasympathetic overregulation would result not in a spasm, but rather in a forced peristaltic movement. Only the cessation of pelvic parasympathetic innervation may be the actual cause. So the direct reason for the syndrome is, theoretically, the interruption of the parasympathetic influence of the S2-S4 segments, leading to the hypomotility of the left colon. The anatomical border of the vegetative innervation is the midgut-hindgut border, i.e., about the left flexure of the colon [5, 6].

Others suggested that, together with the above-mentioned mechanism, the special situation at the fixed and the free portions of the colon may also contribute, through a 'kinking-effect' [7]. This is at odds with the common finding at surgery, namely, that there is no precise cut-off point between the distended and normal bowel.

The impact of humoral factors has also been under discussion – e.g. glucagon, prostaglandins, sex hormones – but few studies have appeared, especially on the acute pseudoobstruction. The well-known influence of tricyclic antidepressants on bowel motility also works in a neurohormonal way [8, 9].

The neural origin of the disease is generally accepted nowadays. The direct events that activate the mechanism are indicated in Table 2. According to the collected data – which are controversial – the cases are clustered among gyneco-obstetrical, urological and traumatological patients. The proportion of pregnant women or who underwent Caesarean section is high in particular.

The rate of 'idiopathic' origin is about 10%.

Clinical findings. After 1–10 days of uncertain or atypical abdominal discomfort, the bowel distension shows progression. The symptoms do not point to either the dynamic or obstructive disorder of motility, but rather to their mixture. The leading sign is meteorism, first with intestinal spasms. The cessation of bowel movement occurs only in about 1/3 of cases; in fact diarrhoea is not uncommon, despite the serios distension. Nausea and vomiting are not typical. Sometimes abdominal tenderness occurs, accompanied by normal or (less frequently) forced intestinal movements with lack of splash. Muscular defence occurs only late, in the case of peritonitis, as a sign of perforation. The rectum mostly contains normal stool.

Radiological findings are crucial. The diameter of the cecum may be up to 22 cm. The distension and gas blow-up have a characteristic cut-off point at the splenic flexture. Nevertheless, usually a small amount of gas collects along the distal colon as well [6, 10].

Table
Patients with

Patients (year)	Former history	Prev. compl.-s	Diagn. at admission	X-ray, cecum diameter
62 female	urolith, appendect., cholecystect., hypertension, diab. mell.	vomiting diarrhoae abd. spasms	mechanic ileus	gases till desc. colon 10 cm cd.
95 female	appendectomy	abdominal spams no stools for 3 d.	mechanic ileus	extreme gas collect. till left colon 11 cm c.d.
80 female	caes. sect., inf. myoc., appendect., hypertension	mild abd. spasms no stools for 7 d.	mechanic ileus susp.	gas collection in the right colon with tenderness, 9 cm c.d.
62 male	appendectomy nephropexy	lobectomy for lung cc. 5 days earlier		gas collection till left colon 11 cm c.d.
31 female	appendectomy	caes. section 10 days earlier	mechanic ileus	gas collection till left colon changing c.d.
63 male	alcohol addiction	lobectomy for lung cc. 6 days earlier		extreme gas coll. in the whole colon

The advantages of irrigoscopy have been emphasized earlier by several authors. Others consider it unnecessary or even harmful. It is also well known that irrigoscopy often fails with older patients in poor condition, and for this reason in particular, the organic obstruction may not be excluded by this method. Nowadays, in the 'colonoscopic era' this latter is prior to the former in differentiation of real obstructive and dynamic ileus.

Serial native abdominal X-ray is suitable where conservative treatment is called for – as for example in cases of toxic megacolon.

The perforation of the colon is the danger of the process. The otherwise high mortality is much higher if perforation occurs. Different authors put the rate of frequency of this complication between 0 and 10 per cent, with about 40% mortality [11].

It has been concluded from serial measures that a cecum diameter over 9 cm, particularly with a competent Bauchin valve, means overdistension and represents imminent complication if its persists for a few days [10]. The duration of the dilation is as important as its diameter.

Recently it has been observed that constant distension at 9–12 cm in diameter, lasting for about three days, almost surely leads to complications. That is why three days is regarded as the limit of conservative treatment [2].

1
Ogilvie syndrome

Irrigoscopy	Indication for surgery	Operative findings	Surgery	Outcome
failed	mechanic ileus	distended small and large bowels	transanal tube decompression and anus sigmoideus	died of pneumonia (7th day)
rectoscopy neg., irrigosc. failed	clinical and radiological progression	extremely distended colon	anus transversus	died of heart failure (30th day)
failed	clinical and radiological progression	distended colon till the left flexure	manually assist. evacuation per anum	healed
not attempted			conservative treatment	sudden death neg. autopsy
not attempted			conservative treatment	healed
not attempted	perforation	extremely blown up cecum with multiple splitting and a single leakage	cecostomy via laparotomy	healed cecostomy closure 6 weeks later

A 'splitting phenomenon' is often found at the time of surgery. Specifically, one or more splits appear along the teniae, often together with mucosal prolapse. This occurs most often, but not exclusively, on the cecum.

It is evident from these facts that the first cause of the cecum perforation or rupture is the overdistension.

Dotted necroses are seen less frequently in the wall of the colon.These are ischemic in origin and may also lead to perforation.

Therapeutic modalities

The tools rather than the principles have changed over the last few decades. Since the syndrome is a consequence of a prior pathology, according to the normal rules of medicine, the prior event must be the first target of treatment. But this is often impossible or unnecessary, as it is not the basic pathology or event, but rather the complication– the APC – which poses the danger. The first task is decompression of the large bowel. For treatment, many methods are at disposal.

*Conservative treatment.*If all other abdominal catastrophes were excluded (organic ob-struction, volvulus, vascular disease, etc.) and/or there were no symptoms of peritonitis

Table 2
Trigger factors for Ogilvie syndrome

Cardiovascular diseases
myocardic infarction, circulatory insufficiency, pulmonary embolism, surgery
Respiratory diseases
acute and chronic hypoxemia, pneumonia, artificial ventillation
Diseases in the pelvic region
urogenital interventions, kidney transplantation, stones in the urinary tract, pregnancy, delivery, gynecological inflammatory diseases, pelvic injuries
Postoperative state
Abdominal inflammatory diseases
cholecystitis, gastritis, pancreatitis
Retroperitoneal processes
bleeding, phlegmone, tumours, kidney-ureter diseases
Injuries
thoracic, abdominal, pelvic, backbone, skull, burns
Systemic diseases
alcohol addiction, toxic states, diabetes mellitus
Infections
pneumonia, gangrene of the extremities, septic state, herpes zoster
Neurologic and psychiatric diseases
brain tumours, degenerative processes, vascular diseases, Parkinson's disease, major tranquillants
Idiopathic occurrence

and/or the diameter of the cecum would not be over 9–12 cm for a period of time, then and only then conservative treatment may be initiated. This means tube drainage of the stomach with continuous suction and evacuation of the lower section of the colon by repeated enemas.

Recently, in a departure from former ideas, phamaceutical products have been administered in order to set the bowels in motion. The first choice may be ceruletid. Others put forward (or just doubt) the administration of erythromycin as it is a direct motilin antagonist [12].

Continuous epidural anaesthesia is also recommended as a means of conservative treatment [13].

Sloyer questions the need for any other method. All but one of his patients were treated in this manner, without any complications [14].

According to the literature the mortality rate is about 20%. Long-term observation is recommended since recurrence is possible within two weeks.

Endoscopic treatment. Kukora was the first to recommend endoscopic desufflation as treatment [15]. It is performed after failed conservative attempt or at the outset in advanced cases. The presence of organic obstruction or the early signs of transmural necrosis are discovered by endoscopy. In such manner, the mostly elderly patients do not need to stay in bed, and further complications are avoided.

The danger of iatrogenic overdistension is prevented by using pressure-limiting valves [16].

The procedure may be repeated if necessary, or a tube may be inserted to drain the whole colon [17, 18].

About fifteen per cent of attempts at this procedure fail as well, because the cecum is unreachable.

The mortality rate in case of this treatment method is as favourable as a few per cent.

Limited access invasive methods provide a new therapeutical approach, which has seen rapid advance. First, Crass described CT-guided needle aspiration [19]. Later, others studied the effectiveness and safety of the transretroperitoneal or transperitoneal insertion of a catheter into the dilated cecum [20]. A third version of the percutaneous drainage is performed in an endoscopically assisted way, i.e. percutaneous endoscopic cecostomy (PEC) [21, 22]. The described methods are probably all equal from the view point of safety and effectiveness, providing means to avoid the more risky open surgery. The disadvantage is that they require highly skilled personnel.

Surgery is needed if all other methods have failed or the disease is in a late stage of peritonitis or perforation. It is also necessary if diagnosis has been uncertain and irrigoscopy or colonoscopy have been considered to be too dangerous, given the enormous distension.

Surgery may be performed with or without laparotomy. Transabdominally, manually assisted transanal insertion of a tube is the simplest and less invasive version, with open surgery. It is obvious that this method carries a certain risk of insufficiency, as do all tube-drainage methods. Cecostomy is the most widely used procedure. It may be performed even under local anesthesia. But it is not advisable in spite of its simplicity, as complications occurring in another section of the colon can be overlooked without laparotomy. The situation is the same with the colonoscopically assisted cecostomy. The limited access does not allow the prevention of further complications.

Laparoscopic cecostomy may be chosen if other minimal access methods are insufficient [23]. This is above all diagnostic procedures, and should be attempted only if a complication is imminent. It is as accurate as open exploration is in diagnostics. Then if a resection is not urged by the findings, the intervention becomes a therapeutic proce-

dure, allowing laparoscopic tube cecostomy. The method is considered to be a safe one and more tolerable than laparotomy. The only problem which may arise is again insufficient tube drainage of the intestine.

The expected results of a stoma come sooner and are more certain if the stoma is a wide one performed via laparotomy. It is the only suitable intervention if minimally invasive methods are not applicable or if a complication has already occurred.

Meticulous exploration seems obligatory when laparotomy or laparoscopy are at issue. It is emphasized that even if the cecum was overextended, perforation or necrosis may occur at the cecum and/or even elsewhere in the large intestine [3]. Nevertheless, the continuous desufflation of the cecum must be dealt with even in these cases, usually by cecostomy. Anus preternaturalis at another section is unsuitable to prevent further complications at cecum-section, as intestinal paralysis may last for 4–14 days after surgery [10].

In cases of extended necroses or necrobioses, surgeons have no other choice than hemicolectomy.

The mortality rate of patients operated on is 20–40%.

Table 1 shows the relevant data of *our six patients*. It is interesting, but probably coincidental, that all but the last patient underwent earlier appendectomy. The abdominal symptoms were acute for five and subacute for one patient. They match the criteria of APC. The trigger factor was not identified even retrospectively in three cases: these are the so-called 'idiopathic' forms. Former lung resection for two patients, delivery Caesarean section for one patient were prior to the abdominal disease. The diagnoses were mechanic ileus of the colon in four, perforation in one and dynamic disorder of the gastrointestinal tract in the sixth case. The X-rays were all typical, showing mostly gaseous distension extending to the left colon. Irrigoscopy was attempted twice, with failures in terms of gaining relevant information.

Endoscopic procedure was not attempted even once. This is because three out of six cases were 'idiopathic' forms – the patients wre admitted as cases of mechanic, colonic ileus; the conservative treatment was successful in one case, perforation developed very rapidly in another case, and sudden death occurred in the last case.

Four interventions were performed. It was avoided in the fifth case because of the quickly changing clinical findings. Two distal colostomies were not the best choices, even though no consequences followed. The other two, a manually assisted insertion of a transanal drain at laparotomic exploration, and a cecostomy, were successful. The same may be said of one of the two conservative treatments.

Three out of the six patients were lost. Two of the deaths were not directly related to surgery: their cause was the polymorbidity of the elderly patients.

The histories of our patients and the literature suggest that APC is not always recognized. The spontaneously healing forms are generally not noticed. Cases with complications are probably registered under other diagnoses.

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PRIMARY MALIGNANT LYMPHOMA OF THE APPENDIX (A CASE REPORT AND REVIEW OF THE LITERATURE)

H. Uncu, E. Erdem and A. Tüzüner

Department of Surgery, University of Ankara, Faculty of Medicine, Büyükesat, 06670, Ankara, Turkey

Authors report a case of a 29-year-old male with primary malignant lymphoma of the appendix with involvement of lymph nodes in the mesenteries. Surgical intervention was performed, adjuvant chemotherapy was applied. No recurrences, metastases or complaints occurred after one year of follow-up. The case is of interest due to the clinical and histopathological diagnostic problems as well as the dimension of the metastatic lymph node in the ileal mesentery.

Introduction

Although the lymphomas are seen in the bowel in 5% of the cases of this disease, only 1–3% of all bowel lymphomas are reported in the appendix [1–3]. Since appendiceal lymphoma is a rarely detected disease with a nonspecific clinical appearance, it is commonly diagnosed incorrectly as appendicitis, retroperitoneal tumours or other diseases. Ultrasonography, computed tomography and double contrast barium enema were performed in the presented case which showed atypical symptoms. However, none of these imaging studies could diagnose the appendiceal lymphoma correctly. The proper diagnosis was established with histopathological studies after surgical intervention.

In the followings, a case of primary malignant lymphoma of the appendix is presented without organ metastasis but with mesenterial lymph node involvement of the ileum and colon, one of them being $9 \times 7 \times 6$ cm in size. A report is also given of the treatment methods and their results, with a review of the literature.

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Patient and Methods

Case Report

A 29-year-old male patient was admitted to hospital with symptoms of mucous stool, dysuria and periodical disturbing abdominal pain of the right quadrantes for the last 2 months. He also had complaints of dyspepdia and slight weight loss for the last 6 month. He did not have hematochezia or any other illness, and was not on medication. There was nothing noteworthy in his personal and family histories. On physical examination, a palpable tumour on the right lower quadrant of the abdomen was evident. Digital examination of the rectum was normal. There was no general lymphadenopathy or hepatosplenomegaly. Upon physical examination, the other systems were normal.

Nothing abnormal showed up on his serologic and haemotologic tests. Furthermore, electrocardiogram showed no abnormal findings. Roentgenologic examinations of the abdomen, thorax and urinary system showed normal results. Ultrasonography revealed a mass 102× 75 mm in dimension with a central heterogeneous echo and peripheral hypoecho in the region of the appendix which was thought to be an appendiceal abscess. Double contrast barium enema revealed a mass in the localization of the ceacum which was pressing on the colon. By the computed tomography of the abdomen, two abdominal masses were determined. One was a hypodense mass 8.5 cm in diameter, in the right lower quadrant, extending to the right parailiac zone, pressing the right ureter and changing its place to the lateral side. The other mass was in the large bony pelvis, 9 cm in diameter and partially necrotic (Fig. 1).

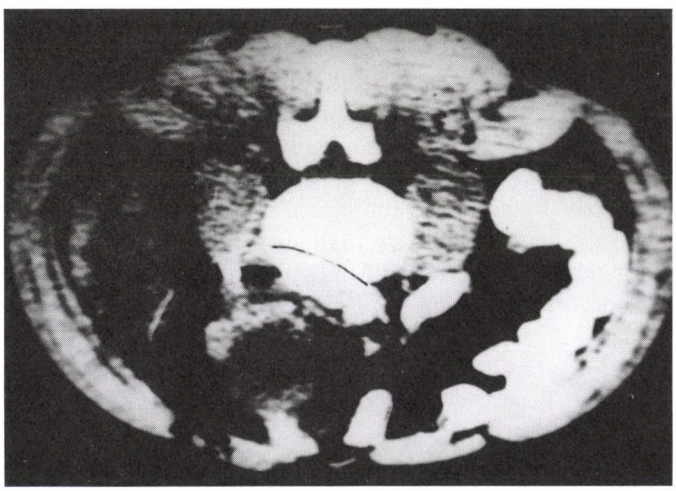

Fig. 1. Preoperative CT section shows abdominal masses

Surgery

After radiological examination, surgery was decided on for diagnosis and treatment. Following median laparotomy, a solid capsulated mass was seen at the mesoileum, 9×7×6 cm in size, pressing the sigmoid colon. It was considered to be a lymph node. The mass showed partially nodular structures and could easily be broken into pieces by means of palpation. The other mass, 11 × 8.5 × 5 cm in size, was semisolid and dirty yellow in colour, observables in the ileoceacal area. In addition, there were small lymph nodes in the mesenteries of the ceacum and ileum. Frozen section histopathological studies of the biopsies of these two masses revealed malignant tissue, infiltrated by atypical lymphoid cells. Therefore, right hemicolectomy and a 25 cm long distal ileal resection with mesenteric lymph node dissection were performed. The appendix was infiltrated by the neoplasm entirely, which was resected totally by the surgical intervention. The other semisolid mass in the mesoileum was also totally, resected conserving the vascular structures. After end-to-end ileotransversostomy the liver and spleen were found to be normal and the operation was concluded.

Pathology

Histopathological examination revealed bleeding areas in the atropic mucosal layer of the thinned wall of the appendix. The normal structures of the appendix were completely destroyed. The appendiceal wall disappeared as a result of diffuse tumoural infiltration. There were malignant tumour areas with atypical lymphoid cells which had multilobar nuclei, nucleoli and narrow cytoplasm. A large number of mitoses were observed (Fig. 2). Accordingly, the result of the histopathological study was high grade centroblastic non-Hodgkin malignant lymphoma according to Kiel's classification. There was no mucosal or muscular pathology in the resected ileum and colon, only serosal odema and hyperemia were found. The histopathological examination of the large mass in the mesoileum showed a lymph node infiltrated diffusely with the same characteristic tumour cells. It also consisted of large bleeding as well as necrotic areas. Five lymph nodes in the mesoceacum and 3 lymph nodes in the mesoileum revealed hyperplasia.

The patient had no postoperative problems and was discharged one week following surgery. He received 6 doses of cyclophosphamide, vincristine, mitoxantrone, corticosteroid combination chemotherapy treatment.

For a period of one year, the patient was controlled once a month. No problems have arisen and he is still working as an English teacher. The findings of repeated computed tomography of the abdomen and thorax have been normal (Fig. 3).

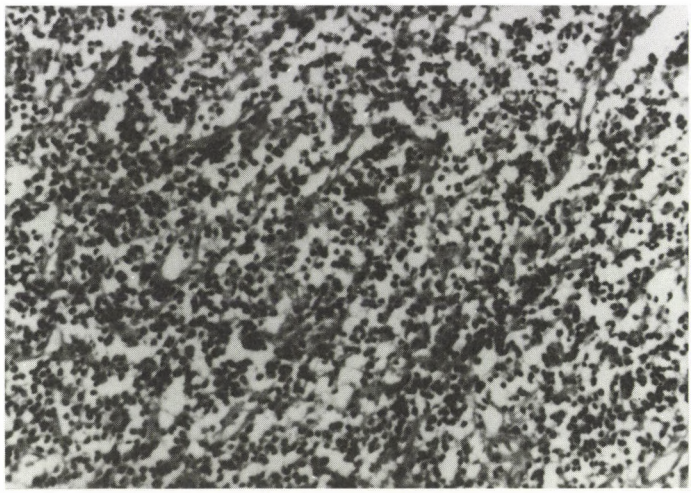

Fig. 2. Histopathologic examination shows malignant appendiceal tissue infiltrated by atypical lymphoid cells

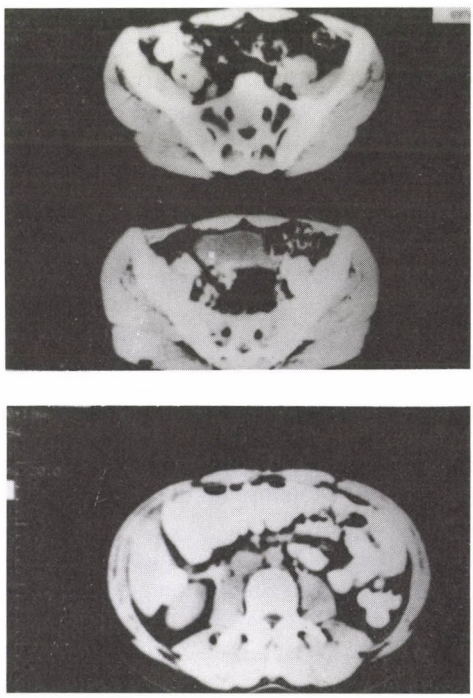

Fig. 3. CT sections of abdomen and thorax were normal in the control of the patient

Discussion

Although extranodal lymphomas are frequently seen in the gastrointestinal tract, lymphomas of the appendix are rare [4]. Schmutzer found 101 appendiceal neoplasms among 8699 appendectomy cases. After metastatic carcinomas with 12 cases, lymphomas took second place with 3 cases in the classification of malignant tumours of the appendix [5]. Mori found 38 primary lymphomas in the literature, to which he added one of his own 70-year-old cases. In his study, lymphosarcoma took the first place among them by 14 cases [6].

The primary lymphoma of the appendix is frequently manifested in the second and third decades, however, it might be seen between the ages of 4 and 70, with a mean age of 25 years [6–8]. Appendiceal lymphomas are seen in younger ages more than other gastrointestinal lymphomas. Its cause is explained with the appendix having more lymphoid tissue in childhood [9]. There are symptoms of patients where the physician cannot make a diagnosis. The chief complaints of the patients are usually similar as for appendicitis. The most frequent complaint is right lower quadrant pain. A few of them have palpable tumours. The patients may also be presented with ileus or peritonitis secondary to perforation of the appendix [3, 10]. Symptoms not usually present, however, were observed in our patient, including dysuria, mucous faeces and weight loss.

Although, there are a lot of imaging techniques, preoperative diagnosis is very difficult. Some cases were found accidently during operation [6]. Ultrasonographic examinations revealed acute appendicitis or localized abscess formation of appendicitis as a confusion [1, 8]. Also, in our case a wrong diagnosis of localized appendiceal abscess was made with the use of ultrasonography, as mentioned above. However, upon surgical procedures this was determined to be incorrect and a lymphoma was discovered. Computed tomography can give more knowledge about the size and wall thickness of the appendix and the presence of periappendicular inflammation. In the report of Balthazar, computed tomography defined 7 abnormal appendices, of which 5 were mucoceles and 2 were primary adenocarcinomas in the 22 cases thought to be appendicitis [11]. There were no pathognomonic findings which could be sufficient for the diagnosis and also for the treatment of our case. There is a wide variety of treatment choices. If the tumour is localized in the appendix, appendectomy would be enough. But it would be necessary to apply chemotherapy or radiotherapy according to the result of histopathological examination. If the tumour has reached beyond the appendix and there are lymph nodes in the mesentery, ileoceacal resection and lymph node dissection would be preferred and chemotherapy and/or radiotherapy should be applied [12]. Since we too, share these opinions on treatment plans, right hemicolectomy was performed with a 25 cm long distal ileal resection and mesentery lymph node dissection. Following surgery, adjuvant chemotherapy was applied. However, it is a difficult task to determine which treatment methods are preferable. The number of cases in the literature until now is not enough to estimate the relationships between the prognosis and different treatment approaches [6, 10].

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THE IMPORTANCE OF ARTHROSCOPY IN DIAGNOSING SYNOVIAL HAEMANGIOMA OF THE KNEE JOINT

Cs. Farkas[1], I. Mórocz[2x], L. Szappanos[1] and K. Szepesi[1]

[1]Department of Orthopaedics and [2]Department of Pathology, University Medical School of Debrecen, H-4012 Debrecen, Nagyerdei krt. 98, Hungary

In connection with one of their cases, authors call attention to the importance of differential diagnosis in synovial haemangioma of the knee joint, a rare condition. They also give a survey of its clinical, radiological and pathological features, review the literature on the topic, with special emphasis on the importance of arthroscopy in making the clinical diagnosis, and describe the treatment applied in their case.

Introduction

Synovial haemangioma is a rare condition. In the majority of the cases it affects the knee joint [15] and usually manifests itself in the form of maemarthroses emerging after minor injuries, or no injuries at all, in early adulthood or childhood. Without treatment, degenerative changes may develop in the joint. The condition is clinically significant, since making the proper diagnosis of a vascular tumour may be difficult even if taking the history and carrying out the physical examination are accompanied by techniques of imaging. Since the introduction of arthroscopy, the method has proved to be the most reliable one in making the clinical diagnosis, which can be justified through pathological investigations, too. Moreover, arthroscopy may also serve as the therapeutic solution [2, 10, 11, 14, 19, 22]. Bouchut first described the condition in 1856 [3].

Patient and Methods

Case Report

Puncture due to synovial fluid of the left knee was performed on Z. É. boy at our outpatient department on three occasions at one-week intervals, one month prior to his admission to the clinic. Puncture always justified haemarthrosis. No trauma was present

[x] At present the author works at the Department of Pathology of Csabai Kapui Kórház in Miskolc.

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in his history. Despite the punctures and compression bandages, the haemarthrosis kept recurring. On February 9, 1979, just a week after punctures, he was admitted to our clinic because of expressed pain in his left knee, swollen joint and disability to move. Based on the laboratory investigations, haemophilia could be excluded. No pathological structure of the bone could be seen in his X-rays. No visceral changes could be detected either.

On admission, his patella could be balloted, the knee joint being capable of performing movement in the range of 0–110°. Despite daily punctures and compression bandages performed and changed on five occasions, respectively, his haemarthrosis recurred, so his left knee was opened through a lateral parapatellar incision to enable us to reveal what the bleeding had been caused by. The articular surfaces, menisci and ligamental system were found intact, but the synovial membrane was slightly thickened and characterized by the presence of haemosiderin in it. Parts of the accessible synovial membrane were removed in an attempt to prevent recurrence.

The postoperative period was free of complications, the wound healing at first intention and the knee regained its full range of movement within a month, following icing and special exercises.

Histological investigations (DOTE 1220/79) of the removed synovial membrane revealed the accumulation of haemosiderin granules underneath the widened synovial cellular layer, together with the inflammatory infiltration in the papillary, proliferative and partly scarred synovial tissue. Pathological vasodilation, ulcerative inflammation or tumour could not be detected.

The patient had been free of complaints for 6 years, but then haemarthrosis emerged again following minor injuries on two occasions. Puncture and conservative treatment resulted in healing on each occasion. The possibility of his being a haemophiliac was excluded again.

After 3-year period, he was admitted for the second time because of a 13 × 3 × 2 cm tumour palpated in the same knee in the region of the suprapatellar bursa.

Nothing pathological could be seen in his X-ray. Catheterized arteriography revealed normal vascular structure. The joint was opened along the lateral surface of the knee; piercing through the old scar we found the menisci, articular surfaces as well as ligamental system to be intact. The substance of the synovial membrane contained a 13 × 3 × 2 cm vascular structure, corresponding to haemangioma dilated laterally in the lateral recess and subpatellar bursa in Hoffa's body. Haemosiderin granules were scattered all over the synoval membrane. Regions of the synovial membrane containing dilated vessels were removed. Stratiform closure of the wound was carried out after haemostasis over the drain tube. The postoperative period was free of complications and the wound healed at first intention.

The histological investigation (DOTE 1005/88) showed multiple sections of several twisted vessels of heterogeneous parietal structure and of wide lumen, filled with erythrocytes, next to capillaries and arterioles, in a 13 × 3 × 2 cm region below the synovial surface. The mass of erythrocytes showed signs of organization (Fig. 1).

Diagnosis: Mixed type of synovial haemangioma.

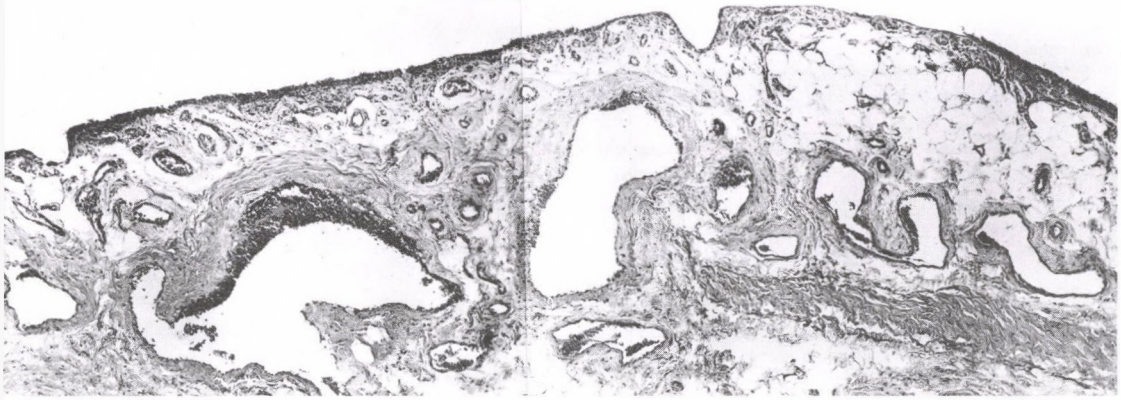

Fig. 1. Synovvial haemangioma of mixed tissue type in the sample removed during the second operation (HE staining, ×63)

Having done special exercises and receiving balneotherapy, the patient was free of complaints in the sixth postoperative week, the range of articular movement being 0–135°.

Over the 9 years since the operation, no haemarthrosis has been detected, the patient's mobility has not changed and he has been free of complaints.

Discussion

Haemangioma is of unknown aetiology, although it is thought to be a congenital lesion by most authors or, according to their supposition, the tumour may develop under certain hormonal effect [12] which is supported by the fact that it may start proliferating during pregnancy [16]. Resulting from the faulty contact among cell groups forming the vascular network, irregular, blind channels may form which are separated from the general circulatory system. Goidanich and Campanacci [7] calls the lesion 'hamartoma', whereas Fairbank [6] classifies it as 'neoplasm' if it is composed of capillaries. Trauma is thought to be a possible pathological cause by Weaver [21].

According to their histological structure, haemangiomata belong to four groups such as capillary, cavernous, mixed caverno-capillary and venous.

Haemangioma may develop anywhere in the locomotor system, the highest incidence being noticed at 60% in the knee joint [5]. The literature surveyed by us listed 208 cases. It is close to equally common in males and females [15]. No cases of bilateral localization have been reported so far. The complaints come in yound adulthood, occasionally in childhood [4, 9, 14, 15]. The various types are found in juxta-articular, intra-articular or intermediate position. Sessile and infiltrative types are distinguished macroscopically, the latter one being difficult to remove, therefore this type has poorer prognosis [18].

Table 1
Differential diagnosis of haemarthrosis of the knee joint

– Trauma
– Foreign body
– Haemophilia
– Sickle cell anaemia
– Dissected osteochondritis
– Osteochondromatosis
– Pigmented villonodular synovitis
– Haemorrhagic arthritis
– Rheumatoid arthritis
– Discoid meniscus
– Meniscal cyst
– Tumour

The importance of synovial haemangioma of the knee joint is underlined by the role it plays in making the differential diagnosis of haemarthrosis of the knee joint (Table 1). The complaints start with the swelling of the joint, haemarthrosis, following a minor trauma or no trauma at all. Pain and restricted articular movement are typical features.

The haemangioma or certain parts of it are rarely palpable, although sometimes it is thought to be a supratellar or mediopatellar plica, due to its location [14]. If ever, it becomes symptomatic only after an injury. Unexplained haemarthrosis should be regarded as synovial haemangioma until other pathological changes or laboratory findings are justified [15]. If the complaints are present for a long time, the muscles around the joint may become atropic, sometimes overgrowth of the extremity is seen due to hypervascularization [15], but this latter feature is absent in changes due to trauma.

If a tumour of the soft parts is palpated in the joint, the detection of phleboliths via radiological investigation may suggest the presence of a vascular tumour and help to distinguish it from tumours of the soft parts, such as the tumour called pigmented villonodular synovitis (PVNS), arborescent lipoma or other benign, juxta-articular tumours, like juxta-articular myxoma as well as the malignant ones, e.g. synovial sarcoma, occurring here.

The bones rarely show radiological changes. In exceptional cases, an uneven surface and/or thickening of the periosteum, atrophy of the femur or tibia, phlebolith, an osteolytic process on the femoral or tibial condyle and thickening of the soft mass surrounding the bone may emerge [15]. In the bulk of the tumour of the soft part, signs of possible calcification may be detected.

Depending on the histological type of the maemangioma, arteriography may reveal hypervascularization or an arteriovenous shunt [15], but it may also present itself in the form of a saturation defect [5], which is also present in PVNS.

Further diagnostic techniques are presented by double contrast angiography [15] which can only inform about the size but not the nature of the tumour. CT and MRI can be helpful, but arthroscopy is regarded to be the best method in the literature in making the diagnosis of the haemangioma of the knee joint [2, 10, 11, 14, 19, 22]. Haemor-

rhagic periods in the history and appearance of synovium during arthroscopy remind of PVNS, which could be another factor making the recognition of the tumour difficult [10]. If the tumour is located beside the body of Hoffa, recognition is made difficult from a technical point of view.

If the presence of haemangioma is suspected, it is imperative to rule out any form of haemophilia using laboratory investigations [14].

Complaints and symptoms caused by synovial haemangioma require a surgical solution in each case. Recently, arhtroscopy has been used both as a modern diagnostic and therapeutic method and a technique playing an important role in the characterization and removal of the lesion [2, 10, 11, 14, 19, 22]. The detected tissue proliferation suggests a diagnosis macroscopically either through biopsy or arthroscopy, although PVNS may have similar morphological features [10]. If the haemangioma is well defined or is a pedicled one, its sheer removal may result in full recovery. Shapiro described the application of holmium YAG laser in one of his cases [19]. Arthroscopic removal of the tumour may be limited by tumour size. If the tumour has invaded a wide area its excision combined with postoperative irradiation may be one of the options [18]. In the case of diffuse tumours, irradiation is recommended as the only method by Reeves [17]. Radiotherapy is contraindicated when the physis is still open. Surveying the major statistical data [1, 15] we found that the excision of the tumour accompanied by synovectomy has been the most effective technique.

In our case, the synovial haemangioma, located in the left knee, was diagnosed after subsequent haemarthroses following minor traumata or no traumata at all. The synovial membrane removed during the first surgical intervention did not provide grounds for making the diagnosis of haemangioma. After a six-year asymptomatic period, haemangioma was diagnosed through histological investigations following another operation on the recessed joint, in the growth phase of the pre-adolescent period.

Our patient has been asymptomatic again, for 9 years, since the removal of his tumour and synovectomy at the age of 18, when he stopped growing.

Synovectomy is indicated not only in the preventive removal of microscopic haemangiomata but also on removing the inflamed and thickened synovial membrane due to subsequent haemorrhages and scattering of haemosiderin, when the membrane can hardly function or it cannot fulfil its physiological role at all.

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RE-EVALUATION OF THE ROLE OF IMPEDANCE PLETHYSMOGRAPHY IN THE DIAGNOSIS OF DEEP VEIN TROMBOSIS IN SURGICAL PATIENTS[x]

M. Cete[1], A. Soran[2], E. Yücel[3], I. Ziraman[4] and S. Hengirmen[5]

[1]*Deputy Chief of 1st Surgical Clinic, Ankara Numune Hospital, Turkey*
[2]*Research Fellow, Surgical Intensive Care Unit in Pittsburgh University Medical Center-USA, Senior Registrar of 1st Surgical Clinic, Ankara Numune Hospital, Turkey*
[3]*Resident, 1st Surgical Clinic, Ankara Numune Hospital, Turkey*
[4]*Deputy Chief of Radiodiagnostic Unit, Ankara Numune Hospital, Turkey*
[5]*Assistant Prof, 1st Surgical Clinic, Ankara Numune Hospital, Turkey*

The clinical diagnosis of deep-vein thrombosis (DVT) is nonspecific and nonsensitive. As a result invasive and non-invasive laboratory tests are needed. In order to detect the diagnostic value of impedance plethysmography (IPG), a widely used non-invasive laboratory test, a prospective clinical trial was performed to compare IPG with color Doppler-ultrasonography (CDUS) and venography.

Seventy-six (41 female, 35 male) high-risk abdominal surgery patients were included in the study. IPG and CDUS were performed preoperatively. During the postoperative period IPG, CDUS and venography were carried out. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy of IPG were all determined. The preoperative IPG was positive in 32 patients, being (+) in 29 patients postoperatively. On the other hand, two of the 29 postoperative IPG (+) patients had DVT diagnosed postoperatively by CDUS and venography. One of 47 IPG (–) patients had DVT diagnosed postoperatively. According to these findings, the sensitivity of IPG was 67%, specificity 63%, and PPV, NPV and accuracy were 7%, 98% and 63%, respectively.

Our study showed that IPG was not a reliable non-invasive laboratory method in the diagnosis and screening of DVT of the lower extremity.

Introduction

Effective treatment of any disease relies on a correct diagnosis. This is particularly true for deep venous thrombosis (DVT) of the lower extremity. The clinical diagnosis is not always reliable in DVT and the symptoms are generally nonspecific and can mimic other nonthrombotic diseases [1–7]. Potentially dangerous venous thrombosis can be silent clinically. Clinical diagnosis of a low specificity as the symptoms of venous thrombosis can also be seen in some other diseases [2]. Additionally the risk of pulmonary embolism, a life-threatening complication of venous thrombosis, makes the diagnosis of venous thrombosis critical [1, 8, 9].

Clinical criteria achieve 50% false negativity and 50% false positivity [9]. Thus, many laboratory tests have been developed for the diagnosis. Invasive techniques in use

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today include I 125 fibrinogen uptake, venography. Non-invasive techniques include color doppler ultrasound (CDUS), and impedance plethysmography (IPG) [10].

In this prospective study, IPG was compared with CDUS and venography, in order to determine the diagnostic accuracy of IPG in surgical patients.

Patients and Methods

Between June and September 1995, patients were prospectively enrolled in this study at the Ankara Numune Hospital, if they were to undergo elective abdominal surgery. Low molecular weight heparin (LMWH-Fraxiparine 0.3 ml) was administered subcutaneously to all patients 12 hours prior to surgery and continued until the 7th postoperative day; the dosage was 0.3 ml/day. The patients were mobilized as early as possible. Those who had a diagnosis of DVT were treated with a high dosage of LMWH and immobilized. All patients underwent surgery under general anesthesia. Measurements relating to fasting glucose, haemogram, thrombocyte count, bleeding time, coagulation time, as well as partial thromboplastin time were all performed preoperatively.

Five days prior to operation, IPG and CDUS were performed on all patients. The same tests were repeated on the 5th postoperative day and venography was performed in patients who had suspicious IPG positivity.

The Toshiba SSH 140 A colored Doppler, 7.5 MHz linear transducer was used for CDUS. Convecs transducer 3.75 MHz was used for thicker extremities. The results were assessed by two experienced radiologists. Venographic examinations were carried out in a standard manner in the Radiology Department of our Hospital.

The IPG 800 (Electro Diagnostic Instruments) was used for IPG examinations. These examinations were performed based on the procedures of Dr. Hull and Dr. Taylor [10, 11]. All the tests were performed by the same technical staff. The patients were in supine position, a special pillow was put under their thighs, so their knees were in a flexed position. Their lower extremities were minimally externally rotated so that the hip joint had a 20–30° angle. Peripheral electrodes were placed on the thighs. Pneumatic cuffs were applied on the legs to occlude the circulation, cuffs were inflated maximally to 50 mm Hg and were kept at this position for 45 or 120 seconds.

During this period, venous capacity (VC) and 3 second "venous outflow" (VO) were automatically measured, and graphically displayed (Fig. 1). VO and VC were considered normal, if the test result was above the dotted line (Fig. 2). Below the line the highest increase and highest decrease values of the parameters were interpreted in order of disease suspected (+) DVT.

Sensitivity, specificity, positive and negative predictive values, as well as accuracy ratios of IPG were determined. Patients were separated into two groups; (–) normal, (+) abnormal.

Results

A total of 76 patients were included in the study, who had undergone abdominal surgery, admitted to our Clinic between June and September 1995 (41 female and 35 male patients in total). The age range of the patients was between 35 to 80 years and the average age was 60 years. Thirty-six of the patients were smokers. None of them were using oral contraceptives, hormones or anticoagulant drugs. Malignant abdominal disease was the cause of hospitalization for 23 patients. One out of the 76 patients had a history of DVT (Table 1). Twenty-three of the 76 patients had a coexisting illness (Table 2).

Blood tests were normal in all patients. Forty-four normal (–) and 32 abnormal (+) results were obtained by IPG preoperatively. Ten patients having (+) IPG test results preoperatively changed to (–) postoperatively. The results of 7 patients were (–) preoperatively and (+) postoperatively.

Table 1
Characteristics of the patients

Number of patients	*76*
Female patients	41
Male patients	35
Average age	60 (35–80) years
Smokers	36
Oral contraceptive use	none
Hormone	none
Anticoagulant use	none
DVT history	1
Gastric cancer	11
Colorectal cancer	10
Pancreas cancer	2

Table 2
Coexistent medical diseases

Diabetes mellitus	6
Chronic obstructive pulmonary disease	3
Atherosclerotic coronary disease	3
Previous myocardial infarction	2
Duodenal ulcus	4
Goiter	2
Total	20

Table 3
Results of IPG, CDUS and venography

No. of patients	Preop. IPG	Preop. CDUS	Postop. IPG	Postop. CDUS	Venography
76	32 (+)	3 (+)	29 (+)	3 (+)	3 (+)
	44 (–)	73 (–)	47 (–)	73 (–)	27 (–)

Preop.: preoperative
Postop.: postoperative
IPG: Impedance plethysmography
CDUS: Color Doppler ultrasonography

Table 4
Analysis of IPG results

Sensitivity	67%
Specificity	63%
Positive predictive value	7%
Negative predictive value	98%
Accuracy	63%

In the preoperative and postoperative periods, lower extremity CDUS was performed in the 76 patients and DVT was diagnosed in 3. Venography was performed in 30 patients whose IPG results or CDUS were (+) postoperatively. DVT was diagnosed in the same patients whose CDUS was also (+) (Table 3). One patient whose IPG was (–) pre- and postoperatively, was shown to have a DVT by venography and CDUS.

Overall, the sensitivity and specificity of IPG was 67% and 63%, respectively. PPV was 7%, NPV was 98% and the accuracy was 63% (Table 4).

Discussion

Lower extremity DVT that can develop in the postoperative period is one of the most frightening complications for surgeons, especially because of the risk of fatal pulmonary embolism [1]. Because the clinical diagnosis may be misleading for DVT, sophisticated laboratory tests are needed [6, 11, 12].

Such a test must have the features of being non-invasive, having no risk of morbidity, being easily applicable and useable at the bedside. In addition, its reliability in diagnosing DVT must be proven in prospective studies, and cost effectiveness must also be considered [7, 13, 14].

No diagnostic or screening tests being 100% sensitive and specific have been developed so far. Although venography is an invasive method and the contrast agents used have undesirable side effects, in the hands of an experienced radiologist the results have

Table 5
Diagnostic studies of deep vein thrombosis

Tests	No. of literature	Sensitivity (%)	Specificity (%)
I 125 FU	8	90	96
IPG	24	56	73
Phlebography	4	97	94
CDUS	20	84	88

I 125 FU: I 125 Fibrinogen uptake
IPG: Impedance plethysmography
CDUS: Color Doppler ultrasonography

more than 90% reliability and the exact localization of DVT can be demonstrated. This test is still the "gold standard" [1, 3, 6]. No complications or side effects were observed in this study during venography, which was always performed by an experienced radiologist. DVT was diagnosed in three patients.

CDUS is a non-invasive method, which can also demonstrate proximal thrombi and has a 90% reliability. The "Triplex-scan" method has been applied widely in recent years. By this method, the location of thrombus, and its anatomy can be successfully observed in many cases [1, 6, 15–21]. CDUS was applied to all our patients and DVT was diagnosed in three of them, postoperatively. These results were confirmed by venography.

Thrombi that form in popliteal, femoral and iliac veins generally block the venous "outflow" and so impair the normal pressure/volume relationship in the leg. Based on this principle, various plethysmographic methods have been developed. Among these, the most widely used is impedance plethysmography (IPG). There are some advantages and disadvantages of IPG. It is non-invasive and bedside usage is possible. Technically its usage needs experience. Technical error can cause false negative as well as false positive results. If the pneumatic cuffs are tightened more than necessary, they block venous return and can mimic DVT. Placement of the peripheral electrodes can cause a similar problem. False results can be caused by abnormal contractions of leg muscles, peripheral vasoconstriction, hypotension, cold weather and pain. False results can also occur during pregnancy, or in patients with leg edema, traction, previous DVT or obesity [22]. Although the device was used in this study by an experienced team, the conditions that could affect the results of IPG and CDUS were minimized, and the test was carried out 5 times for each patient, false negative and false positive results were nevertheless obtained. In our study, pre- and postoperative IPG results were (+) in 22 patients. These positive tests were also confirmed by CDUS and venography in only two patients. In 10 patients preoperatively (+) IPG became (–) postoperatively and the converse occurred in 7 patients in whom the CDUS results were (–). The reason for this discrepancy in 17 patients was not understood. The preoperative false positivity in 20 patients did not change postoperatively.

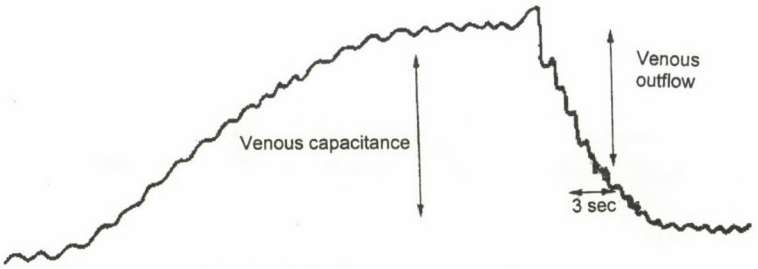

Fig. 1. IPG trace form a chart recorder

In comparative studies of IPG and other laboratory methods, many encouraging results for IPG have been previously published [2, 7, 9, 14, 23–29]. In almost all of these studies the sensitivity and specificity of IPG were found to be more than 90%. In these prospective studies, the results of IPG were better than, or at least the same as CDUS and venography. Recent studies, some before 1992, showed that the sensitivity and specificity of IPG were much lower than in the studies that had been published earlier [3, 18, 20, 21, 30–41]. Table 5 shows the results of IPG compared with the results of other tests. The overall sensitivity of IPG is 56% on average and specificity is 73%. In our study the specificity and sensitivity were found to be 64% and 67%, respectively, similar to other recent literature.

Pulmonary embolism, the most worrisome sequel of DVT, was not seen in our study. On the other hand, in a recent study, Prandoni et al., who have published many studies of IPG with favorable results, advised not to use IPG in clinical diagnosis. They admitted that IPG is insensitive in suspected DVT patients, as they observed false (–) results of IPG in 10 patients with DVT and the development of fatal pulmonary embolism in 4 patients [30]. Other centers have also found unfavorable results of PG in recent years [35, 36]. The technical reason for low sensitivity and specificity of IPG is the existence of non-occlusive or small thrombi [34, 36, 42].

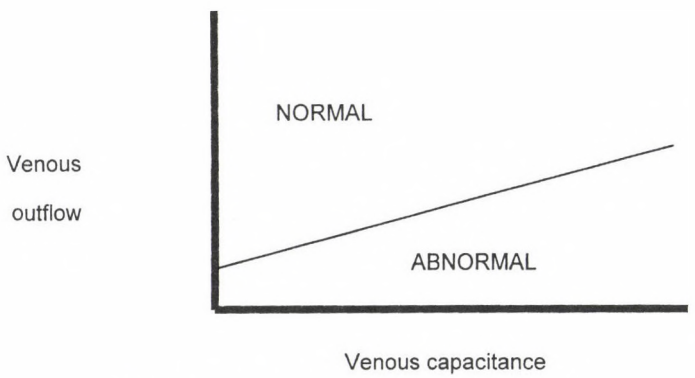

Fig. 2. Line of Huel [43] derived from IPG trace data

The risk of pulmonary embolism is higher in proximal venous thrombosis (P-DVT) than in distal (calf) vein thrombosis. Some authors have stated that IPG is insufficient for the diagnosis of P-DVT but others have emphasized that it is unfavorable for distal DVT [3, 15, 31–34]. In our trial, 3 patients who were diagnosed as DVT had distal venous thrombus (D-DVT). We cannot comment on the accuracy of IPG for D-DVT, since the number of DVT patients was insufficient.

We think that the Triplex scan method is the ideal method for the screening and diagnosis of DVT. It can be used in regions between vein cava and knee, can show the anatomy of the thrombus and compression capacity of the veins, the spontaneous or phasic venous flow, and may be used at the bedside. In addition, it is non-invasive and has 90–100% sensitivity and specificity. Many recent studies of this new method have been published [9, 18, 19, 21]. Venography is the "gold standard" diagnostic test for DVT and must be considered in suspicious cases.

Each medical center should established its own protocol for DVT diagnosis, according to their own economical status and the experience of their staff. Many recent studies of various authors, as well as our own show that plethysmography is not a reliable screening and diagnostic method.

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OVERVIEW OF OUR 13-YEAR-LONG EXPERIENCE WITH COCHLEAR IMPLANTS

O. Ribári and Marianna Küstel

Department of Oto-Rhino Laryngology Head and Neck Surgery, Semmelweis University Medical School, H-1083 Budapest, Szigony u. 36, Hungary

Authors give account of their 13-year-long experience of cochlear implantation. Their results with different devices as well as some observations regarding fitting and rehabilitation are also discussed.

Introduction

During the last decades, cochlear implants have become the treatment of choice for profoundly deaf adults and children who obtain little or no benefit from conventional hearing aids. Since the beginning of the cochlear implant program in Budapest different techniques, devices and speech processors have been consequently used [5, 6]. Significant progress can be achieved with the recently developed continuous interleaved sampling strategy (CYS), which provides improved speech understanding to cochlear implant patients [7]. Attention has also been called to the phenomenon of contralateral hearing improvement [4]. In addition to the usual audiological tests that measure postoperative speech understanding, warble tone sound field thresholds have been established, as well, by means of evaluating cochlear implant performance [6].

Patients and Methods

During a period of 13 years, 75 cochlear implantations were performed; 21 of them on children (63 primary procedures and 12 reimplantations). Thirty patients (18 children and 12 adults) were deaf prelingually, all others had postlingual deafness. Different devices as well as different techniques were used. In 8 cases extracochlear promontory electrodes, in 25 cases extracochlear round window electrodes and in 42 cases intracochlear electrodes were implanted. Considering the intracochlear implants, 2-, 8- or 22-channel intracochlear electrodes were implanted, all of them Med-El devices, with one exception (Nucleus). Having achieved best results with Med-El Combi-40 and

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Combi-40+, we have continued their use not only in patients fitting into the original criteria applied for the ongoing multicenter study with the implant [2] (age more than 18 years, duration of deafness less than 10 years, no signs of concurrent ear pathology, no psychological contraindications, preoperative dynamic range exceeding 10 dB), but in case of all other patients, as well. We have implanted 22 patients with the device so far [6]. Also, different speech processors were applied [1, 3] (both body-worm and behind-the-ear devices); at first a digital pulsatile sound-encoding system, later on analogue processors were in use, while processors operating on the basis of the CIS strategy are preferred nowadays [7]. We have previously called attention to the phenomenon of contralateral hearing improvement after implantation [4]. Because of this, hearing on the contralateral ear of all patients ae routinely checked 3 months after the implantations. In 18 cases, 6 month after the operation hearing improvement was observed on the contralateral ear (Fig. 1). Also implanted patients' warble tone thresholds are established regularly in free-field conditions (Fig. 2).

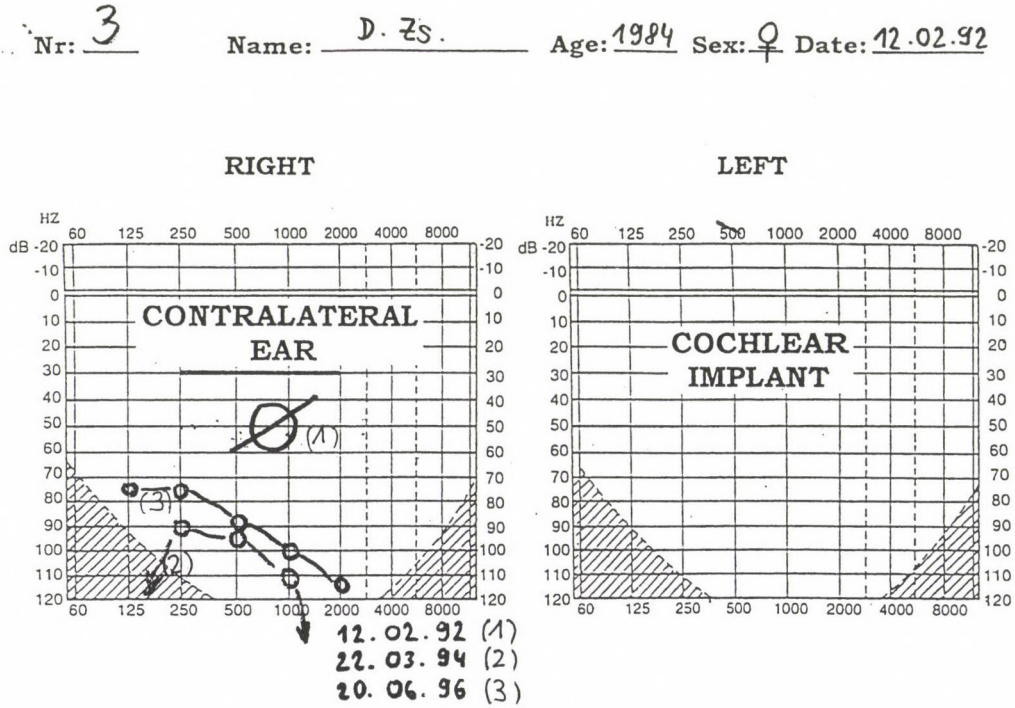

Fig. 1. Contralateral hearing improvement. Recovery of hearing on a previously totally deaf ear

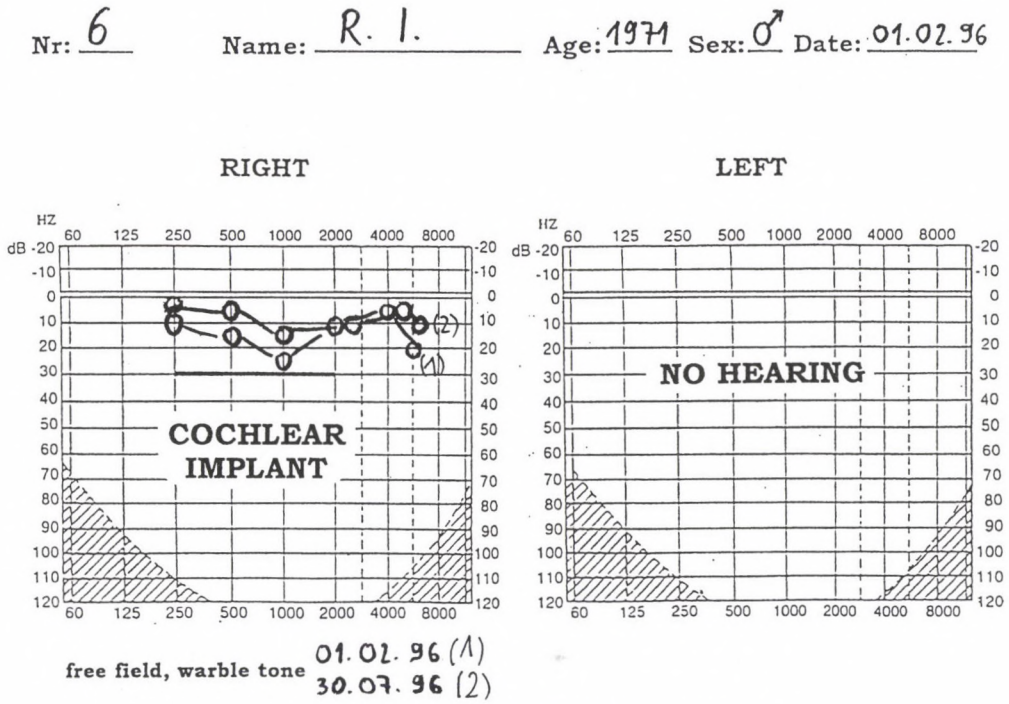

Fig. 2. Warble tone threshold after cochlear implantation

Results and Discussion

Effects of sound-encoding

In our 75 cases different kinds of speech processors were used. Results were compared with both analog and digital speech processors on the same patients. In the majority of cases the analog processors gave better results. Also the patients claimed that they could hear clearer sounds and even better speech discrimination scores were obtained. Best results are achieved with the speech processors working on the basis of the new CIS strategy. This represents a considerable improvement regarding speech discrimination and device fitting. Patients get used to the implants with CIS processor immediately and their speech discrimination is excellent. Based on our experience with Combi-40 patients taking part in a multicentric clinical study, we observed 85–90% speech discrimination without lipreading and rehabilitation; consequently this is our first choice for implantation in case of young postlingual adults.

Contralateral hearing improvement

Previously, attention has been called to the surprising phenomenon of contralateral hearing improvement in the contralateral ear after implantation [4]. Compared to the preoperative hearing threshold, at least a 10 dB SPL improvement could be observed on 2 or more frequencies in 18 cases, or there was a recovery of hearing on a previously totally deaf ear. The hearing improvement was obtained gradually over a period of 12 months on the side using high-performance hearing-aid while the implant was on the other side. The underlying mechanism is still obscure. Hearing on the contralateral ear of all patients are routinely checked 3 months after the implantations. In several cases very high speech discrimination scores could be obtained by a high performace hearing aid on the contralateral side. When a combination of cochlear implant, hearing aid and lipreading was provided, 90–100% speech discrimination could be achieved in all cases. Best results in contralateral hearing improvement were observed in patients who were implanted on their left ear whereas they were right-handed people. It seems that the role of the dominant brain hemisphere cannot be neglected in cochlear implant cases.

Postoperative warble tone thresholds

Evaluating performance with cochlear implants is not easy. Generally, various tests and methods are applied to measure postoperative speech discrimination. On the other hand, there is a considerable difference between being able to detect sounds or to understand speech. While the implant assists the patient to detect sounds, comprehension of speech depends on personal capabilities of the patient itself. Performance is dependent more on the patient than on the implant. It is a common observation, that in case of reimplantation, even if it is with a different implant, the patient who performs well with one device will probably achieve the same level with the other. The wide variability among patients is apparently due to the patient's personal abilities and natural endowments. Therefore, we have begun to detect warble tone thresholds in free-field conditions for 6 months, besides the traditional speech discrimination tests. It seems to make interpretation and documentation of the results easier, on the other hand, it is a tremendous help in fitting the device. Over time a patient's ability to discriminate responds to training and experience, but warble tone thresholds might change only with a more perfect fitting of the speech processor.

Summary

The primary aims were for all our patients to perceive sensations of hearing at normal listening levels, to recognize environmental sounds and distinguish between speech and other sounds. They were promised to understand 90–100% of the speech with lipreading and some of the patients (mostly Combi-40 users) even without that. A considerable improvement in speech intelligibility was also to be expected. As a rule, the

expectations were fulfilled in every case their quality of life improved a lot (marriage, promising new job, university studies with successful outcome amongst normal-hearing students, etc.). Some of the outstanding patients are able to follow rapid conversations, can use the telephone on regular basis, moreover a few of them can even enjoy music.

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SEROLOGIC EXAMINATIONS IN ACUTE APPENDICITIS

A. Antal, B. Kocsis[1], S. Jeges[2], Gy. Hideg and E. Tornoczky[3]

University Medical School and the Brothers of St. John of God Hospital Heart Institute,
[1]Department of Medical Microbiology and Immunology, University Medical School of Pécs,
[2]University Medical School of Pécs, Central Research Laboratory,
[3]Baranya County Institute of National Public Health Service Bacteriological Laboratory,
H-7621 Pécs, Irgalmasok u. 1, Hungary

Authors studied the formation of endotoxic antibody level in healthy adults and in patients with appendicitis with a technique (indirect haemagglutination) not used till now. They found the antibody level against endotoxin to be increased in 91% of their patients in the postoperative period. Decrease in the antibody level against endotoxin was observed in two patients with gangrenous appendicitis and two patients with perforated appendicitis. Summarizing their results, authors consider mixed (aerobic, anaerobic) infection to be of decisive importance in the development of acute appendicitis, contributing to the weakened immunereresponse of the host.

Introduction

The pathogenesis of acute appendicitis is not uniform and clearcut [10]. There are two major factors in the development of the disease: the infection and obstruction of the lumen of the appendix [7, 8]. According to the bacteriologic examination of the inflamed appendix the anaerobic agents have pivotal role in causing appendicitis [3, 11]. According to Latt's opinion there is a mixed infection caused by anaerobic and aerobic bacteria in severe appendicitis [6].

In search of the cause of acute appendicitis in our recent publications, we studied the formation of antibody levels against endotoxins produced in the serum of healthy, as well as diseased patients with various degrees of appendicitis.

Patients and Methods

Fifty-one patients who underwent appendectomy between 1st February, 1996 and 31st December, 1997 were randomly selected and 8 ml of their blood taken on the day of the operation and 11 days after. The serum was separated from the cellular elements of the blood and frozen at –20 °C, then stored till the laboratory studies were performed.

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Laboratory techniques

Indirect haemagglutination. The antigens used were *E. coli* 0–21, 22, 33, 61, 86, 116, *Shigella sonnei* 4350, *Salmonella minnesotta* R 595 (absolute R mutants) strains cultivated in fermentor.

Phenol–water extract was prepared for S bacteria [12] and phenol, chloroform and petrol-aether extract for R bacteria [4]. An amount of 1 mg/ml concentration of purified freeze-dried endotoxin was added to 5% sheep red blood cell suspension washed in 0.9% saline solution three times and incubated at 37 °C for 60 minutes.

For the studies, the sera were diluted and sensibilized red blood cell suspension added. The titers were read in a Takátsy microtitrator. All examinations were repeated. Histology: light microscopic examination, Haematoxillin-eosin staining.

Statistics

The statistics were calculated in the case of samples taken before the operation by sign-test and paired *t*-test. The values for the serum pairs of patients with different histologic samples were checked with the Mann–Withney test and 2-sample *t*-test. Unanimous results were gained by both methods.

Results

The study comprised 34 female and 17 male patients whose age range was between 16 and 88 years. The mean age was 32 years. Inflamed appendix was not found in 7 out of the 51 patients. Thirteen of the 51 patients suffered from appendicitis acute simplex, 31 of the patients had phlegmono-gangraenosus appendicitis. Two cases with grave inflammation had led to perforation. The control group consisted of 7 appendectomized patients without histologic deviation, and 10 unappendectomized healthy individuals with no difference in age and sex compared to the appendectomized patients.

Figure 1 shows the development of antibody level against endotoxin produced from *Shigella sonnei* 4350. According to the figure it can be said that antibody levels had grown in acute, moderate and severe appendicitis. This enhancement had continued during the postoperative period.

Figure 2 shows the antibody levels produced against *E. coli* 0–21. No significant differences are observable between the antibody levels of the control group and patients with histologically normal appendix. An increase in antibody level can be seen in the case of appendicitis in the postoperative period.

Figure 3 shows the antibody levels produced against *E. coli* 0-116. No significant differences are detectable between the control group and patients with healthy appendix regarding production of antibodies. An increase in antibody level against both *E. coli* 0-21 and *E. coli* 0-116 is observable in the serum of patients with inflamed appendix.

Table 1 shows considerable dispersion regarding antibody levels and their change following statistical methods using procedures based on the method worked out earlier

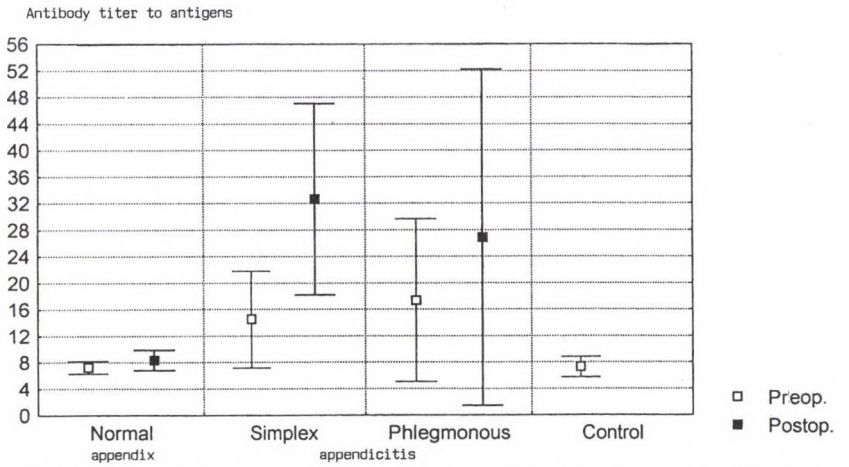

Fig. 1. Antibody levels against absolute R endotoxin produced from *Shigella sonnei* 4350 in healthy, non-appendectomized (control) individuals, and patients with histologically normal appendix, as well as patients with different degrees of inflamed appendices (appendicitis simplex, phlegmono-gangrenosus)

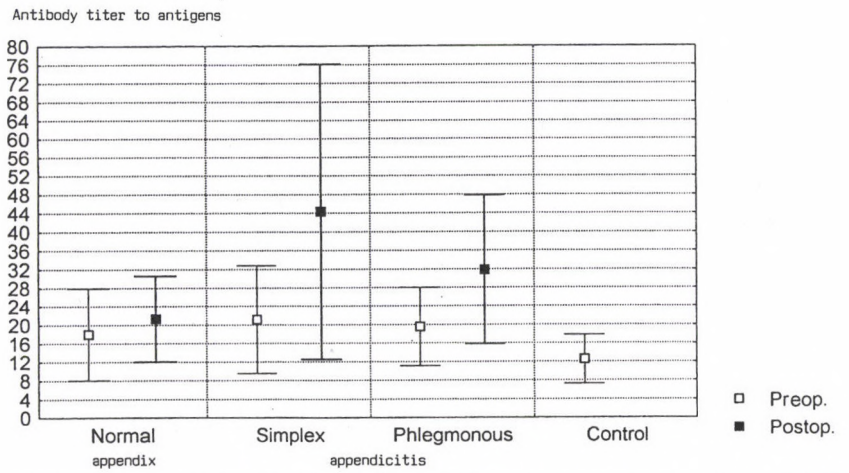

Fig. 2. Antibody levels produced against *E. coli* 0-21, in healthy non-appendectomized (control) individuals, patients with histologically normal appendix, and in patients with differing stages of inflamed appendices (appendicitis simplex, phlegmono-gangrenosus). The sign means the sample prior to the operation

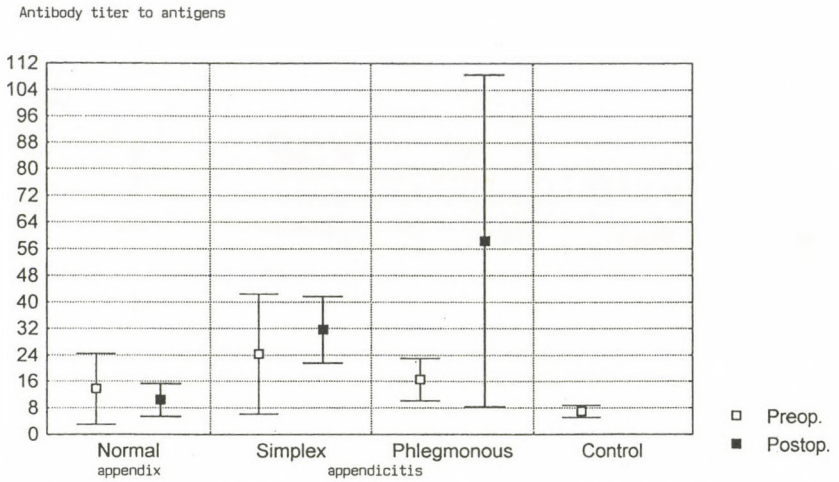

Fig. 3. Antibody levels produced against *E. coli* 0-116 in healthy non-appendectomized individuals, and patients with histologically normal appendix, as well as in patients with different degrees of inflamed appendices (appendicitis simplex, phlegmono-gangrenosus). The sign means the sample prior to the operation

by Pieper and his coworkers [8]. The double value of the mean antibody level in the control group was regarded as significant deviation and its frequency is shown for the patients having various degrees of inflammation (Table 1). It can be concluded that the earlier displayed change on the diagrams is based on how many patients had serum level duplication or multiplication. In 40 of 44 cases with examinations on endotoxins, serum antibody level augmentation (duplication) was observable, while 4 patients we had not found any kind of antibody level increase. Two of the patients had perforated appendix, the case histories of whom are reported in the followings.

An 88-year-old male patient had complaints starting 4 days before his admittance to our Clinic. On the previous day his abdominal pain increased and his temperature had peaked (38.4 °C). When having show up he had right lower abdominal tenderness. His temperature taken from the armpit was 37.4 °C, his white blood cell count read 16.900 mm^3. He underwent immediate surgery, with his perforated appendix taken out. In the vicinity of the appendix ca. 20 ml of pus was found (histology: appendicitis acuta ulcerophlegmonosa). The patient had recovered after an uneventful postoperative period. Regarding antibody levels of the studied serum no multiplication of antibody levels was found either during the operation or in the postoperative period.

Our 45-year-old female patient had complaints 3 days prior to her admittance to our Clinic. She had felt nauseated and vomited on several occasions during this period of time and her body temperature had risen to 38.9 °C on the day before admittance. Her WBC count had been 19.900 mm^3. Upon first examination, the right half of her abdomen felt tender and the punctum maximum was located on the ileocoecal region. Ur-

Table 1
Duplication or multiplication frequency of level of the antibodies produced against different endotoxins

Antigens	App. ac. simpl. (n = 13)	App. ac. phlegm. gangr. (n = 31)	Total (n = 44)
S. sonnei 4350	5	8	13
S. minnesota R 595	3	7	10
E. coli 0-21	7	9	16
E. coli 0-22	8	12	20
E. coli 0-33	5	11	16
E. coli 0-61	5	5	10
E. coli 0-86	3	4	7
E. coli 0-16	9	16	25

gent surgery was called for, during the course of which the perforated appendix was taken out (histology: appendicitis acuta gangraneosa). No increase in the antibody level of her serum was observable by the methods used, and an uneventful recovery period followed.

Discussion

Infection and obstruction of the appendix play a major role in the development of acute appendicitis [7, 8]. In our previous publication, we studied the role of obstruction of many pathogenetic factors from a new aspect. We had stated the decreased peristaltic movement of the organ in appendicitis phlegmonosa which had contributed to rapid progression of the pathophysiology [2].

With the decrease of peristaltics of the appendix, the exposition time of the harmful mix of bacteria causing inflammation expands. There are controversial data regarding whether the bacterium flora of the inflamed appendix is really pathological or not. Roberts had not found any differences in the intestinal flora of the lumen of appendices with histological normal finding and with inflammation [9]. According to Thadepalli, in the case of acute appendicitis the anaerobic bacteria are increasedly colonizing the appendix and ileum [11]. Lau had found mixed aerobic and anaerobic infection in acute appendicitis [6]. The relationship between the intestinal bacterium flora and the host depends on the cellular and humoral immune response. We have been studying the humoral immuneresponse, using *E. coli* 0 antigen extracted from strains occurring most often in faeces and so-called absolute R mutation endotoxins according to our assumption, independent of their source, the absolute R antigens – because of their common antigen component – are able to demonstrate many antibodies produced against Gram negative bacterial endotoxins. We have demonstrated antibody level increase versus *Shigella sonnei* 4350 s endotoxin in acute appendicitis, and have obtained similar re-

sults regarding the *E. coli* 0-21, 116. Kauffmann set up a theory on the pathogenic importance of some *E. coli* serotypes in acute appendicitis [5]. We had already found increased titers to normal control values during the course of surgery, meaning that the antigen stimulus could be a few days old. Eleven days later we found further elevation in the titer level. The immunesystem had met the antigens before the operation, remembering these and producing antibodies against them following surgery. Due to the difference in response actions, our data showed great dispersion, shown in Table 1 prepared after Pipers, method of duplication criterium concerning serum level.

Duplication or increased antibody level against endotoxins were detectable in one-third or half of our patients, respectively. We had experienced significant increase in antibody production in 91% of our patients with appendicitis, taking into consideration all antibody productions studied by us. We consider it of importance that no antibody level increase was found at all in the two patients with perforations. Anderson's point of view regarding the infective origin of acute appendicitis had been reinforced by our study [1]. In accordance with Lau, the inflammation had been regarded as mixed bacterial infection by us. In view of our observations, the course of illness had been aggravated by the lack of immuneresponse by the host

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REVERSE TWO-STAGE PROCEDURE IN THE SURGICAL TREATMENT OF ESOPHAGEAL CANCER

Ö. P. Horváth, M. Kassai, L. Halmos and L. Lukács

First Surgical Clinic, Medical University of Pécs, H-7624 Pécs, Ifjúság u. 13, Hungary

Authors have performed 266 one-stage resections and 6 reversed two-stage operations for the treatment of esophageal cancer during a 10-year-period. In six cases first a substernal bypass with colon or stomach was carried out while the tumourous esophagus was removed only 3–4 weeks later from a right thoracic approach. All six patients recovered.

The reverse two-stage operation for esophageal cancer can be suggested with rare indications (pulmonary abscess, previous abdominal operations, severe malnutrition, etc.) and it is only justified when the advantage gained by increased operability and decreased morbidity and/or mortality is higher than the disadvantage ensuing from oncological, financial and patient demanding considerations.

Introduction

The surgical treatment of esophageal cancer carries a high morbidity and a ca. 10% mortality rate even at highly experienced departments despite the crucial changes of the last decades [4, 17]. Numerous authors have tried to divide the operation into several stages in the hope to reduce the rate of complications and mortality [1, 5]. In the majority of cases they tried to reduce operative risk unsuccessfully because the mortality rate did not decrease. Nakayama [11] is uniquely exceptional, being the first mediator of the multi-stage procedure. He performed gastrostomy first in order to obtain a positive N balance, the esophagectomy itself was performed later via transthoracic approach and then the passage reconstructed by an antethoracic gastric tube in the third step. This method achieved an outstanding result in reducing the mortality rate to 5%. The three-stage procedure, however, did not spread because it needed several months of hospitalization.

In the review of Müller [9] one can read about merely 2% of patients suitable for a two-stage procedure. The sequence of operations was similar to that in Hartman' procedure [6] in colon surgery: thoracotomy and esophagectomy formed the first measure, while reconstruction was accomplished in the second step. However, the reserve two-stage procedure implies primary esophageal replacement with either a gastric tube or a

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colonic segment as the first sep while the tumour-bearing esophagus will only be removed in a second setting. This method has been used by several authors [15] in the fifties in order to improve the patient's general condition by natural nourishment – just like Nakayama's procedure – but intravenous hyperalimentation has superceded this method.

The reverse sequence of operations is a published method also in cases with corrosive esophageal injury [3, 12, 13]. The reverse two-stage procedure was at first accomplished in our Clinic under the compulsion of cases to be discussed later, and then continued in high risk cases because of our favourable experiences.

Material and Methods

An amount of 130 esophageal resections were performed at the Surgical Department of the Medical University in Szeged, the number being 136 at the I. Surgical Department of the Medical Univrsity of Pécs (between 1 April, 1986 and 31 January, 1996). The mortality and morbidity rates for the summarized cases were 14% and 40%, respectively. In most cases the cause of death was connected to severe malnutrition and bad cardiorespiratory function.

A reverse two-stage procedure was performed in 6 cases (Table 1). The indication was established under a special compulsion in three cases, as follows:

1. Pulmonary abscess because of aspiration
2. Esophageal cancer and synchronous gastric cancer
3. Previous pancreato-duodenectomy because of chronic pancreatitis.

For the remaining three cases the indication was established on the basis of a previous gastric resection for ulcer disease with significant malnutrition (Buzby [2] index > 50%) and/or significantly reduced respiratory functions (FEV_1 < 1000 ml/sec), respectively. In all the six patients the localization and stage of the tumour did not allow a transhiatal resection.

We would have preferred a reverse two-stage procedure in four more cases. However, the removal of the esophagus would have been oncologically senseless because of widespread abdominal metastases in the first case. Anastomotic insufficiency and stricture had developed in the second case necessitating dilatations. The second stage was refused by the patient himself in the third case and the immediate postoperative period was utmost wearying for the fourth one, who needed artificial ventillation for three days, therefore unabling us to take the risk of performing the second stage.

Further significant complications occurred only after the second stage: chylothorax in one case and atelectasia in another. All of the six patients operated on with the reverse two-stage procedure have survived.

Table 1
Indications for and operative methods and results of reverse two-stage procedure for esophageal cancer

Age	Sex	Indication	First operation	Second operation	Complications
47	male	pulmonary abscess	gastric bypass	en bloc esophagectomy	–
64	male	synchronous gastric cancer	total gastrectomy esophago-coloduodenostomy	standard esophagectomy	atelectasia
52	male	previous Whipple operation	colonic bypass	en bloc esophagectomy	–
48	male	previous gastric resection Buzby index > 50%	colonic bypass	en bloc esophagectomy	chylothorax
62	male	previous gastric resection FEV_1 < 1000 ml/s	colonic bypass	standard esophagectomy	–
58	male	previous gastric resection Buzby index > 50%	colonic bypass	standard esophagectomy	–

Discussion

The reverse two-stage procedure had already been used in the early era of esophageal surgery but later it became forgotten [15]. The advantage of separate stages could not be proved by anyone but Nakayama [11]. Siewert [14] performed replacement procedure 48–72 hours following esophageal resection, however, he did not find any differences between randomised groups of one-stage and two-stage procedures. Even a longer interval (4–7 weeks) between two stages did not matter at all. Imre [7] performed 38 esophageal resections with collar esophagostomy, cardia closure and gastrostomy, but he could successfully complete them by replacement in only 14 cases. Nabeya [10] performed esophagectomy and esophagogastropexy in the first stage (half reconstruction), with the anastomosis being completed in a second setting. With this method he was able to significantly decrease both the anastomotic leakage rate and pulmonary complications, too.

It can be put on record that performing a two-stage procedure in cases with malignancy is probably no longer justified due to the recent pre- and postoperative intensive treatment facilities.

However, the reverse two-stage procedure may have a role in the surgical treatment of extraordinary cases with esophageal cancer. These are the indications we call compulsory.

Our first patient was admitted with a right-sided pulmonary abscess whereby a middle third esophageal cancer was diagnosed causing total inability to swallow. The patient had continuous aspirations. A right thoracotomy would have been a mistake in

case of a pulmonary abscess and aspiration was also to be eliminated at the same time. A bypass procedure proved to be the best solution. The abscess was healed after three weeks and the esophageal resection could be performed via transthoracic approach without any complications.

The second patient had a III. stage esophageal and a synchronous III. stage gastric cancer. The resectability of both tumours was questionable, based on the investigations. Abdominal exploration seemed to be a less troublesome procedure, so a total gastrectomy was performed together with substernal colonic replacement during the operation and the esophagus was only excluded at both ends. Three weeks later the esophagus was removed via transthoracic approach. If we had started with a thoracotomy and with the gastric cancer being unresectable, the patient would have been subjected to a lower loading procedure and the operation should have been finished according to Torek [16].

The stomach was surely unsuitable for replacement in the third case after a previous pancreatoduodenectomy. Suitability of the colon is questionable in such cases, too, therefore it seemed more advisable to start with the abdominal stage and carry out the substernal colonic bypass.

Due to favourable experiences with our first three cases we went on with the reverse two-stage procedures also in patients who had had previous gastric resections and/or the operative risk was utmost high due to their poor general condition and/or cardiopulmonary status and the localization of the tumour did not allow transmediastinal resection.

Compulsory indications of the reverse two-stage procedure underline the justified suitability of this procedure in rare, selected cases. Pulmonary abscess due to aspiration caused by a middle third esophageal cancer constitutes an absolute indication. If the patient has a synchronous esophageal and gastric cancer or previous abdominal surgery would make the possibility of esophageal replacement questionable, the procedure should always be started with the abdominal stage. Otherwise the surgeon would be compelled to complete the operation according to Torek [16], since following the removal of the esophagus there would be no suitable organ for replacement. Of course, a thoracotomy following a bypass procedure can be carried out at any time in one sitting, thus the second and third indications are not absolute.

A further advantage of the reverse two-stage procedure is the fact that if there is no hope for a R0 resection after the first stage, there is no need to remove the esophagus. The second stage can be abandoned if the loadbearing capacity of the patient cannot be estimated or serious complications, have developed after the first stage. We have examples for each situation among our cases.

Between the two stages both the respiratory function and nutritional state can improve so that the patient may become suitable for a transthoracic esophagectomy. Thus the operability rate may increase because a bypass can be performed in borderline cases, but not in a one-stage fashion, however.

In our practice both morbidity and mortality rates were lower in patients undergoing a two-stage procedure than in the whole clientel subject to esophageal resection.

The lack of "timepress" is called by Siewert [14] being that an advantage of the procedure for the surgeon is that he/she does not need to spend 6–7 hours in the operating theatre with all its mental and physical disadvantages.

The disadvantages of the procedure from the patient point of view is that they need to undergo surgery twice, the tumour remains 3–4 weeks longer in the body, during which time it obviously grows. The patient generally cannot be discharged between the two stages so that the hospitalization time increases to the double or more, hence the expenses ought to be reconsidered.

We performed colonic replacement in five cases and used a gastric tube replacement in one patient. Colonic bypass is a widely used and tested procedure. However, more time is needed to perform it and it carries a higher morbidity rate, but there is no other choice in cases with an unsuitable stomach.

Gastric bypass with exclusion of the esophagus is a safe procedure [8] especially when there is no hazard of developing mucocele because the time between the two stages is only 3–4 weeks. Because of its simplicity it can be held the method of choice. In the second stage we have usually performed an en bloc esophagectomy, supposing that there was hope for a R0 resection, otherwise we have carried out a standard esophagectomy.

As a summary, it could be said that the reverse two-stage procedure can be applied rarely for treatment of esophageal cancer. This procedure is only justified when the advantage of increased operability and decreased morbidity and/or mortality is higher than the disadvantage originating from oncological, financial and patient demanding considerations.

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PHARYNGEAL DYSPHAGIA CAUSED BY ISOLATED MYOGEN DYSTROPHY OF MUSCULUS CRICOPHARYNGEUS

Ö. P. Horváth[1], J. Zombori[1], L. Halmos[2], B. Bozóky[2] and T. Oláh[3]

[1]*I. Surgical Clinic Medical University, Pécs, H-7633 Pécs, Ifjúság u. 13, Hungary*
[2]*Surgical Clinic and Institute of Pathology, Albert Szent-Györgyi Medical University, Szeged, H-6725 Szeged, Vedres u. 6, Hungary*
[3]*Department of Pathology, Municipal Hospital Hódmezővásárhely, Hungary*

Five patients suffering from idiopathic cricopharyngeal dysfunction (without Zenker's diverticulum) were treated surgically. Together with cricopharyngeomyotomy biopsies were taken at the level of the cricopharyngeus. Histological, enzyme hystochemical and electronmicroscopic examinations were performed on all patients. In two cases the histology revealed myogen dystrophy (presence of necrosis, myophagocytosis, abnormal fiber structure, basophilic fibers, fibrosis, mild cellular reaction and predominancy of fiber type I). Since the complete patient evaluation (clinical features, electromyography, serum creatinin phosphokinase level, etc.) could rule out any general, muscle disorders, the cause of the idiopathic pharyngeal dysfunction must have been in these two cases an isolated myogen dystrophy of the cricopharyngeus.

Introduction

Pharyngeal dysphagia is caused by a disturbance in the coordinated neuromuscular events during the initiation of swallowing and the propulsion of the swallowed material from the oropharynx to the cervical esophagus [7]. Asherson [1] labeled it as achalasia failure of relaxation of the cricopharyngeus in the absence of mechanical obstruction and neurogenic origin.

If the mechanical and neurogenic origin is excluded from the causes of pharyngeal dysphagia there remain the following [7]:

1. Disorders of striated muscle.
2. Idiopathic dysfunction.

The diagnosis of primary muscle disorders can be established by clinical features (weakness), electromyography, laboratory investigations (creatinine phosphokinase, thyroid function test) and muscle biopsy.

Idiopathic dysfunction is the intrinsic abnormality of the cricopharyngeus. The diagnosis is based mostly on manometry and exclusion of other diseases. But very little is known about the morphological aspects of the cricopharyngeus [2, 11].

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Patients and Methods

Between 1 January, 1987 and 31 December, 1989 we have treated 10 patients suffering from pharyngeal dysphagia. The classification of these patients is presented in Table 1.

Table 1
Classification of patients

Idiopathic dysfunction	5
Neurogenic origin	3
Zenker's diverticulum	2

All patients underwent a cricopharyngeal myotomy. Biopsy specimens were obtained from all patients with a diagnosis of idiopathic dysfunction. Biopsies were taken at the site of the cricopharyngeus and at the level of the inferior pharyngeal constrictor muscle. Sections of paraffin embedded and frozen materials were stained for HE, PAS and Gömöri trichrome. The enzyme reactions SDH diaphorase and ATP-ase (at pH 9.2, pH 4.6 and pH 4.3) were carried out on frozen sections according to Dubowitz and Brooke [3]. For electronmicroscopic examination (EM) the semithin sections were stained with methylene blue and basic fuchsin, the thin sections with uranyle acetate and Reynolds's solution.

Morphology

In three of our five cases (with idiopathic dysfunction) no specific findings were obsrvable. The histologies of the two remaining cases are presented in this paper.

By light microscopy, in the stenosed pharyngeal tract the myofibers exhibited a moderate and/or strong atrophy. The atrophic fibers were arranged haphazaradly, without any grouping tendency. The rate of the atrophic fibers was 74% (case 1) and 86% (case 2). 3% (case 1) and 0.5% (case 2) of the fibers were mildly hypertrophic. A large number of the fibers were necrotic with signs of myophagocytosis. In many fibers splitting could be seen. So-called rimmed vacuoles were not demonstrable with Gömöri trichome staining in any of the cases. A mild cellular reaction occurred only in case 2. A few basophilic (regenerating) and moth eaten fibers were also found. The enzyme histochemical reactions revealed a predominancy of the fibers type I (61% in case 1 and 49% in case 2). The type I predominancy could also be demonstrated for the atrophic and hypertrophic fibers.

In the proximal (dilated) pharyngeal wall the structural lesions could be seen in a mild form and the predominancy of type I fibers was absent (Fig. 1).

On EM picture, in addition to normal myofibers, the atrophic ones showed the following ultrastructural changes in both cases: parallel with the degree of the atrophy the number of myofibrils decreased, they become narrowed and desorganised and exhibited splitting (occasionally up to the Z band). The Z band showed "widening and smearing".

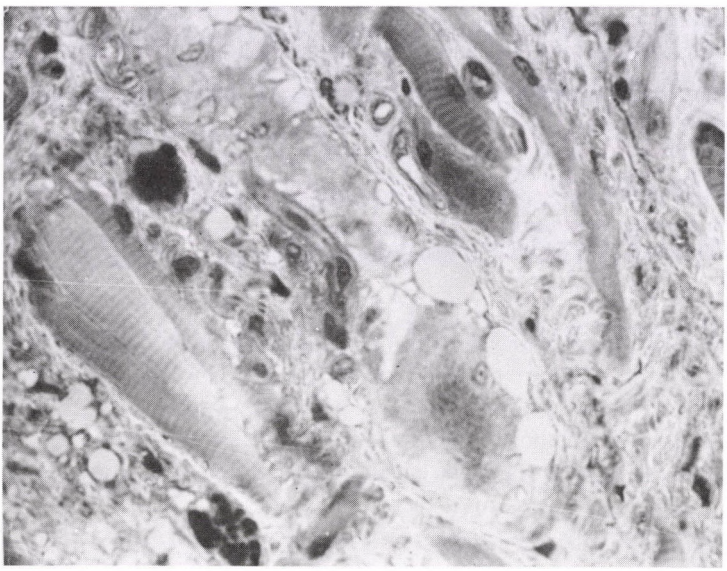

Fig. 1. Various forms of the dystrophic muscle cells separated by increased amounts of fibrotic tissue (case 2). (Semithin section, methylene blue and basic fuchsin staining, ×560)

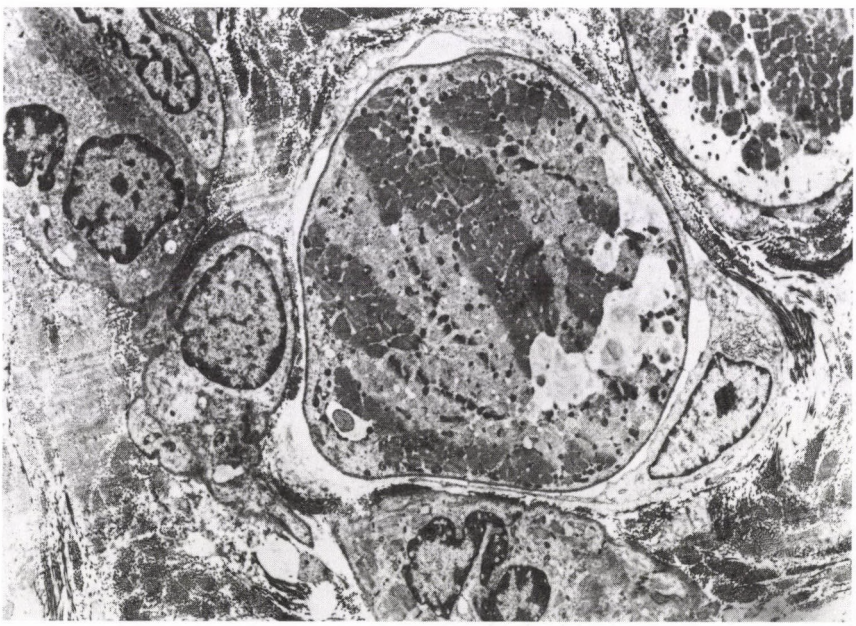

Fig. 2. Dystrophic muscle cells surrounded by collagen filaments (case 1). (EM, ×5780)

The cysternae of the sacroplasmatic reticulum were dilated, some fibers contained lipid droplets in the sarcoplasma. The lamina basalis of the atrophic fibers were reduplicated. The nuclei and mitochondria were normal (Fig. 2).

Case reports

1. A 72-year-old male patient had suffered from gradually increasing dysphagia for years. On admission he could swallow liquids only slowly. At night and during eating he had coughing fits. Two months earlier he had become hoarse. His weight loss was 20 kg.

The laboratory parameters were normal except for the htc (32%) and erythrycyte sedimentation (60 mm/h) – the creatinine phosphokinase level was also normal.

Both the vocal cord function and swallowing reflex were poor. Neurological investigations did not find any pathological deviations.

Cineradiography of deglutition revealed a prolongation of swallowing and weakened pharyngeal contraction. The contrast medium pooled in the vallecular folds and the hypopharynx was extremely distended. Aspiration could be observed at each swallow (Fig. 3).

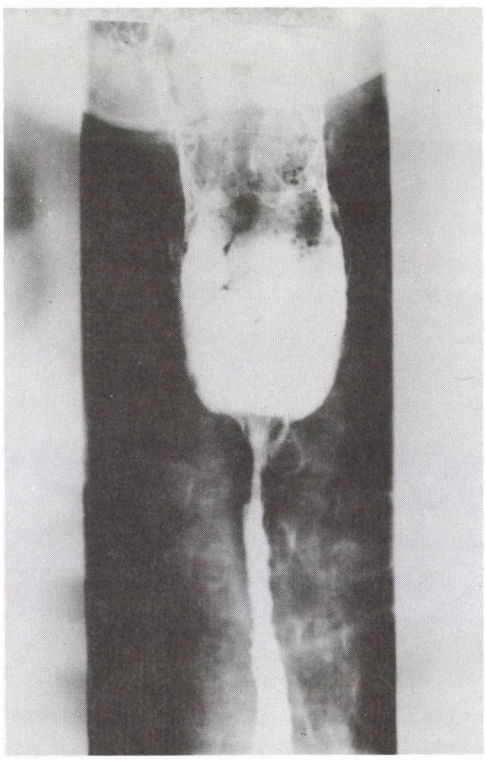

Fig. 3. Extremely distended pharynx (case 1)

Manometric evaluation of the UES showed an incomplete, delayed relaxation. The resting tone was normal.

Endoscopy ruled out other diseases in this region and a 24-hour pH-metry did not show pathological gastroesophageal reflux.

The electromyography demonstrated a normal tone in the skeletal muscle.

Radionuclide study (20 Mbq 99m – Tc – IDA in semisolid food) revealed an enlarged phaynx with a significant hypopharyngeal stasis. The pharyngeal emptying time was 330 s.

A cricophanygeomyotomy was performed with excellent late results. Two months after the operation the pharyngeal emptying time was 22 s.

2. A 67-year-old male patient had had swallowin difficulty for 8 months. He complained of food sticking in the cervical region and of coughing immediately after swallowing. After recurrent pulmonary infections he was referred to our Clinic.

Radiography showed a delayed passage into the esophagus with aspiration. A lateral view revealed a cricopharyngeal bar (Fig. 4).

Manometry demonstrated a normal resting tone at the UES with incomplete relaxation.

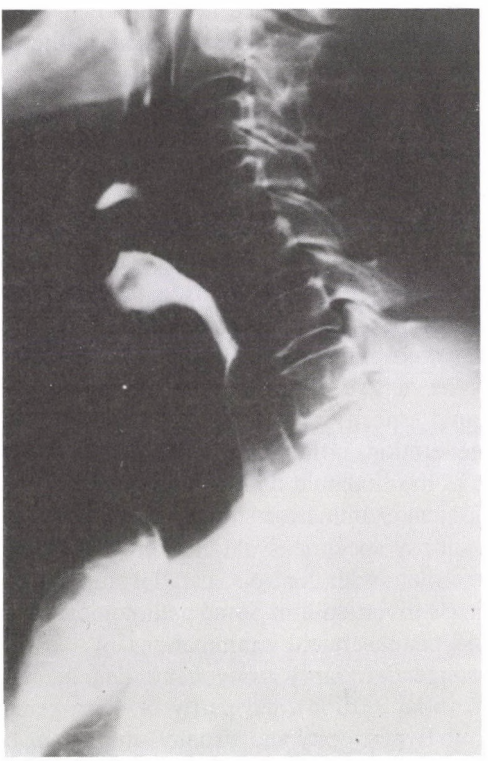

Fig. 4. Cricopharyngeal bar (case 2)

Pharyngeal emptying time with the radionuclide study was 120 s.

The electromyography did not find abnormalities in the function of the skeletal muscle.

Following special consultations, endoscopy, pH-metry, as well as laboratory investigations, other disorders could be ruled out in this area and with a diagnosis of idiophathic dysfunction the patient was operated on. Six weeks after the cricopharyngeomyotomy the patient could eat normally and emptying on the pharyngo-esophageal scintigram was normal as well. The pulmonary infection has not recurred since then.

Discussion

The cause of oropharyngeal dysphagia can usually be identified from the clinical presentation. A careful history will lead to an accurate diagnosis in about 85% of cases and the addition of diagnostic procedures increases this accuracy to around 95% [5]. Neurogenic and myogenic causes account for 85% of cases while the rest are due to local structural lesions (idiopathic dysfunction) [9]. In these patients the malfunction is either identified on its own or is accompanied by complications of the functional abnormalities (Zenker's diverticulum).

The etiology of cricopharyngeal dysfunction is unknown. First Cruse [2] reported on the histological examination of cricopharyngeal muscle in the case of pharyngeal dysphagia. The main pathological changes were the following:

1. Interstitial fibrosis.
2. Extensive accumulation of phagocytes in some muscle fibers suggesting a degenerative process.
3. Large internal nuclei in other fibers indicating regeneration.

They compared these results with those of the control group (biopsies were taken from fresh autopsy specimens or from patients with other cervical operations). The morphological aspects did not show clear differences between controls and patients. The histological findings were the same with the exception of interstitial fibrosis. On the basis of their results the cause of dysfunction could not be explained.

Skinner [11] also found aspecific histological changes (fibrosis, atrophic and hyperplastic muscle, myodegeneration, inflammation and edema) in biopsy specimens taken from patients suffering from idiopathic dysfunction (without diverticulum). In five out of 24 patients the histological examination showed normal skeletal muscle.

Lerut [8] exanubed biopsy specimens obtained from 14 patients with Zenker's diverticulum and compared them with controls. Parallel studies showed a slower and less forceful pattern in Zenker's diverticulum. Some pathological changes were found in the histological and enzyme histochemical examinations of the cricopharyngeal muscle. Certain changes were suggestive partly ofmyogenic degeneration (necrosis, nemalide rods, ragged red fibers, inflammation) and partly of neurogenic disorders (fiber type domination, size variation, hypertrophy and atrophy, absence of cholinesterase and neurofilaments). On the basis of these data it could not be assessed whether these changes

are a primary cause in the genesis of the diverticulum or are secondary to compression caused by the diverticulum.

A further important question is whether the two types of idiopathic dysfunction (with and without diverticulum) are the same disease or not.

In our two cases, after thorough investigation, we set up the diagnosis: idiopathic cricopharyngeal dysfunction. But the histological examination of the biopsy specimen taken during cricopharyngeomyotomy from the cricopharyngeal muscle revealed and isolated muscle dystrophy (presence of necrosis, myophagocytosis, abnormal fiber structure, basophilic fibers, fibrosis, mild cellular reaction in case 2 and a predominancy of fibers type I). Compared with the usual morphological picture of oculopharyngeal dystrophy [3, 10], our cases are "atypical" (lack of so-called rimmed vacuoles and small angulated fibers and presence of basophilic regeneratic fibers). To our knowledge such a pathography – pharyngeal dysphagia caused by isolated myogen dystrophy – has not been published hitherto.

Oculopharyngeal muscular dystrophy is a similar disorder in which ptosis of the eyelids and progressive dysphagia are the cardinal features. It was first described by Hutchinson [6] in 1879 and studied in depth by Taylor [12] in 1915. The disorder is most common in French Canadian families and is transmitted as an autosomal dominant gene. Manometric studies show low pharyngeal contraction pressures, and abnormalities in cricopharyngeal relaxation may be observed. An isotopic deglutition scan demonstrates the problems associated with poor pharyngeal contraction and stasis in the pharyngeal recesses [4].

The etiology of this rare disease remains unknown. Patients with isolated myogen dysrophy respond well to cricopharyngeal myotomy.

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FUNCTIONAL IMPROVEMENT AFTER KNEE ARTHROPLASTY WITHOUT RESURFACING OF PATELLA

M. Abd-El Wahab, K. Szepesi, G. Szűcs, Cs. Farkas and Z. Csernátony

Department of Orthopaedics, University Medical School
H-4012 Debrecen, Nagyerdei krt. 98, Hungary

There has been no universal agreement so far regarding the necessity of patellar resurfacing in total knee arthroplasty. As resurfacing has been reported to be associated with high incidence of complications, this practice has been avoided in our Department. A report is given on the analysis of the functional outcome of 60 knee arthroplasties without patellar resurfacing in 53 patients (7 bilateral) followed up for twelve to thirty months, with special regard to the functions closely related to patelloformal articulation. The underlying diagnosis was osteoarthritis in 78.3%, rheumatoid arthritis in 13.3%, and posttraumatic arthritis in 8.3% of the patients. Graded according to the modified knee-rating system of the Hospital for Special Surgery, excellent or good results were obtained in the case of 55 knees (91.6%) and the mean score improved from 53.6 points preoperatively to 82.6 points following arthroplasty. Subjective and objective functional assessment of stair climbing and transfer activities have shown no functional deficit attributed to the patellofemoral joint of the replaced knee.

Introduction

The early designs of total knee prosthesis did not include a patellar-resurfacing component and were reported to be associated with 40 to 58% incidences of patellofemoral pain [19, 21, 29]. In the mid-1970s, patellar resurfacing became an optional part of total knee arthroplasty [18, 19]. Early studies suggested that only 15% of patients who had total knee replacement needed patellar resurfacing as judged intraoperatively by the condition of the articular surfaces. However, patellar resurfacing has been reported to be associated with complication rates of up to 20%. The complications have included fracture [6, 8, 15, 16, 33, 35], loosening [4, 6, 22], dislocation and subluxation [5, 6, 13, 14], avulsion of the ligamentum patella [7, 31], and separation of the polyethylene beading from its metal backing [3, 4, 6, 11, 24, 25].

Because of this potential for major complications, some surgeons have abandoned resurfacing the patella [1, 10, 23, 34, 36]. According to the reports of Soudry et al. [38] the results are the same whether the patella has been resurfaced or not, except for patients without patellar resurfacing, who had difficulty in climbing stairs. Insall et al. [20], as well as Soudry et al. [37]. Basing their opinions on a larger series of studies, re-

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ported that patellar resurfacing was associated with major complications, recommending that it not be routinely performed in patients who are overweight, very active and relatively young [6, 28, 34]. Other authors have reported more favourably on patellofemoral replacement [4, 9, 27]. Ranawat reported good or excellent results in 90 to 95 per cent of cases where patellofemoral replacement was carried out. Because of the risk of major complications with resurfacing, we have avoided patellofemoral replacement. To evaluate this practice, we reviewed our experience with 60 total knee arthroplasties that had been done without patellar resurfacing and determined the functional outcome of these patients.

Patients and Methods

Between February 1993 and March 1995, 60 total knee arthroplasties were performed without patellar resurfacing in 53 patients (7 bilateral) who had knee arthritis refractory to non-operative management. Among the 53 patients, 40 were females (75.5%) and 13 were males (24.5%). The underlying diagnosis was osteoarthritis in 47 knees (42 patients, 78.3%); rheumatoid arthritis in 8 knees (6 patients, 13.3%), and posttraumatic arthritis in 5 knees (5 patients, 8.3%). The mean age of the patients was 64 years (36–81), with no difference between males and females. The operations were performed under general anaesthesia and midthigh tourniquet. Anatomic Modular Knee prosthesis (AMK, De Puy–Warsaw–Indiana) was used in all patients. Standard anterior mid-line skin incision was used in all but 5 patients, in whom earlier anteromedial incisions of previous surgeries were followed. Patelloplasty was performed by the marginal circumferential trimming of osteophytes and hypertrophic synovium from the borders of the patella, reconstructing an as nearly as normal patellar contour. As a partial denervation of the patella, electrocauterization was carried out all around the inner surface of the patella, few millimeters from its edges, except at the supero-lateral corner, the site of the superior lateral geniculate artery. In cases where the patella was tending to dislocate or excessive pressure with the thumb on its lateral border was needed to maintain central tracking, a lateral release was considered to be in need. This was done, from inside the joint, in 8 patients. The tibial component was cemented, but the femoral component was applied without cement (Hybrid technique). Low molecular weight Heparin (Fraxiparine), and Cephalosporines derivatives were used in thromboembolic, and antibitic prophylaxis. Continuous passive motion (CPM) machine was used from the first postoperative day, and partial weight bearing was allowed with a walking frame on he third day, after drain removal. When the patient was able to actively flex the knee 90° (usually within two weeks) he or she was allowed home to continue the exercises taught. At follow-up interviews (two months, six months and one year postoperatively, and twice yearly thereafter) the patient was examined clinically and radiologically. The modified knee-rating scale of the Hospital for Special Surgery [20] was used in evaluating the patients. A score of more than 85 points was considered to be an excellent result; 70 to 84 points were regarded as a good result; 60 to 69 points as a fair result; and less than 60 as a failure.

Results

Total score

Table 1 shows the averages and ranges of the total score (preoperatively and following arthroplasty) for the 60 knees as a whole, and in groups with different diagnoses. There are no marked differences between the various groups in the mean postarthroplasty score, although patients with rheumatoid arthritis had a relatively lower preoperative score. Table 2 shows the number and percentage of excellent, good, fair and poor results in respect to all patients and in the groups with different diagnoses. Patients with rheumatoid arthritis still have the lowest incidence of excellent results, while those with osteoarthritis have the highest. Table 3 shows the preoperative and postarthroplasty scores (averages and ranges) gained by patients for each item of the modified HSS knee rating system.

Pain. Preoperatively, all patients complained of pain. In 39 knees the pain was generalized involving the entire knee. In the other 21, the patient could localize the pain to one or more compartments of the knee; there was medial pain in 16 knees; lateral pain in 11 knees; anterior pain in 12 knees and posterior pain in two knees. So 51 knees (85%)

Table 1
Total score (preoperative and after arthroplasty), for patients with different diagnosis

	Total (60 knee)	O. A (47 knee)	Rh.A (8 knee)	Post. Traum. (5 knee)
Preoperative Score	53.6 (33–79)	54.5 (36–73)	48 (35–72)	54.2 (33–75)
After arthroplasty Score	82.6 (51–96)	83.9 (62–96)	80.3 (71–91)	79.8 (54–94

Table 2
Final results after arthroplasty. Number and percentage of knees (HSS Scoring System)

	Total (60 knee)	O. A (47 knee)	Rh. A (8 knee)	Post. Traum. (5 knee)
Excellent	34 (56.6%)	30 (63.8%)	2 (25%)	2 (40%)
Good	21 (35%)	14 (29.8%)	6 (75%)	1 (20%)
Fair	4 (6.6%)	3 (6.4%)	–	1 (20%)
Failure	1 (1.6%)	–	–	1 (20%)

Table 3
Patient scores for the items of H.S.S. rating system* (60 operated Knees)

Item		Preoperative score		After arthroplasty score	
Pain	(30)	7	(0–20)	29	(20–30)
Walking	(12)	6	(4–10)	10	(4–12)
Stair climbing	(5)	2.6	(2–5)	3.2	(5)
Getting out of a chair	(5)	3.3	(2–5)	4.1	(2–5)
Range of motion	(18)	11	(6–16)	12	(8–16)
Flexion deformity	(10)	7	(0–10)	9.5	(5–10)
Instability	(10)	6	(0–8)	8	(5–10)
Total	100	53.6	(33–79)	82.6	(51–96)

*Muscle strength (10 points) not shown.

had anterior knee pain, either as a part of generalized pain or combined with other sites. Postarthroplasty: no patient had pain while resting or severe pain when walking, and there was no pain related to the patellofemoral joint. Four patients, however, had mild to moderate pain on occasions of prolonged walking.

Function

Walking. Postarthroplasty: 6 patients can walk unlimited distances, 34 can walk up to one kilometer; 9 up to 500 meters and 4 patients can walk indoors only. The causes of walking distance limitations are diseases involving other joints; generalized debilitating diseases and poor general condition but in 4 patients (6.6%%) the cause is mild to moderate pain in the replaced knee after prolonged walking.

Walking aids. Twenty-one patients needed a stick or cane preoperatively and 9 still use it following arthroplasty.

Climbing stairs. Patients were evaluated in more detail regarding this activity to evaluate patellofemoral function. They were categorized according to their stair climb ability into five groups: normal (using both feet in reciprocating manner); one step at a

Table 4
Patient's ability to climb stairs (53 patients)

Ability to climb stairs	Preoperative	After arthroplasty
Normal	0	15
One step at a time	11	18
With handrail	20	10
With handrail and stick	21	9
Unable	1	1

Table 5
Ability to get out of a chair. Number and percentage of patients (53 patients)

Getting out of a chair	Preoperatively	After arthroplasty
With ease	12 patients (22.6%)	39 patients (73.5%)
With difficulty but with assistance	19 patients (35.8%)	5 patients (9.4%)
Assistance or aids needed	22 patients (41.5%)	9 patients (17%)

time; with the help of handrails; handrails and sticks; and unable to climb stairs. Table 4 shows the number of patients in each group both preoperatively and following arthroplasty. After arthroplasty, 33 patients (62.26%) are able to climb stairs without assistance (normal, or one step at a time) compared to 11 patients (20.75%) preoperatively. This improvement occurred mainly when the replaced knee was the main cause of preoperative disability dut to pain, instability, or sense of insecurity in the knee. The underlying diagnoses in these patients were either mono-articular forms of arthritis or arthritis that predominantly manifested in the replaced knee. The 9 patients still using sticks during stair climbing also use these aids during walking.

Getting out of the chair. Depending on the ability to get out of a chair, patients were grouped into the followings: those capable of this with ease, those with difficulty but without assistance, and those in need of assistance or aids (cane or stick). Table 5 compares the number and the percentage of patients in each group preoperatively and following arthroplasty, and shows that after replacement 44 patients (83%) need to assistance to get out of a chair, although 5 of them are still doing this with difficulty. However, this difficulty could be omitted when using a chair with arms.

Range of movement (ROM). Mean ROM increased from 91° (50–120°) preoperatively, to 97° (65–125°) following arthroplasty. All the patients can flex the knee more than 90°, except one patient with limited flexion to 65°. Full extension up to 5° is posible in 45 knees; and 5 knees have extensor lag between 5 and 10°.

Flexion deformity. Preoperatively 29 knees (48%) had flexion deformity (16 below 5° between 5 and 10° and 6 between 10 and 20°). After arthroplasty, 5 knees (8.3%) have flexion deformity, and all are between 0 and 10°.

Varus–Valgus instability. Following arthroplasty 40 knees are stable, 19 have mild (0–5° and 1 has moderate (5–15°) instabilities. No knee has severe instability (more than 16°).

Complications. Deep infection or thromboembolism was not encountered in our series, otherwise we had 4 complications (6.6%), 2 of which were successfully treated. The first was a patient with poor wound healing and secondary sutures. The second was a case of undisplaced supracondylar femur fracture caused by falling of the patient on the ground one month after the operation, which was treated conservatively. The third was a case of stiff knee in extension (poor score), in a patient with post-traumatic arthritis, with past history of previous knee surgeries (ilio tibial tract tenoplasty and two

arthroscopic arthrolyses). The fourth complication developed in the 'second' knee of the patient with bilateral knee arthroplasty, one month after operation by persistent knee effusion, redness and swelling of the whole leg with low grade fever. Repeated cultures from the knee aspirate revealed no growth, the condition was diagnosed by a dermatologist as erysipelas. One year after arthroplasty, exploration and debridement of the joint, as well as change of the prosthesis were carried out but the condition did not improve (fair score). No complication releated to the patella or the extensor mechanism was encountered.

Discussion

Functional improvement gained by the patient after arthroplasty is the main object aimed for by the surgeon and the patient, and to achieve this, avoidance of complications is of prime importance. The most frequently reported complications of knee arthroplasty in recent reports are those associated with the patella and extensor mechanism, which occur with varying frequency with different implant designs and even without patellar resurfacing [1, 10, 23, 36]. On the other hand, patients with patellar resurfacing are claimed to have a better function and less pain during activities that stress the extensor mechanism such as raising from a chair and walking up or down stairs. We studied the functional improvement after knee arthroplasties with AMK prosthesis in 60 knees (53 patients) without patellar resurfacing. Our overall results are comparable with other clinical results of knee arthroplasty presented in the literature with or without patellar resurfacing [4, 6, 28]. Figgie et al. [11] related postoperative anterior knee pain to three variables, the position of the prosthetic joint line, the height of the patella, and the anteroposterior location of the tibial prosthesis on the tibial plateau.

We assume that our reasonable results are more likely secondary to several factors, including the precise technique in dealing with the extensor mechanism and patella; the implant design features; and the proper positioning of the prosthetic components. The anterior flange of the AMK femoral component, with its lateral rise, divergent groove, and adequate width seems to stabilize patellar tracking. The intraoperative rotational orientation of the femoral component contributes also to the stability of the patellofemoral articulation [2, 12, 26, 30, 32]. Regarding the functional improvement in activities which cause patellofemoral stress, such as stair climbing and getting out of a chair, one can notice that marked improvement in such activities has occurred in patients in whom the replaced knee was the predominant cause of preoperative disability, in spite of non-resurfacing of the patella. On the other hand, in the majority of patients showing little improvement in such activities, the limiting cause of improvement was mainly the result of multiple joints affection and not the replaced knee alone. Finally, although it is difficult to draw definitive conclusions from such a study involving a limited number of cases, our results show that, the use of appropriate prosthesis design and careful surgical technique can provide satisfactory results after knee arthroplasty while avoiding the potential complications of patellar resurfacing. The minimal functional deficit, which is claimed to accompany non-resurfacing must be carefully weighed against the suspected complications of resurfacing.

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METHODS HELPING THE DIAGNOSIS OF "ACUTE SCROTUM" BASED ON MEDICAL PRACTICE IN OUR DEPARTMENT

Z. Szabó, I. Pásztor and E. Ficsór

Department of Urology, Bács-Kiskun County Hospital
H-6000 Kecskemét, Hungary

Authors have analysed the case records of their patients admitted in the last 2.5 years. The color-doppler US is stated to be the most efficient method in differential diagnostics, but the conventional ultrasound + Doppler + scintigraphy can also help in establishing quick and reliable diagnosis as it has been proved in practice.

Introduction

The differential diagnosis of patients having pains that come within the term "acute scrotum" represents a significant challenge for every practitioner. The cause of the syndrome can be testicular torsion of various level, epididymitis, trauma as well as the rarely definable appendix torsion. A more efficient examination should be carried out, since the efficiency of physical examination is not more than of 50 percentage and quick diagnosis is essential because of the nature of the disease [2–4, 6].

At the HUA Congress (16–18 October, 1997 in Debrecen) an account of results was given regarding our 2 years' experience observed during the examination of acute scrotum with testicular scintigraphy. After evaluating the patients in full, our aim was the comparison of the results of physical examination, ultrasound (in some cases color Doppler as well), testicular scintigraphy and the operative findings.

Patients and Methods

Thirty-eight male patients with acute scrotum were treated in our Department between 1 January, 1995 and 30 December, 1997. Their mean age was 17 years. All patients underwent routine physical examination and ultrasound examination (Doppler), besides routine laboratory examinations, scintigraphy and color Doppler ultrasound examinations were carried out as well. Patients who seemed to be ill with epididymitis had conservative treatment, but even in their cases we repeated the ultrasound exami-

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nation a week and a month later. The ultrasound examination was carried out with 7.5 linear transducer on Toshiba SSA-270 apparatus.

Results

Every patient underwent conventional ultrasound + Doppler examination after the routine examinations (we have the facilities for this in our Department day and night). In each case an immediate diagnosis was established after the first examinations:

Epididymitis:	21 cases
Testicular torsion:	12 cases
Strangulated hernia:	1 case
Testis tumour (suspicion):	1 case
Haematoma (post-traumatic):	2 cases
Testis abscessus (suspicion):	1 case
Total:	38 cases

Testicular scintigraphy was carried out in 16 cases. In 11 cases the examination results were in accordance with the results of the ultrasound and Doppler examination. Observable differences could be seen only in 5 cases. In 3 cases results awakened the well-grounded suspicion of testicular torsion, 1 case appeared to be epididymitis, and in one case abscessus seemed to be taking shape. The exploration showed epididymitis and appendix torsion in the case of these patients (3 cases), while in the other 2 cases it showed torsion. Among the 12 patients having been operated on because of testicular torsion there were 3 cases when we had no other choice but to have orchiectomy, while in 9 cases orchidopexia occurred. As the testicle's strangulated time had different periods and rates, these cases had to be observed after the operation for 3 months. The Doppler, the ultrasound examination and the repeated scintigraphy showed the formation of testis atrophia of medium degree in only 2 cases (Table 1).

Table 1 does not show those patients who did not undergo the three examinations mentioned above (ultrasound, Doppler + scintigraphy). Establishing the diagnosis of these patients, there was no doubt regarding differential diagnosis, since they were admitted as a consequence of casualty and received immediate surgical care because of strangulated hernia.

Discussion

The diagnosis of acute scrotum involves great difficulties and represents a day-to-day "challenge" in our work. The anamnesis is often very poor, thus not being of much help. The efficiency of physical examination is notmore than of 50 percentage, so with the object of quick diagnosis more efficient examinations should be seeked. Simple ultrasound detects the deviation of testis structure quite well, but it does not give inform relating to the flow conditions [1, 7, 9, 11]

Table 1
Some facts about the 16 patients who underwent testicular scintigraphy, US, and Doppler examinations

No. of patients	Age (years)	Diagnosis on the basis of physical examination, US, scintigraphy, Doppler US	Testicular pain in former case records	Findings of exposure	Operative event	The beginning of treatment from the beginning of symptoms (hours)
1	15	epididymitis, abscess	no	torsion	orchiectomy	72
2	27	torsion	yes	torsion	orchidopexy	4
3	16	torsion	no	epididymitis	orchidopexy	7
4	2	torsion	no	appendicular torsion	appendix testis exstirpation	4
5	28	epididymitis	no	torsion	orchiectomy	17
6	20	torsion	yes	epididymitis	orchidopexy	3
7	19	torsion	no	torsion	orchidopexy	7
8	41	torsion	no	torsion	orchiectomy	38
9	13	torsion	no	torsion	orchidopexy	5
10	18	torsion	no	torsion	orchidopexy	18
11	8	torsion	no	torsion	orchidopexy	2
12	31	torsion	yes	torsion	orchidopexy	6
13	19	torsion	no	torsion	orchidopexy	4
14	22	torsion	yes	torsion	orchidopexy	5
15	16	torsion	yes	torsion	orchidopexy	7
16	24	torsion	no	torsion	orchidopexy	3

The Doppler ultrasound examination is reliable in a percentage of 60–65. The most efficient examination is the color Doppler, which according to some authors, can help the differential diagnosis of testis torsion in 100 percentage [10, 12].

Analysing our cases, we realized that the ultrasound + Doppler + scintigraphy is a very precise and reliable diagnostic method, which can become routine in practice.

Among our patients there were only 5 cases, when the preoperative diagnosis was not in accordance with the findings of the exploration.

In our opinion, the scintigraphy in the case of testis torquatio can be misleading by giving rather false positive results, while in the case of epididymitis by giving false negative findings. (In the last half year the color Doppler examinations carried out by us have presented the same results as those reported in the literature [5, 10, 12].

Finally, it is our view that among the techniques helping the diagnosis of acute scrotum, the color-Doppler ultrasound examination is the most efficient. However, where there are no facilities for this, a combined ultrasound + Doppler + scintigraphy examination can be very useful in establishing the right decision. Scintigraphy is also a perfect method for the postoperative observation of patients.

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EIGHT-YEAR EXPERIENCE IN TREATMENT OF HEMORRHOIDAL DISEASE

A. Nagy, P. Willner, M. Jankovich and P. Török

Department of Surgery, Vaszary Kolos County Hospital
H-2500 Esztergom, Petőfi u. 26–28, Hungary

During an eight-year period 887 patients with symptoms of hemorrhoids were treated at the Department of Surgery and Outpatient Care of the Vaszary Kolos County Hospital, Esztergom. 178 patients with first degree hemorrhoids received only conservative treatment. Rubber band ligation (RBL) which can be performed on outpatients was applied in 324 patients with first, second and third degree hemorrhoids. Trombosed external hemorrhoids were treated by excision in 215 patients. Hemorrhoidectomy (H) was mainly carried out in 91 cases for treatment of circular 3rd and 4th degree nodules involving complications. More than 80 per cent of the patients receiving rubber band ligation and hemorrhoidectomy were followed up. 65% of the RBL group and 85% of the H group were symptom free, while 76% of the RBL group and 91% of the H group showed great improvement after the treatment. Personal results, complications, and review of the literature are discussed in detail.

Introduction

Description of various methods in the treatment of hemorrhoids dates back to the Babylonian times. The use of cautery in the management of hemorrhoidal bleeding was first described by Hyppocrtes which must have been exceptionally painful in the preanaesthetic era. In the twentieth century a wide variety of techniques were applied in the treatment of this disease [1–17]. Although hemorrhoidectomy is a well-established treatment for hemorrhoids producing excellent results, it does, however, require a period of hospitalization and some form of anaesthesia and may be complicated by urinary retention, hemorrhage and anal stenosis. Thus, it is not surprising that alternative techniques for the management of piles have been developed. Much interest has been focused on other forms of treatment like rubber band ligation, cryotherapy, infrared photocoagulation, bipolar diathermy coagulation and laser therapy. In our practice we apply rubber band ligation, closed and open radical hemorrhoidectomy. Our paper assesses the effectiveness of our treatment during an eight-year period.

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Patients and Methods

Between September 1986 and 1994, 887 patients with symptoms of hemorrhoids were treated at the Department of Surgery and Outpatient Care of the Vaszary Kolos Hospital, Esztergom, Hungary. A total of 178 patients with first degree hemorrhoids received conservative treatment (suppositories, sitz bath, high fiber diet, bowel regimen). Acute perianal thromboses with histories of no more than two weeks were treated by excision of the piles using local anesthesia, leaving the wound open in 215 patients. Initial evaluation included digital examination, anoscopy proctosygmoideoscopy and in the case of patients exceeding 50 years of age, barium enema examination and colonoscopy were often performed. Grading of hemorrhoids were defined according to the Standards Task Force American Society of Colon and Rectal Surgeons [14].

Rubber band ligation was applied in 324 patients with first, second and third degree hemorrhoids. Banding was performed with a suction ligator developed at our surgical Department using size O rubber bands [12]. The intervention was carried out after the emptying of daily stool without any special preparation or anaesthesia. In most cases banding with two elastic rings in one direction per session was carried out. One month after all the treatments were completed every patient was requested to return to the Department for check up.

Surgical hemorrhoidectomy was carried out in 91 patients with second (more than 6 elastic ligations with residual protrusion and bleeding), third (persistent protrusion outside the anal verge in more than one direction) and fourth (irreducibly circular prolapsed trombosed) degree hemorrhoids and internal hemorrhoids associated with benign

Table 1
Main complaints before intervention

	Group of ligation (n = 324)	Hemorrhoidectomy (n = 91)
Bleeding	288/89%	78/86%
Protrusion	233/72%	85/93%
Pain	156/48%	63/69%
Discharge	–	34/38%

Table 2
Classification

Degree	Group of ligation (n = 324)	Hemorrhoidectomy (n = 91)
First	29/9%	–
Second	259/80%	18/20%
Third–fourth	36/11%	73/80%

anal lesions (fissura, fistula, hypertrophied anal papilla). Open radical hemorrhoidectomy (according to Milligan Morgan) and closed radical hemorrhoidectomy (according to Eisenhammer) were performed [8]. Only a small enema given to the patients on the morning of the intervention proved to be sufficient preparation. Two spoons of mineral oil administered after the operation helped effortless evacuation of stool. Leading complaints, symptoms and grading of hemorrhoids before intervention are shown in Tables 1 and 2.

Results

During an eight-year period, a total of 324 patients underwent 1,070 ligations. The average in this group was 41.3 years (21–68). Every patient was checked one month following treatment and 262 patients were followed up by means of a questionnaire 4–92 months after completion of the banding. Complications were confined to discomfort (47), bleeding (47) and protrusion (43). Nine of 47 patients required observation and admission to the surgical department. Two of them were given blood transfusion. There patients noticed perianal swelling, none of them required surgical intervention. Duration of postligation discomfort lasted one to three days. Fifteen patients of the ligation group were operated on because of persistent complaints (protrusion and bleeding after more than 6 banding sessions), and 170 patients had no complaints.

Table 3
Residual complaints after intervention

	Group of ligation (n = 262)	Hemorrhoidectomy (n = 77)
Bleeding	47/18%	3/4%
Protrusion	43/16%	–
Skin tag	–	6/8%
Discomfort	47/18%	8/11%
No complaint	170/65%	65/85%

Table 4
Opinion of patients concerning therapy

	Group of ligation (n = 262)	Hemorrhoidectomy (n = 77)
Satisfied	199/76%	70/91%
Partly satisfied	53/20%	7/9%
Dissatisfied	10/4%	–

A total of 91 hemorrhoidectomies were performed. The average age was 43.2 years (25–75 years). Seventy-seven patients were followed up based on questionnaire (8–91 months). Three patients reported bleeding. In two cases reoperation was necessary due to excessive postoperative bleeding. Urinary retention, on the day of operation, occurred in four male patients and required catheterisation. No septic complications occurred. Sixty-five patients had no complaints. Residual complaints after intervntions are described in Table 3. The opinions of the treated patients concerning therapy are shown in Table 4.

Discussion

Outpatient management of hemorrhoidal disease is mutually beneficial to the patient and the social insurance organization. Rubber band ligation is successfully applied in patients presenting 1st, 2nd and 3rd degree hemorrhoids, the latter with protrusion in one direction only [2, 3, 9, 10, 13–17]. Advantages of the method are the followings:

– no special preparation, anesthesia necessary,
– the technique involves a single, low cost,
– there is minor discomfort for the patient,
– possibility of reapplication following recurrence.

Bartizal and Slosberg [3] published the follow-up of 670 patients in 1977. The number of ligations in their report was 3208. 96% of the studied patients were free of complaints, 4% returned with episodic bleeding, 4% with pain.

Steinberg [15] followed up 125 patients by means of questionnaire. Five years following ligation 88% of those treated were satisfied with the result although only 44% were free of symptoms: occasional bleeding, minor prolapse occurred. Wrobleski et al. [17] were able to follow up 266 out of 352 patients during an average period of 5-years. 80% of the patients reported major improvement, although several have residual complaints. Murie [9], in his randomized study, compared the results of the Milligan Morgan procedure with rubber band ligation in patients with grade II–III hemorrhoids. Regarding grade II hemorrhoids no major difference was found, operative management of grade III hemorrhoids showed significantly better results.

Recent publications have given account of two relatively new methods: infrared photocoagulation and bipolar diatherny coagulation [1, 5, 6, 10]. Ambrose et al. [1] studied the therapeutic efficiency and complications of photocoagulation and rubber band ligation based on the follow up of 268 patients. Success of therapy was identical in the two groups, postoperative pain was more frequent in those who underwent ligation. In their similar study Weinstein et al. [16] found the therapeutic efficiency of rubber band ligature superior.

In their meta-analysis MacRae et al. [8] compared the results of 18 randomized studies. According to their assessment efficiency of hemorrhoidectomy surpasses any other type of outpatient therapy, though the number of postoperative complications was higher. Rubber band ligation applied in grades I–II–III hemorrhoids gave better results

than sclerotherapy or photocoagulation, despite the postoperative pain being greater. Photocoagulation proved to bemore effective than sclerotherapy. They recommend rubber band ligation as the first choice in grades I–III hemorrhoids. Our strategy in treatment of hemorrhoids is similar to the recommendation of the Society of Colon and Rectal Surgeons of USA [14]:

first degree:	conservative treatment, repeated bleeding-rubber band ligation,
second degree:	rubber band ligation, associated with benign anal condition, surgical hemorrhoidectomy, closed repeated complatins (protrusion, bleeding after more than six ligation sessions), hemorrhoidectomy closed,
third degree:	protrusion in one direction-rubber band ligation, protrusion in more than one direction-hemorrhoidectomy closed
fourth degree:	radical open hemorrhoidectomy, acute interacted circular, thrombosed hemorrhoids with considerable swelling, infiltration with Hyase + bupivicain and reposition, next day open hemorrhoidectomy

Conclusion

During an eight-year period only 10% of patients required surgical hemorrhoidectomy. Almost 90% [7, 9] of patients underwent outpatient treatment. Elastic band ligation proved to be a very successful therapy in our practice in first, second and third degree hemorrhoides. Hemorrhoidectomy was mainly performed in circular third-fourth degree hemorrhoids with complications.

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UNSTABLE PELVIC FRACTURES IN CHILDREN

E. Hargitai, J. Szita, J. Dóczi and A. Renner

National Institute of Traumatology,
H-1081 Budapest, Fiumei út 17, Hungary

A total of 3561 freshly injured children received treatment at the paediatric trauma department of the National Institute of Traumatology between 1984 and 1994. Out of these 38 (approx. 1%) had pelvic fractures. Based on the classification of Tile and Laer, 15 pelvic fractures were diagnosed to be unstable, from which 8 were polytraumatised, 4 shocked and 1 was a casualty. Run downs could be considered as the main cause of these fractures

Conservative treatment was provided for 13 unstable cases (bed rest: 5, band suspension: 1, femur skeletal traction: 4, femur traction and band suspension: 3). Surgery was performed in 2 cases (symphysis cerclaige: 1, acetabulum plate o.s.: 1). Eleven patients were called in for late controls (after 3 years). Subsequent complications were: pain: 3, limb shortening: 4, lumbal scoliosis: 1, minor pelvic deformations: 4, partial necrosis of caput femoris: 2. The subjective complaints of 3 adolescent cases seem to be small in number, however, it is a fair assumption that the control period of 3–6 years later is not enough to form a comprehensive conception on the nature of early degenerative deformations occurring later, e.g. during adulthood. Because of further surgeries and examinations, correct traction and suspensional treatment can only be carried out with great difficulties regarding children. Therefore, posterior stabilisation of the pelvic ring must be planned with percutaneous sacroiliac pinning or screwing in unstable cases.

Introduction

A pelvic fracture occurring in a child involves significant trauma, the high energy nature of these fractures is reflected in the significant incidence of associated injuries [1, 4]. Besides the urgent treatment of life threatening abdominal and major vessels, and urological injuries, treatment of pelvic fractures is of course not the highest concern at the beginning. This may be the reason why treatment of children's multiple, unstable injuries of the pelvic bones is characterized by numerous diagnostic mistakes, contradiction of tactical purposes and imperfect reductions and retentions of the pelvic ring fragments [5, 8, 14]. Keshishyan's comparison of postmortem and radiographic investigations showed that only 20 per cent of fractures in the lateral area of the sacrum and 13.5 per cent of sacroiliac disruption injuries had convincing radiographic signs [5].

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Insufficient diagnosis and lack of due treatment, furthermore, a too short a period of restriction from any weightbearing, may result in the cure of unstable pelvis fractures with permanent deformities.

Tile classifies the pelvic fractures according to the force of injury and its directions and stability [14].

Laer considers permanent late consequences for classification: injuries to the growth zones only give rise to minor deformities in the pelvic, while injuries to the pelvic ring rather to more serious irreversible deformities [7]. The classifications of Tile and Laer are coincidental: injuries above and beneath the linea terminals (avulsions of the apophyseal nuclei, isolated fractures of the o.s. ileum. o.s. ischii) are stable and do not result in severe late complications. Out of the pelvic ring fractures transacetabular fractures can cause permanent deformities.

Regarding the fact that there is only slight correlation between post-traumatic pelvic deformities and clinical complaints [3], our aim was to review the fate of our former patients in view of the efficiency of the mainly conservative treatment employed.

Patients and Methods

During the last decade (1985–1994), at our Department of Paediatric Traumatology there were 38 cases of pelvic fractures (1%) out of 3561 acutely injured children under the age of 15.

In accordance with the afore-mentioned Tile classification, 15 cases were potential unstable fractures (0.42%), 8 males and 7 females. The seriousness of our material is confirmed by the fact that 8 children had polytrauma, 4 of them with shock, 1 child was lost. Our treatment of unstable pelvic fractures was mainly conservative, only two cases were stabilized primarily by surgery. Subsequent follow-up examinations were performed in 11 cases, the follow-up time ranges being from 3 to 6 years. Our results are illustrated in Tables 1–9.

Table 1
Causes of unstable pelvic fractures
(n = 15)

Runover by car	10
Car passenger	3
Motorcycle passenger	1
Fall	1

Table 2
Severity of injuries

Polytrauma	8
with shock	4
without shock	4
Multitrauma	6
Monotrauma	1

Table 3
Fatal outcome: 1

Shock	
Ruptures of	urinary bladder
	rectum,
	descending colon,
	external iliac artery
	perineal muscles
Fractures of vert. L III–IV	
Open fracture of pelvic (lateral compression)	

Table 4
Classification of unstable pelvic fractures (according to Tile)

Type B	
1. Separation of symphysis	1
AP compression	
2. Anterior-posterior pelvic ring fractures externally rotated (open book)	4
Lateral compression	
3. Anterior-posterior pelvic ring fractures inward rotated (bucket handle)	
4. Transacetabular fractures	3
Type C	
Vertical shear	4

Table 5
Associated injuries

Craniocerebral	11
Thorax	4
Abdominal organs	2
Retroperitoneal haematoma	5
Urogenital	3
Intraabdominal artery	1
Vertebral	2
Upper limb fractures	4
Lower limb fractures	6
Dislocation of the hip	1

Table 6
Treatment of unstable pelvic fractures

Conservative	
Bed rest	4
Band suspension	1
Femur skeletal traction	4
Femur skeletal traction and suspension	3
Surgery	
Cerclaige of the symphysis	1
Plate osteosynthesis of the acetabulum	1

Table 7
Treatment of associated injuries

Laparotomy	3
Craniotomy	2
Suction drainage of the thorax	1
Tracheotomy	1
Osteosynthesis	2
Amputation of the lower limb	1

Table 8
Late complications

Pain	
hip	2
sacro-iliac	1
Limb shortening	
absolute	3 cm (after varus osteotomy)
	1 cm (after varus osteotomy)
functional	1 cm
	1 cm
Scoliosis	1
Moderate deformity of pelvic ring	4
Partial necrosis of the head of the femur	2 (with restriction of hip movements)

Table 9
Treatment of late complications

Varus osteotomy	2 (after partial necrosis of the head of the femur

Discussion

No correlation was found between sex and severity of injury in our material, similarly to others [6]. The most common injury was auto-pedestrian collision: 10 out of 15 cases. This rate shows correlation with the literary data [3, 6, 9]. Apart from bony stability, there is ligamental stability, too: unstable fractures put an end to bony stability, however, displacement may be prevented by the strong posterior sacroiliacal ligaments and strong periosteum, with bed rest. We ought to know that there is a good remodelling for the deformities of the single bones, but there is no or only very moderate remodelling for the deformities of the whole pelvic ring [7]. Most paediatric pelvic fractures are stable and require only supportive management [2]. In our material there were 23 stable and 15 unstable cases.

The treatment of unstable pelvic fractures was conservative until the last decade. Some publications also prefer this nowadays [6, 10, 12]. Regarding the fact that orthopaedic complications (leg length discrepancy, growth arrests, ring deformities, sacroiliac ossifications, etc.) are consequences of unstable forms, it is obvious that minimal invasive fixation methods (external fixation, pelvic clamp, sacroiliacal percutaneous screw-, wire fixation) have been more and more frequently used in recent years [2, 5, 14]. Although mortality in adults with pelvic fractures (especially the ones posterior position) is related mostly to haemorrhage, head injury is the primary cause of death in

children with pelvic fractures [1]. An unstable pelvic fracture in a hemodynamically unstable child with ongoing pelvic bleeding may require urgent external fixation [13], although there are no prospective randomized trials demonstrating the value of fracture stabilization for control of pelvic haemorrhage. Early pelvic fixation was applied in ten of McIntyre's patients of the unstable type and clinically the bleeding was controlled in six of his cases [9]. Given the inherent instability of posterior disruption of the pelvis, closed reduction and minimal external fixation frames allow easier nursing care [11].

Follow-up examinations of our 11 cases revealed only minor deformities of the pelvis and shortening of the limb, which may be an explanation as to why we only found 2 cases with hip complaints and 1 with SI complaints. This may be attributed to the conservative and at the same time active treatment.

Conclusions

The time of our follow-up was between 3–6 years, which is more than the necessary 2 years given for children, but is still not enough to assess the tendency for early degenerative alterations later, in adulthood. We think, similarly to Schwarz et al. [12], that for this reason it is necessary to make an effort to examine the anatomical position. Minimal intervention can be performed (percutaneous SI writing in younger children, percutaneous SI screw fixation in older ones, external fixation, pelvic fixator clamp) in order to stabilize the posterior part of the pelvic ring, since the continuous traction, suspension treatment can rather frequently be performed with only great difficulty because of further operations and examinations. Posterior percutaneous wire fixation has also been recommend by Tile [14], while good results have been obtained by Ogden using SI screw transfixation [11]. In view of the small number of cases, a prospective multicenter study of this issue should be considered.

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HOW EFFECTIVE IS THE ROUTINE MEDIASTINAL BLOCKDISSECTION IN THE SURGERY OF NON-SMALL CELL LUNG CANCER?

G. Egri, Zs. Mészáros, Gy. Vass and M. Juhász

Department of Thoracic Surgery, Bajcsy-Zsilinszky Hospital, H-1106 Maglódi út 89–91, Hungary

The performance of ipsilateral mediastinal blockdissection as a routine in every non-small cell lung cancer (NSCLC) operation gives us a chance to judge the accuracy of the preoperative CT examination. The accuracy rate of the CT in our 316 cases was 70.6%, the false positive rate was 69.6%, the false negative rate was 18.2%. Taking into account the 18.2% false negative rate and the slightly better survival of patients operated with routine blockdissection compared to the survival of a group of patients who had mediastinal blockdissection only if suspicion of tumour spread arose, we consider the procedure reasonable in every NSCLC operation.

Introduction

The removal of the locoregional lymph nodes is a widely used method in many fields of oncological surgery (breast, gastrointestinal tract, melanoma malignum, etc.). The main reason for performing mediastinal lymphadenectomy in the surgery of NSCLC is that the metastatic state of the lymph nodes is a major prognostic factor. Mediastinal blockdissection provides the best surgical staging. Besides this aspect some auhtors reported a positive effect on survival, too [4, 8, 10, 11].

The aim of our study was to evaluate the need of blockdissection. We concentrated on two aspects:

1. How accurate is the CT examination in the preoperative evaluation of mediastinal metastases of NSCLC?
2. Does mediastinal blockdissection improve survival?

Patients and Methods

Since the 1st of July 1992, mediastinal blockdissections have been performed a routine in the surgery of non-small cell lung cancer at our Department (Fig. 1). In this study, after 4.5 years we evaluate the effectivity of the procedure. From the 1st of July

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1992 till the 31st of December 1996, we have performed 265 lobectomies or bilobectomies, 51 pneumonectomies and 47 explorations, or palliative wedge resections (363 operations because of NSCLC altogether). Correct mediastinal blockdissection was accomplished in all operable (316) cases (Table 1).

The basic method of systematic ipsilateral mediastinal blockdissection has been described by Martini, Naruke and others [2, 5, 9]. Since their publications a number of modifications have been published, all proposing greater extension of the dissection [7, 12, 13]. We use the original method. In the right hemithorax we open the mediastinum widely along the vena cava and dissect the fatty tissue containing the lymph nodes, from the vena azygos, upwards to the cupula and downwards to the diaphragm. So we remote the nodes at sites 2, 3, 4, 7, 8 and 9, numbers according to the lymph node mapping of the American Thoracic Society [1]. On the left side, we open the mediastinal pleura above and under the aortic arch and remove the mediastinal tissues with the lymph nodes found there. Following this method, we have noticed only two recurrent nerve paresis as a complication of 319 cases. Both complications arose after the dissection of the subaortic region. We have not noticed any other adverse effects in the dissected group. The procedure added only about 20 minutes to the operating time.

I. First, the results of the preoperative CT scan have been compared with the histologic examination of the excised mediastinal lymph nodes. Our aim was to evaluate the accuracy of the preoperative computer tomogram, concerning mediastinal metastases.

II. Second, our intention was to survey the effect of mediastinal blockdissection on the survival of patients operated because of NSCLS.

For this second purpose, the survival of our patients operated before and after 01. 07. 1992 could be compared (Fig. 1). Before this date mediastinal blockdissections were not performed in every case, only where the preoperative CT scan or the intraoperative palpation indicated the need. So this period could be regarded as the occasional

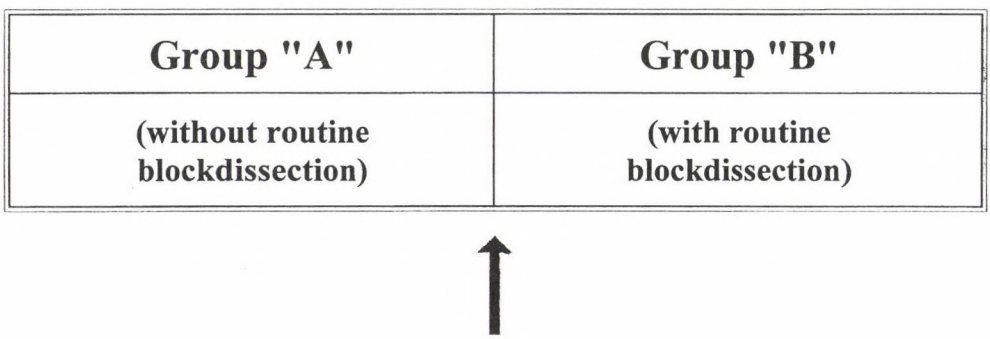

Fig. 1. Our surgical practice before and after 01. 07. 1992

Table 1
NSCLC patients, operated 01. 07. 1992–31. 12. 1996
(n = 363)

Lobectomy, bilobectomy	265
PNO	51
Exploration or palliative wedge	47
Total	363
Mediastinal blockdissectiuon	316
N2 positive	66 (20.8%)

or non-routine blockdissection era. Since then we have performed the procedure in every operable lung tumour case.

To examinate the difference between the routine and non-routine blockdissection groups, 100–100 patients of operable NSCLC of both groups were selected. We did not randomize our patients, the way of getting into the trial was simply to be in the range of 100 patients operated before and 100 operated after the mentioned date. There were no significant differences in the two groups in terms of age, stage or side of the tumour. In order to visualize the differences in the survival of the two most frequent histologic types, only clear adenocarcinomas and the squamous cell carcinomas were included.

In the interest of gaining correct information, pneumonectomy cases were excluded. PNO-patients were not suitable for comparison since we performed blockdissection in their cases at an earlier time point as well. Therefore the 200 patients were operable adenocarcinoma and squamous cell carcinoma cases, who had lobectomy or bilobectomy without routine mediastinal blockdissection in group 'A' and with routine mediastinal blockdissection in group 'B'.

Information was obtained from our patients by means of personal interview, telephone or letter, with a response of 58–60%.

Using the life table and the Kaplan–Meier methods [3, 6], the survival of patients belonging to group 'A' (non-routine blockdissection group) and group 'B' (routine blockdissection group) could be represented on a graph.

Results

I. Radiology regards lymph nodes as negative, if their contours are normal and their transverse diameter is 1 cm or less by the computer tomogram.

The preoperative CT scan of our 316 patients judged their mediastinal lymph nodes as positive in 69, and as negative in 247 cases. The postoperative histological examination of the dissected lymph nodes proved positivity in 66, negativity in 250 cases. This means that about one fifth of the cases (21.9%) were suspected to be N2 positive preoperatively and the same rate proved to be N2 positive postoperatively (20.8%). If we

Table 2
Correlation of CT scan with histology

	CT scan (n = 316)	
Histology (n = 316)	positive (> 1 cm) (n = 69)	negative (< 1 cm) (n = 247)
positive (n = 66)	21	45
negative (n = 250)	48	202

Table 3
Evaluation of CT scan in dg. of mediastinal lymph nodes

Accuracy rate	70.6%	(223 from 316)
Predictive rate of positive findings	31.8%	(21 from 66)
Predictive rate of negative findings	88.0%	(202 from 250)
False positive rate	69.6%	(48 from 69)
False negative rate	18.2%	(45 from 247)

look at the individual cases, however, it can be seen that histology-positive nodes are not the same as CT-positive ones. CT results did not correlate with the histological findings to a certain extent (Table 2). The accuracy rate of the CT was in fact 70.6%. The positive predictive rate was 31.8% (= true positive findings), the negative predictive rate was 88% (= true negative findings), the false positive rate was 69.6%, the false negative rate was 18.2% (!) (Table 3).

II. Evaluating our data on survival, it can be pointed out that mediastinal blockdissection (group 'B') produced a non-significant, but still noticeable positive effect on overall survival of patients after 1 year (Fig. 2).

If we look at the data of survival in cases of the two most frequent tumour types, adeno- and squamous cell carcinomas, we find the same non-significant, but noticeable improvement in survival, if we perform blockdissection (Figs 3, 4).

In Fig. 3 (adenocarcinomas) we can observe an interesting rise in the curve of the routine blockdissection ('B') group, compared to the non-routine blockdissection ('A') group in the first two years. From this, the suggestion arises that in cases of adenocarcinomas blockdissection would improve survival particularly in the first two years.

We can see in Fig. 5 and Fig. 6, that the survival of adenocarcinoma patients is worse than that of squamous cell patients, whether blockdissection was performed or not.

As expected, the survival of N2 negative patients was found to be much better than in N2 positive, or in all patients (Fig. 7).

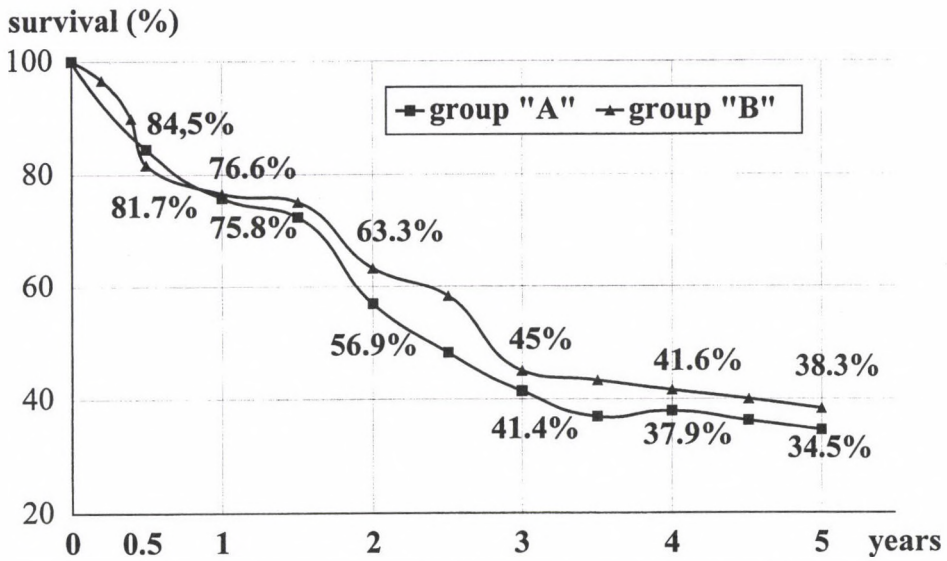

Fig. 2. Survival of patients in group 'A' (n = 88) and group 'B' (n = 60)

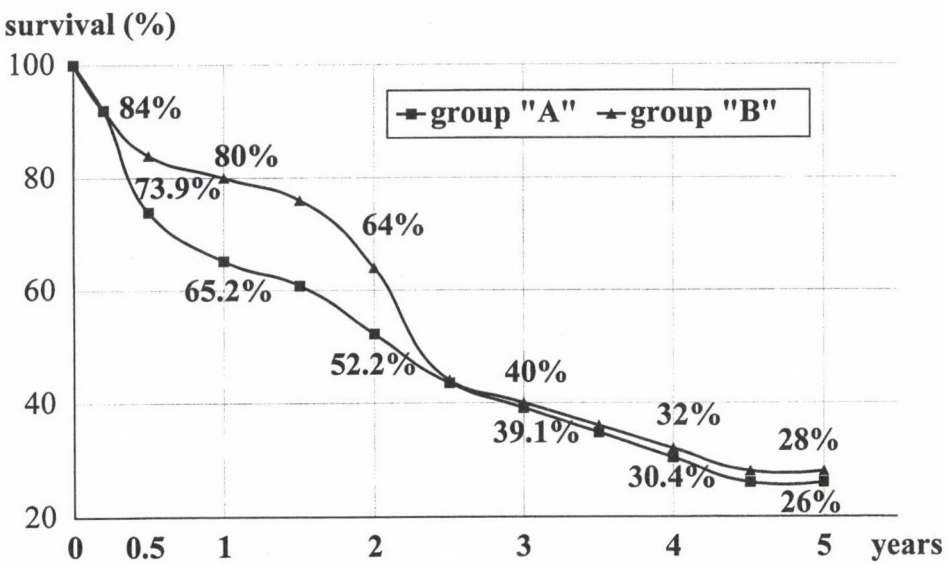

Fig. 3. Survival of adenocc. patients in group 'A' (n = 23) and group 'B' (n = 25)

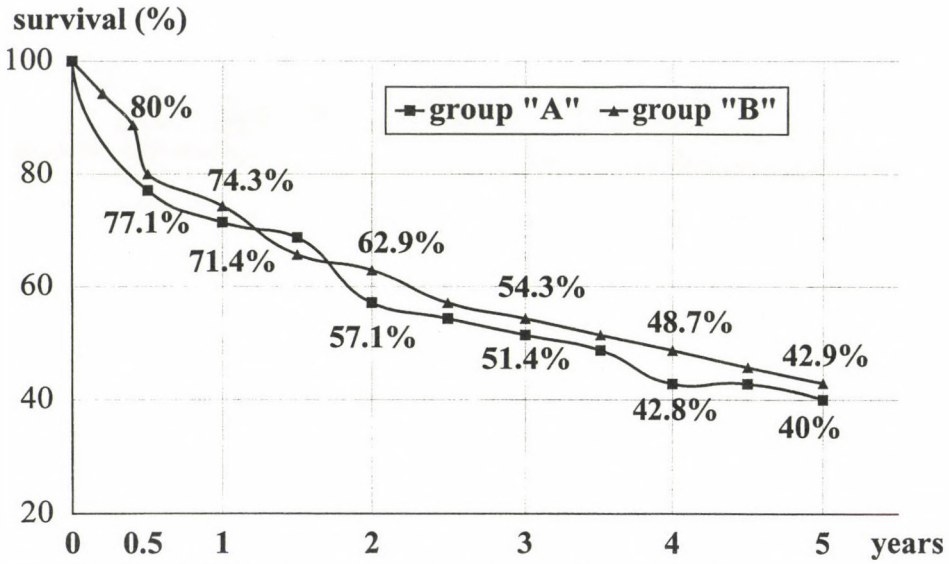

Fig. 4. Survival of squamous cell cc. patients in group 'A' (n = 35) and group 'B' (n = 35)

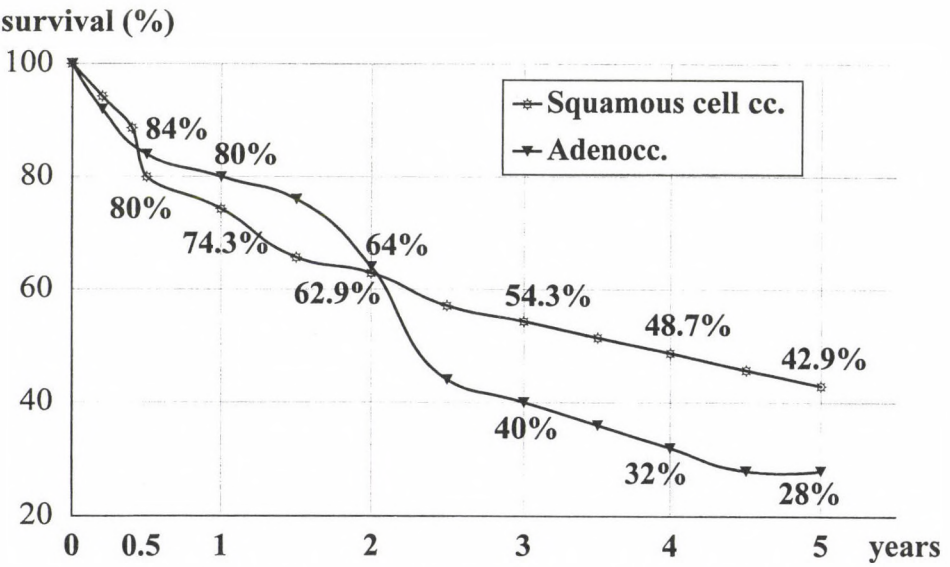

Fig. 5. Survival of adenocc. (n = 25) and squamous cell cc. (n = 35) patients in group 'B'

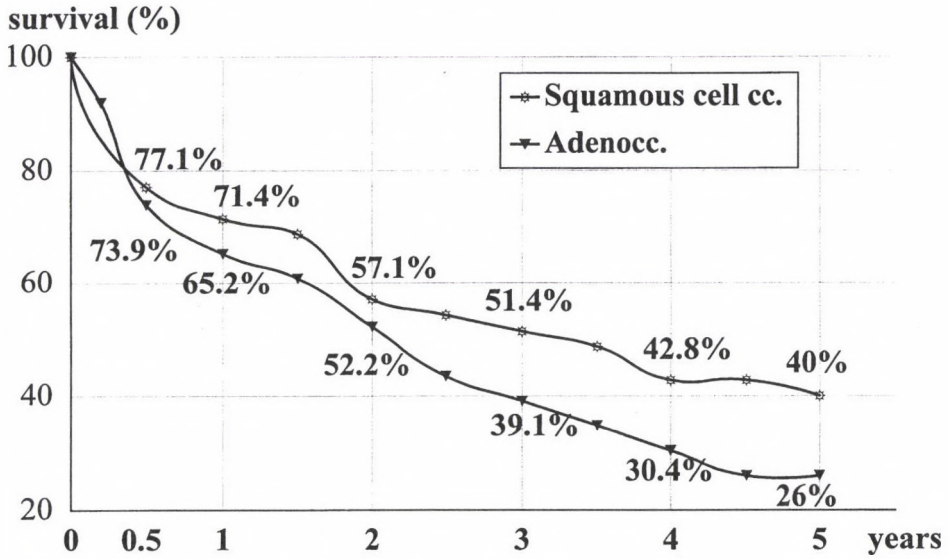

Fig. 6. Survival of adenocc. (n = 23) and squamous cell cc. (n = 35) patients in group 'A'

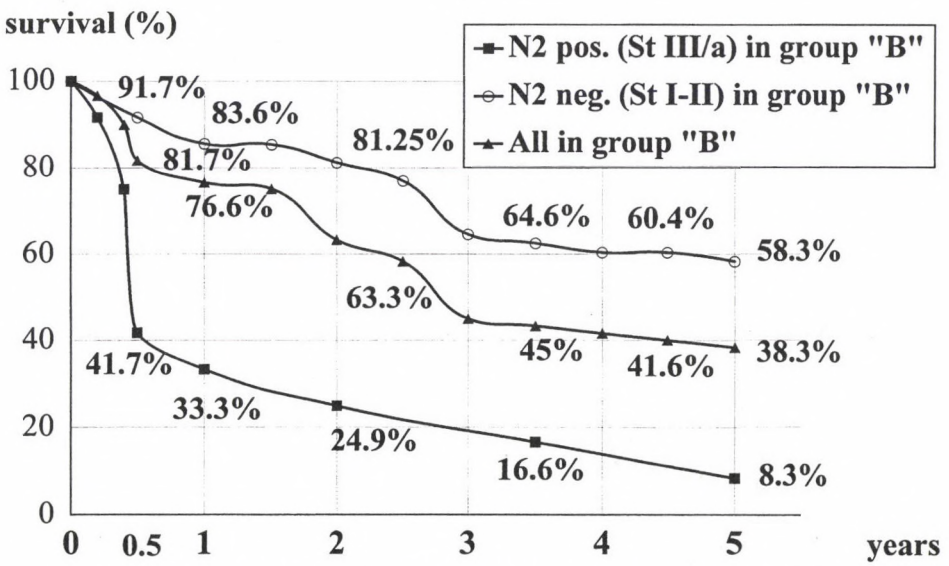

Fig. 7. Survival of N2 positive (n = 12) and N2 negative (n = 48) patients (group 'B' n = 60)

Discussion

I. From the data of the first part of our examination, two items can be emphasized:

1. In cases of greatly enlarged mediastinal lymph nodes (positive CTs), where the evaluation of the CT scan can even influence the indication of the operation, the histological examination in 69.6% (!) of the cases did not prove tumour but showed inflammation. This indicates that when making decision on operability we have to be careful interpreting CT, especially in cases of squamous cell carcinomas. (The false positive Cts occurred mostly in cases of squamous cell carcinomas (43 from 48).)

2. The mediastinal lymph nodes, regarded as negative by CT were histologically positive in 18.2%. On the one hand this means that N2 positivity is proved in a number of cases only postoperatively ("unexpected disease"), and on the other hand that if mediastinal lymphadenectomy had been omitted, the tumour would have been left back in 18.2% of the patients, preoperatively assessed as N2 negative. These false negative cases occurred mostly in cases of adenocarcinomas (40 from 45).

II. From the data of the second part of our examination, the conclusion can be drawn that mediastinal blockdissection slightly improves the survival of patients.

Conclusions

On the basis of our observations, taking into account the 29.4% inaccuracy rate of the preoperative CT, the possibility of a more appropriate staging, and the slightly better survival after the procedure, we recommend that mediastinal lymphadenectomy be performed as a routine in the surgery of NSCLC.

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BIOPSY-BASED DIAGNOSIS OF PROSTATE CANCER IN 1290 PATIENTS REFERRED FOR PROSTATE EXAMINATION: RESULTS ACCORDING TO THE PSA LEVEL, DIGITAL RECTAL EXAMINATION AND ULTRASONOGRAPHY

J. Szabó, A.Végh, D. Gasman, A. Hoznek, D. K. Chopin and C. C. Abbou

Department of Urology, Central Military Hospital, H-1134 Budapest, Róbert K. krt. 44, Hungary

Authors present their retrospective study of 1290 patients referred for prostate evaluation. The risk of cancer was analysed according to PSA, rectal palpation and ultrasound examination. Among the 1290 patients, 54.8% had cancer. The risk of cancer was multiplied by 2.8 when the PSA was between the normal limit and 10 ng/ml, by 7.5 when it exceeded 10 ng/ml, by 4.0 when rectal palpation was abnormal and by 1.6 when a hypoechogenic zone was present. Although a hypoechogenic zone does not improve the detection of cancer compared to PSA and rectal palpation, an increased PSA level even lower than 10 ng/ml indicates biopsies.

Introduction

Early diagnosis of prostate cancer is a priority, as only localized forms can be cured. The use of PSA, endorectal US examination and improvements in biopsy techniques, when combined with digital rectal examination, all enable prostate cancers to be diagnosed when still clinically localized.

In the followings we review a series of 1290 prostate biopsy specimens obtained in routine urological practice. The results were assessed according to the PSA, rectal palpation and US examination. Complications and therapeutic implications are also reported.

Patients and Methods

The data of 1290 patients were collected in quotas concerning the biopsy technique used, the number of specimens and antibiotic propylaxis, the PSA level, results of rectal palpation, presence of a hypoechogenic zone, and all complications which were all recorded. The histological results and their therapeutic implications were also noted. Given the variety of PSA assay methods and their normal range, the results were categorized as follows: PSA < normal (N), n < PSA < 10 ng/ml, and PSA > 10 ng/ml. Rectal palpation was considered abnormal when the prostate was firm or nodular.

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Predictive factors (candidates: PSA level, rectal palpation and presence of a hypoechogenic zone) for biopsy positively were identified by means of stepwise logistic regression (BMDP statistical software).

Results

The data of 1290 patients were analysed during the course of 1994. The mean age was 68.8 years (43 to 95 years). 87.6% (1130) of the biopsies were done by the transrectal approach with US guidance, 5.4% (n = 70) of which were combined with digitally guided biopsy. The other biopsies (12.5%, n = 160) were either guided digitally or involved the perineal approach. In 78.3% (n = 1010) of cases, six or more randomized specimens were taken, with or without biopsy of the hypoechogenic zone(s). Antibiotic prophylaxis was prescribed routinely by 95.3% (123/129).

The biopsies were indicated (Table 1) by abnormal rectal palpation in 67.7% of cases (873 patients) and/or a high PSA value in 88.7% of cases (1143 patients). In 2% of cases (25 patients) rectal palpation and the PSA value were normal; the biopsy was indicated by isolate hypoechogenic zones in 1.1% of cases (n = 14) and various other reasons in 0.85% of cases (n = 11).

Table 1
Indications of prostate biopsy

	TR normal	TR abnormal	
PSA < N	25* (1.9%)	122 (9.5%)	147 (11.3%)
N < PSA < 10 ng/ml	118 (9.2%)	201 (15.6%)	319 (24.7%)
PSA > 10 ng/ml	274 (21.2%)	550 (42.6%)	824 (64%)
	417 (32.3%)	873 (67.7%)	1290 (100%)

*Patients with isolated hypoechogenic zone, n = 14 (1.1%); miscellaneous, n = 11 (0.85%).

Table 2
The rate of tumour occurrence in PSA and RDV

	Negative RDV	Positive RDV	Average
PSA < N	4% (1/25)	30.3% (37/122)	25.8% (38/147)
N < PSA < 10 ng/ml	28% (33/118)	50.7% (102/201)	42.3% (135/319)
PSA > 10 ng/ml	40.9% (112/274)	76.7% (422/550)	(64.8% (534/824)
	35% (146/417)	64.3% (561/873)	54.8% (707/1290)

Table 3
The predicative value of hypoechogenic zone in case of negative RDV

	Hypoechoden +	Hypoechoden –	Statistic
PSA < N	7.1% (1/14)	0% (0/11)	ns
N < PSA < 10 ng/ml	37.5% (18/48)	21.4% (15/70)	ns
PSA > 10 ng/ml	43.2% (32/74)	40% (80/200)	ns

ns – non significant

Table 4
Therapeutic implications after biopsy-based diagnosis of prostate cancer

	No.	%	Mean age	Min. age	Max. age
Hormontherapy (Hth)	267	37.8	75	45	95
Radical prostatectomy (RP)	246	37.3	65	46	78
Radiotherapy (RT)	79	11.2	69.3	51	83
Follow-up	43	6.1	74	62	88
Hth + TURP	27	3.8	75	49	91
TURP	7	1	74.5	62	93
Hth + RT	6	0.8	63	46	72
RP + Hth	5	0.7	72	57	84
RP + RT	3	0.4	68	68	68
Repeated biopsies	3	0.4	60.5	58	63
RT + TURP	2	0.3	70.5	67	74
RT + TURP + Hth	1	0.2	72	72	72

The diagnostic yield of the biopsies for prostate cancer was 54.8% (707/1290). The mean age of the patients with cancer was 70 years (45 to 95 years). The prostate was considered normal in 112 cases (8.7%), adenomatous in 271 (21%), inflammatory in 146 (11.3%), dyplastic in 33 (2.6%) and bore various lesions in 21 (1.6%). Depending on PSA value and RDV the prostatic biopsies occurred with a frequency as shown in Table 2. If RDV was negative and PSA > 10 ng/ml the presence of the hypoechogenic zone had no further predictive value, but if N < PSA < 10 ng/ml in the presence of the hypoechogenic zone, more than 1.5 cases of prostate cancer were noticed than without it (Table 3).

Examinations with the x^2 probe, the PSA, the RDV and the presence of the hypoechogenic zone statistically, showed significant correlation with positive biopsies ($p = 0.001$). With multichanging regressive analysis (odd ratio) the relationship of the same parameters with each other were calculated.

Again, biopsy showed strong positive correlation with a high PSA value, abnormal rectal palpation and the presence of a hypoechogenic zone. The risk of prostate cancer was 2.8 (1.8–4.4) times more when the PSA was between normal and 10 ng/ml, 7.5 times more (4.9–11.3) when the PSA was above 10 ng/ml, 4.0 (3.1–5.2) times more when rectal palpation was abnormal, and 1.6 (1.3–2.1) times more when there was a hypoechogenic zone.

No complications occurred in 1008 patients (78.1%). The rate of frequency for the following complications was as follows: hematuria 196 cases (16.2%), rectal bleeding 71 cases (5.5%), both of which were generally moderate and transient, with urinal infections in 15 cases (1.2%).

The therapeutic implications of prostate biopsy were analysed in the subgroup of 707 patients who had prostate cancer (Table 4).There were two main approaches: hormone therapy was used in 37.8% (n = 267), and radical prostatectomy in 37.3% of the cases (n = 264). Radiation therapy was used in 11.2% (n = 79) of the cases. Other approaches were rarely used.

Discussion

Overall biopsy-based prostate cancer detection rate

In our material biopsy was reasoned by high PSA value, positive RDV or the presence of hypoechogenic zones. The obtained results were similar to those reported by Hammerer and Huland [1] in a comparable population of 651 patients in whom random biopsies were positive for cancer in 45% of cases. In contrast, Cooner et al. [2] reported a positivity rate of 14.5% when the target of biopsies was the hypoechogenic zone in 1807 patients seen routinely. These results underline the superiority of random biopsies over target biopsies.

Value of rectal palpation

When the RDV was positive, the rate of prostate cancer occurrence was found to be 64.3%, or according to the odd ratio the risk of cancer presence was 7.5 times more.

Random systematic US-guided biopsies have proven superior to directed US-guided biopsies when rectal palpation was abnormal [3]. Daniels et al. [4] found 42% of patients to have a carcinomatous zone in the lobe contralateral to the palpated lesion, with prognostic implications. This superiority was confirmed by Shinohara's study [5] in which 21% of palpated nodules were isoechogenic and difficult to target, while Hodge et al. [6] and Lippman et al. [7] reported that 53% and 9.1% of cancers respectively, were diagnosed by US-guided biopsy after manually guided biopsy proved to be negative.

Accordingly, positive RDV is an unambiguous indication of biopsy, all the more because according to the odd ratio the possibility of finding cancer rises 4-fold.

Value of PSA

Biopsy is clearly indicated when the PSA level exceeds 10 ng/ml because the ratio of cancer occurrence is 64.8%. It is difficult to determine the indications for biopsy when rectal palpation is normal and PSA values are between normal and 10 ng/ml. The low positive predictive value of PSA in this range has led to the development of new tools such as PSA D, age-related PSA and PSA velocity. The PSA D, introduced by Benson et al. [8], is obtained by dividing the PSA value by the US volume of the prostate. If PSA D exceeds 0.15, biopsy is indicated. Age related PSA was first proposed by Oesterling et al. [9] and simply gives normal PSA values per age range. Finally, biopsy is indicated when the PSA value increases by 0.75 ng/ml [10] or 20% per year [11]. In this series the positive predictive PSA value between normal and 10 ng/ml, combined with normal rectal palpation, was 28% indicating the need for biopsy.

Value of US examination

The most frequent US aspect in prostate cancer are the hypoechogenic zones. It is, however, difficult to consider isolated hypoechogenic zones as warranting biopsy. In this series, hypoechogenic zones were very significantly linked to cancer ($p = 10$; odds ratio 1.6), but only rectal palpation and the PSA value indicated biopsy. Abnormal palpation or PSA levels indicate biopsy regardless of US findings. Finally, only zone of the 14 patients with a normal PSA level, normal rectal palpation and a hypoechogenic zone had a positive biopsy, giving a positive predictive value of only 7%. This is comparable to the PPV of 5% obtained by Lee et al. [12]. Therefore, an isolated hypoechogenic lesion does not seem to be an adequate basis for biopsy.

Therapeutic implications

Radical prostatectomy was performed on 37.3% of the patients whose cancer was diagnosed by biopsy, making this approach as frequent as hormone therapy and reflecting the increasing number of prostate cancers diagnosed at an early, localized stage.

Conclusions

Indication for prostate biopsy is based on a combination of abnormalities on rectal palpation, PSA value and ultrasound findings. Biopsy is not indicated when the PSA and rectal palpation are normal, even if a hypoechogenic zone is present but it is indicated when the PSA titer is between normal and 10 ng/ml and rectal palpation is normal. Hypoechogenic zones observed upon intrarectal ultrasound examination are significantly associated with cancer, but only rectal palpation and PSA can indicate biopsy, especially since the US examination does not improve significantly the cancer detection rate. Complications of biopsy are rare and minor. Finally, prostate cancer is diagnosed at an increasingly early clinical stage thanks to PSA and systematic rectal

palpation, and improvements in biopsy technique; radical prostatectomy is thus increasingly feasible.

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DATA TO THE CLINICAL MANIFESTATION OF THE KRUKENBERG TUMOUR

S. Csömör Jr., Zs. Melczer and Z. Kazy

Second Department of Obstetrics and Gynaecology, Semmelweis University Medical School, H-1088 Budapest, Baross u. 23, Hungary

Ovarian cancer is one of the most frequent malignant tumours in the female population. The screening of this tumour type is unsolved. The tumours are usually diagnosed in the advanced stage; thus the results of survival are unfavourable. Their histopathological appearance has a wide variety, with the occurrence of numerous metastatic forms. In these metastatic cases the choice of treatment is more difficult and prognosis is also worse. Among the metastatic tumours, the primary tumours of the gastrointestinal tract occur the most frequently. They are known as the Krukenberg tumour. Authors present two cases of Krukenberg tumours in order to summarize our knowledge on this rare tumour type and to give some practical advice.

Introduction

It is not rare for metastatic tumours to occur in the ovary. From the extragenital regions, mostly tumours of the breast [1] and the gastrointestinal tract [2] – mainly those of the stomach and colon – are to be reckoned with. Ovarian metastases of cervical cancer are quite rare, while the transtubal spread of the tumours makes them more frequent in the case of endometrial carcinoma [3]. The most well-known tumour among the metastases of the ovary originating from the gastrointestinal tract is the Krukenberg tumour.

In 1896, Krukenberg [4] reported on six of his cases, naming the tumours "fibrosarcoma ovarii mucocellulare carcinomatodes". The histopathology of this tumour interested many around the turn of the century, but the Krukenberg tumour has the attention of pathologists even in this century. All agree that the tumour in question is a so-called signet-ring cell carcinoma metastasis [5, 6]. The naming of signet-ring comes from the finding that the cytoplasm of these tumour cells is quite tightly filled with mucous substance [6], the nucleus is excentrically located at the edge of the cell; thus the microscopic picture of the cell resembles a signet-ring.

During the past few decades, between 10–20 new cases of ovarian cancers are diagnosed each year at the Second Department of Obstetrics and Gynaecology of the Semmelweis Medical University. In the past four years, two cases of Krukenberg tumours were diagnosed to our surprise, giving the notion to summarize our knowledge and learn from the cases regarding this carcinoma type.

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Patients and Methods

Case I

A 19-year-old unmarried female was admitted to our Department in April, 1994. There was nothing worthy of note in her case history, she had not yet been pregnant. Her menarche was at the age of 12, with regular cycles ever since. The patient was referred to our Department because of a tumour detected in the true pelvis during the course of a screening test.

Findings at admission: mediumly dilated vagina, in the continuation of the portio, normal sized uterus in retroflexion. A solid terime was palpable mainly to the right, before and above the uterus right up to the navel. Medical examination revealed no pathological findings. The laboratory values were within the normal range. Ultrasound exam of the true pelvis showed a 135 × 70 mm sized ovarian mass located mainly to the right.

Following standard preparations, lower median laparotomy was performed. Situs: a completely mobile, partly solid, partly cystic, rough surfaced, encased tumour with an approx. 3 cm thick stem, originating from the right ovary. The tumour was removed by means of 1.a. oophorectomy. The left ovary was slightly enlarged with an appearance similar to the tumour found on the right side. On this side, resection was performed leaving intact ovarian tissue. On both sides the intact tubes and the normal healthy uterus were preserved. No tumour-suspicious accumulation was found upon re-examination of the stomach organs. Since the appearance of the tumour was suggestive of possible malignancy, frozen sections were requested (II. Institute of Pathology, Semmelweis University, Register No.: 2815/8664). As the results did not refer unambiguously to malignity, the abdominal cavity was closed. The postoperative period was undisturbed. The final histological result was carcinoma sigillocellulare metastaticum; but the possibility of Krukenberg tumour was raised by the pathologist (II. Institute of Pathology, Semmelweis Medical University, Register No.: 2860/8741). In the possession of the histological findings – before any further therapy – the following studies were performed in search of the primary tumour.

Abdominal ultrasound exam: The liver was not found to be larger, it was of homogeneous structure, with no observable circumscribed alterations. The bile ducts were not dilated. The gall-bladder was plump with normal walls and no signs of any stones. The spleen was normal sized, homogeneous. The right kidney revealed no alterations; the left kidney was of normal shape and size, the pyelon and calyxes showed slight dilatation. Free abdominal fluid was demonstrable in the stomach.

Abdominal X-ray exam: Swallowing was unhindered. The stomach was hook-shaped and normal sized. The pylorus was intect, the bulbus was regular, emptying was at normal rate. No organic alterations were detectable.

Irrigoscopy: The colon could be filled without hindrance, the retrorectal space was free. The colon was of normal course and size, haustration was preserved. No organic alterations were observable.

Intravenous urography: The kidneys showed regular shape, size and location. Secretion was uniform and of good intensity. The ureters had regular course and size.

Postoperative CT exam of the true pelvis: The uterus showed a localization slightly right of the median, a shadow corresponding to the resected ovary was observable on the left. Enlarged lymph nodes were not detectable in the retroperitoneum.

In order to free the patient of any tumours, based on the final histological results and the above-detailed examinations – which failed to reveal a primary tumour – relaparotomy was performed, due to the evidently tumourous left-sided ovary which was not cut out completely. In contrast to the findings 12 days earlier at the first operation, about 1½ liters of reddish tumourous ascites had to be drawn out from the abdominal cavity. The true pelvis was reached after the sharp and blunt loosening of widespread adhesions, where the enlarged resected ovary was found. Left-sided adnexectomy and right-sided salpingectomy were performed. Histological results: carcinoma sigillocellulare metastaticum, Krukenberg tumour (II. Institute of Pathology, Semmelweis Medical University, Register No.: 3500/9437). The utreus – which is to this day healthy and tumour-free – was untouched in the interest of the young patients' chance for later pregnancy by means of reproductive method. Careful re-examination of the abdomen has to the present day not revealed any tumour-suspicious alterations in the abdominal cavity. Following an eventless postoperative period, the patient was referred to the National Institute of Oncology for further examinations and combined chemotherapy treatment, respectively. According to our information, with the rapid progression of the process, the patient went home after a few months.

Case II

A 50-year-old female patient was admitted to our Department in August, 1997. Her case history included two births and one spontaneous abortion. The patient underwent fractionated abrasion twice due to irregular menstruation (hyperplasia glandularis cystica symplex and proliferative endometrium, respectively). In 1992 subtotal gastrectomy was performed due to a stomach tumour (histology: carcinoma sigillocellulare). This was followed by years without any complaints or symptoms. The lumbosacralis spondylosis of the patient has been known for a long time, causing her periodical pain and movement difficulties.

With respect to her lumbago, the patient requested admission to the Saint Margaret Hospital for the examination of her abdominal and lumbar pains. During the course of the examinations she was diagnosed with an ovarian tumour, and thus transferred to our Department.

Findings at admission: The scar of an upper median laparotomy on the abdomen. Slightly lacerated portio tending towards the breast. In the continuation large, retroflected uterus. Before it, a tight cystic resistance reaching the pelvic wall and protruding from the true pelvis approx. till the navel. The Douglas was not raised or nodular.

Colposcope: intact epithelium around partially epithelizating ectopium. Tu cyt: P_2, II°. Ultrasound exam (TAS as well as TVS): The full bladder was caudally dislocated, behind it large uterus in normal retroflexion, with 5 mm thick mucous membrane. A solid mass surrounded by a regular capsule was observable above the bladder and the uterus filling in the true pelvis, partially in the free abdominal cavity, pushing the small

intestines cranial-wise. Two fluid-filled cavities 30 and 50 mm in diameter were found within the mass.

The medical state of the patient did not show any pathological changes, her laboratory findings were within the normal value limits. The patient could be anesthesized and operated on. In knowledge of the previous events, suspecting Krukenberg tumour, lower median laparotomy was performed following standard preparations. Situs: originating from the left ovary, a partly solid, partly cystic encased tumour was found corresponding in size to previous exams. The right adnexum and the uterus were both of normal appearance. Bilateral adnexectomy – including the tumour – and hysterectomy were carried out. The abdominal cavity was carefully explored in search of any tumour-suspicious alterations on other organs; no ascites was found. Extensive adhesions were observable from the previous gastrostomy. Histology: carcinoma sigillocellulare metastaticum ovarii, adenomyosis uteri (II. Institute of Pathology, Semmelweis Medical University, Register No.: 7552/8001). The postoperative period was eventless. According to our information, the patient is presently without any complaints, being checked regularly at the I. Department of Surgery, Haynal Imre Postgraduate Medical School.

Discussion

The typical heterogeneity of ovarian tumours is a characteristic feature of metastatic tumours, thus the Krukenberg tumour as well. As mentioned in the Introduction, diagnosis is based on the demonstration of the specific signet-ring cells. However, these are only manifest retrospectively, upon the histological processing of the surgical specimen. Until then the wide variety of misleading clinical symptoms may direct towards a different diagnosis. In addition to the morphological characteristics, it is a known fact that in case of Krukenberg tumours the stromal luteinization of the ovary takes place, thus the clinical picture is frequently dominated by hormonal symptoms [7]. In case of virilization symptoms, the suspicion of Sertoli-Leydig cell tumours is quite often raised [8]. The tubular types of the Krukenberg tumour can be mistaken for certain tumours of the germinal epithelium [9, 10]. A case of Krukenberg tumour has been reported in relation to pregnancy by Fox et al. [11]. In a woman in her 32nd week of pregnancy – complaint-free right up until then – sudden virilization symptoms appeared together with ovarian terime palpated beside the pregnant womb. Histological examination of the surgical specimen determined Krukenberg tumour. The question arises whether the form of a Krukenberg tumour is primary or metastatic. This needs further studies and is under debate. The metastatic tumour is mostly bilateral, but the unilateral form also occurs; furthermore, on occasions the normal sized ovary may also have microscopic metastases [9]. It is also of interest to mention the rarity from literature according to which Krukenberg tumour has also been found in a male patient [12]. It can be stated that this is a tumour presenting a variety of symptoms, with a frequency of occurrence below 1% in comparison to all malignant tumours of the ovary. Within this, the number of "clear" Krukenberg tumours is even less [13–15]. In regard to the relevant national

literary data, there are few publications concerning the Krukenberg tumour. The manual-type monograph of László and Gaál [16] should be emphasized, in which a basic pathological survey is given of this tumour, together with a comprehensive literary review. Earlier, Kontsek [17] wrote a case report in 1930; then much later Illei [18] provided a summary of the histopathological characteristics and clinical manifestations of the Krukenberg tumour, based on two rare cases.

Based on the literary data as well as our own experiences it can be determined that the Krukenberg tumour is a disease of rare occurrence and bad prognosis, causing diagnostic and therapeutic difficulties. The treatment of the primary tumour is firstly surgical, the ovarian tumour should be treated according to the general principles. Chemotherapy is of great importance; for example, Kásler [19] suggest the FAV combination. As concerns the origin of the tumour, the most frequent are the metastatic forms deriving from the gastrointestinal tract. Nevertheless, the primary ovarian origin cannot be excluded either. In compliance with this, the Krukenberg tumour should be diagnosed and treated jointly within the field of surgery and gynaecological oncology.

Reviewing our two cases makes it possible to draw a few conclusions: in case of our 50-year-old patient the previous stomach carcinoma raised the possibility of Krukenberg tumour, i.e. a metastatic form even before the gynaecological operation – which unambiguously meant the bilateral removal of the adnexum as well as that of the uterus. In this case progression was slow, since years passed following the abdominal process before the alterations appeared in the ovary. At the same time, in case of our 19-year-old patient, the possibility of Krukenberg tumour was not even thought of in light of the negative previous case history. The patient's treatment caused serious dilemma; bringing to accord radical surgical intervention with the possible preservation of the reproductive capability. The situation was further complicated by the fact that histopathological study of the frozen section prepared during surgery did not give definite answer to the nature of the tumour. Thus, relaparotomy with removal of the remainder of the tumour was only accomplished in possession of the final histological finding, besides a propagated process. A lession was drawn that in a similar case, radical surgery should be chosen as solution rather than preservation of reproduction, by which means relaparotomy under the more disadvantageous abdominal situs could be avoided.

It is known that despite the widespread imaging processes (ultrasound, CT, MRI), there is no solution to the early diagnosis of ovarian cancers. Screening of the complaint-free female population can obviously not be accomplished. However, women with a case history of gastrointestinal tract tumours could be picked out from the average population. This group is at high risk for the development of metastatic ovarian cancer and should be checked regularly – which is made possible by the various modern methods of examination. In a given case of surgery due to a malignant tumour of the gastrointestinal tract, a debate and surgical-gynaecological consultation could be held over whether the adnexum should also be removed in order to prevent possible ovarian metastases at a later stage.

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URETER AND BLADDER REPLACEMENT FOLLOWING RADICAL CYSTECTOMY

S. Csata and D. Répássy

Department of Urology, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary

During the course of Hautmann-type bladder replacement, left sided ureter damage necessitated ureter replacement as well, modifying the removal of the ileum-bladder. The proximal 20 cm length of the 70 cm long isolated ileum portion was not detubularized; instead it was slipped through the mesosigma and mesocolon to the left side of the colon and the left ureter stub was anastomized without tautness to the ileum according to Le Duc. The implantation of the right ureter was accomplished according to Hautmann. For similar cases authors recomment this procedure, since neither stricture, nor reflux could be detected at later examinations.

Introduction

Radical cystectomy is curative surgical therapy for infiltrative bladder tumours. One of the best modes of orthotopic bladder replacement following cystectomy is the Hautmann-type ileum-bladder. The method's most sensitive part includes the implantation of the ureters, a condition of which is that the ureters are of suitable length, of free course and can be well mobilized [2, 4–8].

In the followings, authors report on a case where the left-sided ureter was also replaced, for which purpose modified surgery was performed.

Patients and Methods

A 78-year-old male patient was admitted to our Department on 9th September, 1996. His only complaint was painless, clotty haematuria lasting over 4 weeks.

The cystoscopic image showed a solid, wide peduncular, coagulum-covered tumour the size of a peanut behind the trigonum on the posterior wall, and a smaller tumour of similar structure on the left-sided wall.

The tumour in the bladder was resected on 12th September, 1996.

Histology showed transitional cellular carcinoma T_3, G_3.

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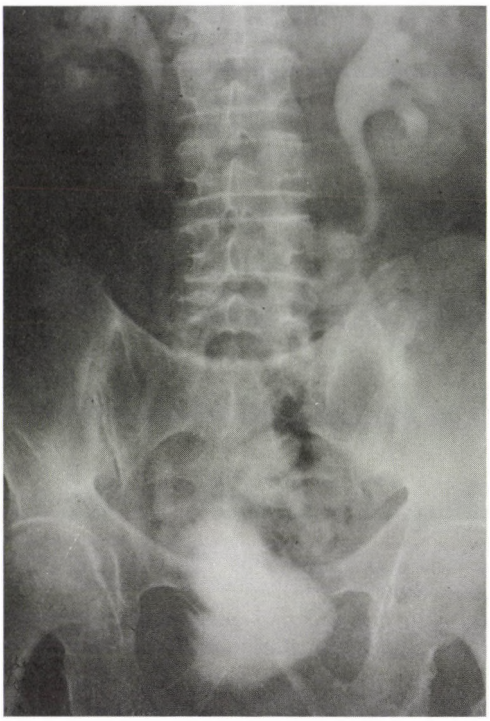

Fig. 1. Iv. picture of the renal cavity system in the continuation of which the thin ureter can well be seen, proceeding into a wider section of the inestine above the ilium. No reflux or stricture is observable. The ureter on the right side is completely intact

Based on the above, radical cystectomy was indicated. Approach was with usual lower median laparotomy, lengthened upwards to the left evading the umbilicus. Pulling away the peritoneum-lamella covering the bladder and cutting through the ducts, the bladder was freed till the lateral peduncles. Then in the retroperitoneal space, dissecting beneath the coecum, the right ureter was opened, then mobilized and resected almost till the bladder. The left ureter was rather gracile and thin-walled, damaged at several places during the dissection behind the adherings of the sigma. Only the upper section of the ureter, located proximally to the arteria iliaca communis, remained intact with unimpaired adventitia.

Due to the shortness of the new bladder, implantation of the left ureter became impossible using the Hautmann method since it would have had to be pull through under the sigma as well, and medialized.

Therefore, following the radical removal of the bladder and prostata the ileum-bladder was cut out in a modified manner: the proximal 20 cm of the 70 cm long isolated ileum section was not detubularized according to Studer [10, 11]. A wide tunnel was prepared under the mesosigma and mesocolon and this is where the proximal ileum section was pulled through to the left side of the colon. Then the left colon was anasto-

mosed without tension according to Le Duc, also securing the ureter extraintestinally [3] and the intestine was closed in two layers. Implantation of the right ureter was performed according to the Hautmann method. Placement of the orthotopic intestinal bladder, urethra-anastomosis was finished off as usual. The left-sided ureter plate (K-32) was also led through the non-detubularized ileum and brought out through the intestinal bladder and stomach wall.

The postoperative period was eventless; the ureter plates were removed on the 12th, the permanent catheter on the 18th postoperative day.

Throughout the period of the later controls the bladder emptied without any residue and there was a slight incontinence for a few months. One year after the operation, the patient's incontinence became minimal, only occurring occasionally (weekly) during the night. Neither reflux nor stagnation was observable on either side (Fig. 1). The slight acidosis of the patient has been kept under control and in balance with Bicarbonate.

Discussion

Following radical cystectomy due to urothelial carcinoma of the bladder, the mode of urine-drainage is to be chosen individually. The most important aim is that urine storage and uresis resemble the natural state, which can be achieved by low pressure orthotopic intestinal bladder formation [2, 4–7, 9].

The bladder replacement method worked out by Hautmann – Ileum Neoblase – has become a classic due to its simplicity and relative good results [4, 5, 8]. Naturally, it has its disadvantages as well as advantages – which is more or less true for any other bladder replacement method. One of the most important difficulties of the method is the implantation of the ureters. Studer has a rather ingenious solution to eliminate the danger of both reflux and stricture. He ensures functional antireflux of the non-detubularized isoperistaltic ileum-section, the more dilated ureter anastomosis can prevent stricture development, and the distal detubularized ileum ensures the low pressure of the "pouch" with adequate capacity [10–12]. Our opinion is that besides low pressure, there is no need for antireflux implantation; simple Le Duc anastomosis is sufficient [3]. Care should be taken, however, that both ureters be implanted in a fairly distal part of the intestinal bladder, since that area is less mobile; i.e. mostly the fore- and upper walls move during the filling of the intestinal bladder. This movement must not be followed by the adhered ureters because it may cause periodical rupture, resulting in possible stagnancy. This is especially valid for the left ureter, where most of the time its length is not sufficient to ensure the above condition due to central placement.

If the left ureter becomes short due to other causes (e.g. stricture, damage, etc.), the above solution is recommended: the ureter can be replaced in a similar mode to the Studer kind of ileum bladder. This also goes for the right ureter. In case of both ureters being short, the original Studer-type bladder replacement may be chosen [10–12]. Such a case is rare, however, there were 25 cases of bladder replacement at our Department during a period of two years, and the presented case was the only one where the reported modification was necessary.

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ORGAN-PRESERVING SURGERY OF RENAL CELL CARCINOMA: REPORT OF FOUR CASES

S. Csata and D. Répássy

Department of Urology, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary

Authors removed the renal tumour of four patients by means of resection in an organ-preserving manner. Of the four patients, one had bilateral carcinoma. The right-sided carcinoma of this patient was removed by resection while the other kidney was removed radically, by transabdominal approach. In three of the four cases which were in the process of stages T_1 and N_0M_0, organ-preserving surgery was performed in the presence of intact opposite kidneys. Authors point out the fact that the resection method might be indicated even in the case of early (T_1) stage tumours with intact opposite side kidneys. Furthermore, they do not recommend the enucleation of renal carcinomas for the surgical treatment of kidney tumours, since experimental studies have proved that these tumours can be transferred into the parenchyma of the kidney through the pseudocapsule of the tumour.

Introduction

The modern treatment for malignant renal carcinomas is radical nephrectomy [1, 2, 6, 12, 13, 22]. The majority of the tumours are resistant to radiation, effective cytostatics are not available and the effects of immune- and hormone-therapy are also unsatisfactory [12, 13]. Thus, effective treatment can only be expected from ablastic and radical surgical intervention carried out in the earliest possible stage [1, 2, 14, 22].

This basic principle of tumour surgery should be modified, however, in the following cases:

– bilateral renal carcinomas,
– solitary tumourous kidneys,
– unilateral tumourous kidneys and opposite side afunctional kidneys.

In case of a bilateral process, the therapeutic possibilities in principle are as follows:

– treatment with pharmaceuticals without surgery,
– bilateral radical nephrectomy and consecutive haemodialysis,
– nephrectomy on one side and organ-preserving surgery on the other side,
– organ preserving surgery on both sides.

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In case of a solitary tumourous kidney:

– treatment with pharmaceuticals without surgery,
– radical nephrectomy and consecutive haemodialysis,
– organ preserving surgery.

Radical nephrectomy can be disregarded – though it is not compulsory to do so – if the tumour is in the T_1 stage and its location allows for the technical execution of organ-preserving surgery.

In the followings, a review is given of four cases.

Patients and Methods

1. A 67-year-old male was admitted to our Department on 1st September, 1996 because of clotty haematuria and kidney spasms.

I.v. urography demonstrated deformity and dislocation of the median and upper calyx stems of the left kidney.

Ultrasound exam showed two echo-deficient, unhomogeneous solid tumours; one ca. 4 × 5 cm in diameter in the median third of the left kidney, and another about 2.5 cm in diameter in the upper third of the right kidney.

The *CT exam* verified the above findings (Fig. 1). The lymph noded did not show any pathological alterations. Diagnosis: Tu. ren. 1. u.

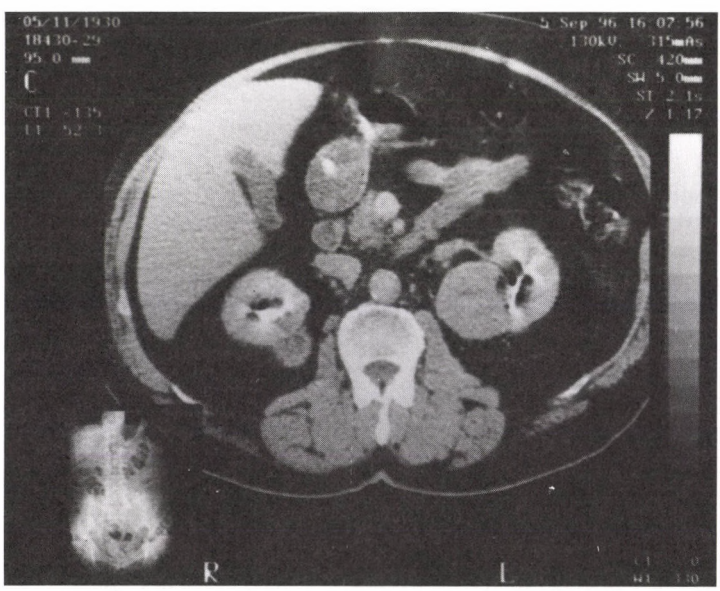

Fig. 1. CT: A mass filled with contrast material, 3 cm in size is observable in the upper third of the right kidney; another, 4 × 5 cm in size can be seen in the median third of the left kidney

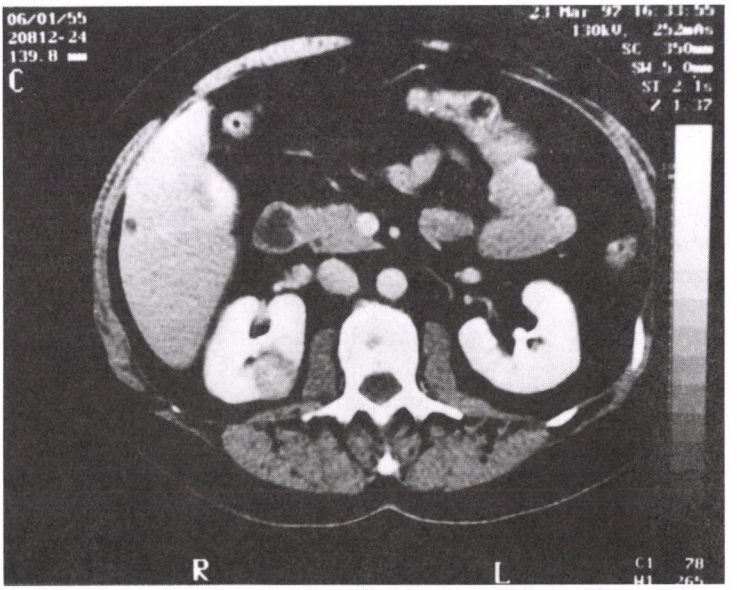

Fig. 2. CT: An 18 mm, sharp-edged solid mass can be seen slightly protruding from the upper part of the right kidney

Since the renal carcinoma was two-sided, the smaller right-sided, approx. 2.5 cm sized tumour was resected on 17th September, 1996. The tumour was cut out from the parenchyma after holding down the hilum (12 minutes). Then the tumour base and the parenchyma were closed with parenchyma stitches.

Histology. Dg.: Clear cell renal carcinoma.

On 28th October, 1996 the patient was admitted again to our Department for left-sided radical kidney removal by means of transabdominal approach.

Histology. Dg.: Renal carcinoma, clear cell type.

The patient left our Department with a healed wound, supplied with medication.

2. A 41-year-old female patient was transferred to our Department on the 3rd April, 1997 because of a kidney tumour found during examination at another Department.

Anamnesis: A striking 3 kg loss of weight within 3 months.

CT exam showed a sharp edged solid mass 18 mm in diameter, slightly protruding from the upper part of the right kidney. The mass was natively isodense, with moderate accumulation of contrast material (Fig. 2). No lymph node alterations were observable in the retroperitoneum. Dg.: Tu. ren. 1.d.

On the 7th April, 1997 an oblique lumbar cut was performed on the right kidney. With the hilum prepared and the renal arteries held down by soft clamps, the approx. 2 cm sized tumour located on the median and upper part of the kidney was removed. The cavity system was joined together by atraumatic 3/0 Vicryl thread and the parenchyma

was closed using mattres stitches. After 12 minutes the hilum was let to rise with no bleeding observed.

Histology. Dg.: Carcinoma renis sinistri, eosinophilic type, well-differentiated form.

No complications arose after the operation, so the patient was allowed home on the 10th postoperative day with a healed wound.

3. A 59-year-old male patient was transferred from another Department to us.

The *abdominal ultrasound exam* showed several parapyelar, 2-3 cm sized cysts in the right kidney. More cortical cysts were detectable in the parenchyma on the convex side. At the back, near the lower pole, an approximately 6 cm sized conglomerate containing several cysts was observable, protruding from the parenchyma, but with no signs of malignancy. The dorsal part of the left kidney also revealed a cyst 2 cm in size.

The *CT pictures* did not show any retroperitoneal lymph nodes. The 5 cm sized, almost encapsulated cystic system manifest in the right kidney corresponded to cystadenoma; therefore, exploratory surgery was performed (Fig. 3). The right kidney was reached by means of supracostal retroperitoneal lumbotomy. A smaller first sized multicystic matter appeared in the median-lower third. This was incised and the multilocular tumour was removed. Peripherally a small area was suspected of being tumourous. The acute, histological study of frozen sections revealed proof of hypernephroid appearance.

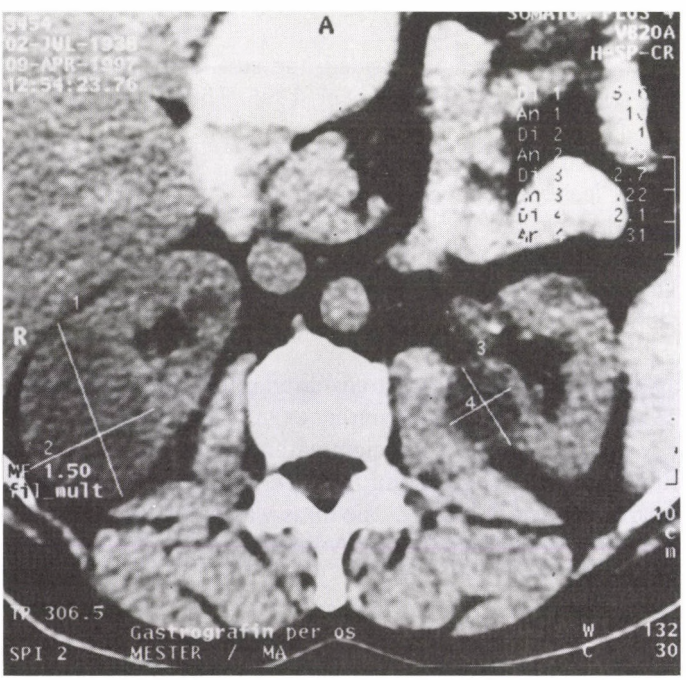

Fig. 3. CT: A 5 cm sized encapsulated cystic-like mass can be observed in the right kidney. An adenoma 5 mm in size is visible in the left adrenal gland

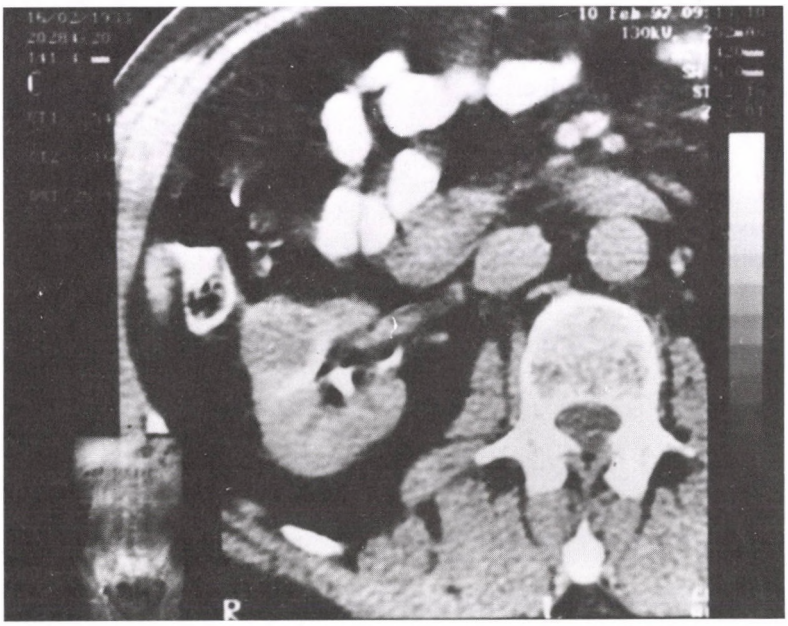

Fig. 4. CT: On the outer contour of the right kidney a sharp-edged, non-cystic solid mass with moderately accumulated contrast material is observable on the confines of the median lower calyx group, dislocating the median calyx group

The parenchyma in the intact area was resected, the arteries and cavity system were closed with 6 3/0 8-s, the parenchyma by means of several mattress stitches.

Histology. Dg.: Hypernephroid cystic tumour.

With no occurrence of any complications, the paient left for home recovered on 23rd May, 1997.

4. A 64-year-old male patient gained admission to our Department on 4th March, 1997 diagnosed with Tu. renis l.d.

Anamnesis: examinations related to his psoriaris revealed cholelithiasis and a right-sided kidney tumour. Thee were no other complaints referring to disease other than his psoriaris and cholelithiasis.

The *abdominal ultrasound exam* showed a normal sized homogeneous liver. The gall bladder was large, with a 16 mm sized stone in it. The lymphatic epithelium in the surroundings was found to be isolately swollen, with a few smaller stones nearby. The fluid content of the gall bladder was of average. A solid mass, 20 mm in size, was found attached to the lower pole of the right kidney.

According to the *abdominal CT examination following administration of 100 ml of Ultravist,* a sharp edged solid mass was visible on the median lower confines of the calyx group, moderately accumulating contrast material, and dislocating the median calyx group (Fig. 4). The liver did not show any alterations. Stones were found in the gall bladder, The pancreas head was slightly thicker (most probably the remnant of an

earlier inflammation). The gall bladder wall was also concentrically thicker, especially in the environs of the stones.

Dg.: Tu. renis l.d. Cholelithiasis.

On the 5th March, 1997 the patient was operated on. A subcostal incision was medially lengthened, the kidney was freed from the fatty capsule and mobilized by being released from the peduncles. The tumour, the size of a walnut, was detected on the central part of the lower pole. The hilum was held down with soft clamps and the visible walnut sized tumour was resected. The bleeding arteries were stitched down, the cavity system was joined together by knotty stitches, and the kidney parenchyma was closed with mattress stitches.

Then the peritoneum was opened and the thicker walled gall bladder was removed together with the smaller walnut sized stones.

The postoperative period was eventless, and on the 10th day the patient left our Department with healed wounds.

Histology. Dg.: I. Benign oncocytoma (oncocytic cortical adenoma). II. Cholecystitis chronica.

Discussion

According to the literary data, renal carcinoma patients who have undergone organ-preserving surgery have a better chance of survival than if irradiation, hormone- or immune-stimulating treatments are given instead of surgical intervention [6, 10, 12, 13, 16–18, 22]. Conservative treatment gives the patient an average of 6 months' survival [6, 12, 22]. Grabstald and Aviles reported on 30 patients who were tumour-free and well for 1-10 years after partial resection [6, 7, 11–13, 17, 20, 22].

The functional state of the kidney following surgery is significant. Based on literary data, 15% of nephrons is sufficient for survival, if they are healthy. In case of solitary kidney tumours prognosis depends on whether the opposite kidney was removed due to a benign alteration or because of a tumour [4–6, 11, 12, 21]. The success of surgery and the prognosis are greatly influenced by the macroscopic as well as microsopic structure of the tumour [1–3, 12, 13]. The clear cell tumours with their firous capsules can be well defined from the renal tissues and if the tumour is located on the periphery, it can easily be resected.

From prognostic point of view, it is essential in case of bilateral renal carcinomas whether the tumours appeared simultaneously or as metastases [6, 14, 22].

It is a case of metastasis if the tumour appears in the form of multiple bone- or lung metastases. If after removal of a kidney carcinoma on one side a tumour soon appears on the other side, it might be a case of a tumour of metastatic origin. A tumour of varying tissue structure does not exclude simultaneous appearance, however, bilateral similar structure does not prove metastasis either [1, 2, 22].

Decision regarding the mode of intervention necessitates exact registration of anamnesis, physical examination, inclusion of diagnostic tools, exact staging, e.g.: i.v. urography, ultrasound, CT, MRI, scintigraphy, selective angiography and if necessary, cavography [6, 12, 13, 17]. The mode of preoperative intervention – surgical tactics – is

decided on the basis of the afore-mentioned examinations. From the resection type of surgical interventions, *in situ* resection seems the better; – extracorporal intervention involves more complications [6, 15, 22]. It is essential to apply careful surgical techniques (kidney-sparing stitching, careful controlling of haemorrhage, short period of holding down the peduncles, etc.), and to use up-to-date threads (Dexon, Vycril, etc.) [6, 8, 9, 15, 19, 22].

Although renal carcinomas are generally circumscribed by a well-defined capsule – contrary to others – we do not consider enucleation to be a radical method, not even in the case of small tumours [4–6, 13, 22]. The justness of this standpoint has been verified by the microangiographic and histological studies of Rosenthal et al. [15].

Due to our small case number as well as the short period of time elapsed since the operations, we are unable to draw far-reaching conclusions. Based on the literature at our disposal, it is our viewpoint as well that regarding renal carcinomas in the T1 stage, satisfactory results are gained by resection of the tumourous kidney in case of an intact opposite side kidney [1, 4–6, 10, 11, 22].

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BILATERAL URETERIC REPLACEMENT WITH ILEUM

D. Répássy, S. Csata, Gy. Tamás and T. Weninger

Department of Urology, Szent István Hospital,
H-1096 Budapest, Nagyvárad tér 1, Hungary

In connection with a report of a case, authors discuss in outline the possibilities of ureter replacement. If both the ureters are injured, they can be substituted with one single segment of the intestine, as it happened in their case. Authors raise the idea that a longer segment of the intestine used for substitution provides sufficient capacity and isoperistaltic function, and this may protect from the negative effects of possible vesicoileal reflux. In this case, the reflux does not spread to the kidneys even if the ureteroileal was not made with anti-reflux technique.

Introduction

In case of the stricture of a long segment of the ureter, ureter replacement is necessary. This can be solved with isolated small intestine: with the skeletonization of the mesenterium providing proper supply, the segment of the ileum is placed and located in an isoperistaltic manner. Sometimes both the ureters are injured and occluded (for example: due to radiation of the pelvic area). In such cases, the ureters can be substituted with one single ileum segment. In the following, we describe such a case.

Patient and Methods

A 58-year-old female patient, was operated due to cervical carcinoma (Stage II/B) in 1993 at a Gynaecological Department. After the surgery according to Wertheim, X-ray and chemical treatments were performed. As a complication resulting from these therapies, the lower- and middle sections of both the ureters became partly stricturized and were gradually closed off. As a result, dilatation in the system of the renal cavity developed. For this reason, percutaneous transrenal drains were placed into both kidneys, and these drains were regularly cared for 4 years. Due to recurrent pyelonephritis, and upon request of the patient (social problems) reconstruction surgery was performed. Both kidneys were exposed by means of median laparotomy. The ureters were found to be stricturized, their upper section was intact. First, the retroperitoneal lamina was

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opened from the ligament of Treits's to the coecum, then further on at the colon ascending at the Toldt line, then elevated at the coecum, the colon and a part of the mesenterium. The right ureter was resected, the intact section was mobilized and pulled in the middle in the height of the ligament of Treit's. The left ureter was also resected, isolated and placed in the middle under the mesocolon cranially from the inferior mesenterical artery so that we preserved the intact nature of the inferior mesenteric vein. After the reconstruction of the retroperitoneum, the two ureter-ends – already in the line of the intra- and retroperitoneal space – were stitched together in a slit-like manner according to Wallace, and anastomosed with the proximal end of the selected small intestine (Fig. 1). A loose mesenterium was prepared and a 30 cm long ileum was selected about 25 cm from the coecum. The continuity of the intestine tract was reconstructed with the help of end to end, two-layer seromuscular suture anastomosis. After laying the ileum in the isoperistaltical position it was implanted into the bladder. By means of sectio alta, slits were made both sharply and bluntly on the posterior wall, and the ileum was pulled into these.

Prior to this, its 3 cm long last section from the mesenterium was cleaned, spatulated at 2.5 cm length on the antimesenterial side, then, folding it as a cuff and fixing it with stitches, a double wall was prepared. This way, a 2.5 cm intravesical nipple was created in order to prevent possible reflux (Fig. 2). The implanted ileum was also fixed extravesically to the bladder wall with four stitches. The anastomoses were prepared along the previously implanted K-32 stents, which were led out through the bladder and the abdominal wall. A 24 Ch Foley catheter was fixed into the bladder. The stents and the catheter were removed on the 24th postoperative day. Upon later control examinations good drainage was detected from both kidneys, with no jam or stagnation detectable. The peristaltic of the intestinal ureter forwarded the urination well. In the course of the reflux examination, minimum reflux was found in the intestinal ureter, but this did not extend to the kidneys. Five minutes after filling the bladder, the contrast material repeatedly flew into the bladder. The patient left the hospital 16 days after surgery with healed wounds.

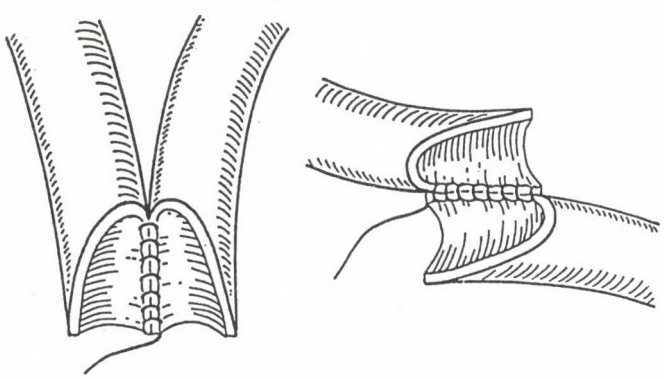

Fig. 1. Ureteroileal anastomosis (Wallace: a) side by side, b) end to end)

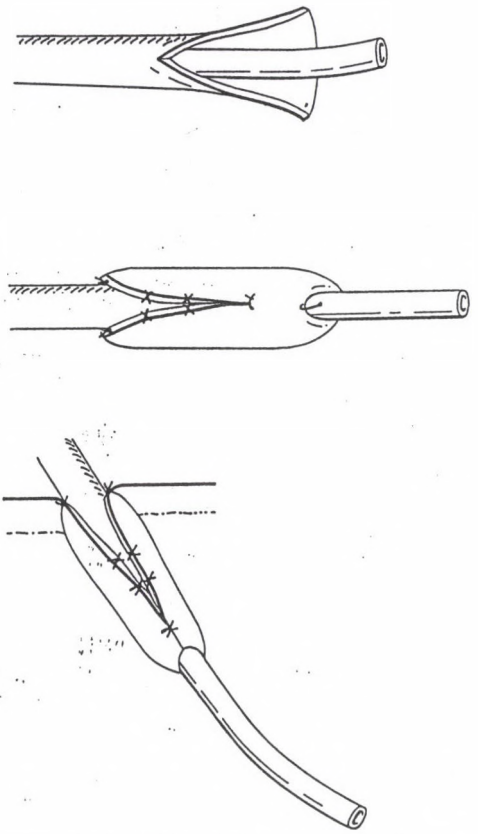

Fig. 2. "Split-cuff nipple" anastomosis

Discussion

If the lower segment of the ureter is damaged, neoimplantation, Boari flap, and psoas hitch might be the solutions for reconstruction. However, cicatrization of a long segment necessitates replacement, which can be solved with selected small intestine [4, 7, 13]. The most important objective is to drain the urine and the mucus efficiently towards the bladder. For this reason, the segmentof the small intestine is placed isoperistaltically by guaranteeing mesenterium providing for proper supply [3, 9]. The three most important steps of the surgery are the following:

1. Selection of the small intestine in well-chosen length;
2. Correct anastomosis of the ureter (or ureters) to the substituting bowel;
3. Implantation of the small bowel into the bladder.

i) It is a basic principle of surgery that any anastomosis should be free from tension. This can be guaranteed with the proper length of the intestine. It is also very important

that the skeletized mesenterium should contain at least one artery body and should be long enough, namely the distal end of the ileum should largely reach the bladder.

ii) Ureteroileal anastomosis can be accomplished in several different ways:

– non-antireflux:	end to end;
	end to side – according to Bricker – [2];
	Wallace (I: "66", II: "69") [12];
	Barzilay [1];
– antireflux:	Le Duc [6] method;
	Intussusceptional method (Kock [6]);
	According to Leadbetter [5].

iii) At the implantation of the small bowel into the bladder the antireflux technique is of basic importance, as there is high pressure in the bladder upon drainage of the urine.

The antireflux methods are the followings:

– Leadbetter [5];
– Stone ("split-cuff nipple") [9];
– Intussusceptional method according to Kock [8].

Two basic problems may occur with the above anastomoses: either a reflux, or stagnation due to stricture may develop. We have to note that the reflux is dangerous if it is caused or sustained by high pressure [10, 11].

In our case we acted according to the following hypothesis:

As high pressure if frequent in the bladder, we performed the implantation of the ileum in an antireflux manner with "split-cuff" technique [9], and the only change was that the nipple was smaller, as we are on the opinion that congestion due to narrow anastomosis is more dangerous than periodical reflux. Keeping the latter in mind, we have used an ileum segment much longer than the distance (30 cm), and its capacity and peristaltic movement counter-balances periodical reflux very well. We used the Wallace [12] method for the ureteroileal anastomosis, as this provides spacious connection, but has no antireflux function. In spite of this, due to relatively low pressure guaranteed by the long small intestine, we did not detect ileoureteral reflux.

Based on one single case, we are not in the position to form an opinion, but would like to raise the following ideas:

– In the case of ureter replacement, ureteroilealis anastomosis may miss the antireflux technique;

– The higher capacity and better peristaltics of a longer ileum segment may counterbalance periodical reflux;

– Ileum substituting the ureter (ureters) has to be implanted into the bladder in an antireflux manner, but we have to take into account that vesicointestinal reflux may develop even in spite of this.

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KIDNEY ONCOCYTOMA

S. Csata[1], D. Répássy[1], A. Iványi[2] and B. Járay[2]

[1]*Department of Urology and* [2]*Department of Histopathology, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary*

Authors review the case history of three patients with kidney tumours which had been surgically removed. In two of the cases radical nephrectomy while in one, organ-preserving surgery was performed. In all the cases histology revealed benign kidney tumours – oncocytomas. In light of the available literature authors indicate that preoperative diagnosis is almost impossible. Furthermore, it is their opinion that this benign kidney tumour has a less frequent occurrence than earlier thought.

Introduction

The rare, benign form of kidney tumours of epithelial origin is oncocytoma (oncocytoma tubulaire renis, mitochondrioma, oxyphilic adenoma). Similar tumours occur mainly in the glandular organs (parotis, thyroid gland, parathyroid, adrenal gland, liver, pancreas, etc.). It rarely develops in the kidney and is practically impossible to diagnose prior to surgery. Intravenous urography, ultrasound, and even CT exams merely provide information characteristic to the tumour [1–5, 7].

The tumour is mostly an unilateral process: two-sided kidney oncocytomas are rare, though it may occur [21]. The tumour develops from the epithelial cells of the tubules due to genetic damage. If the tumour exceeds 10 cm in diameter it may break into the veins, infiltrating the renal capsule and can become malignant according to some authors [7, 22–24].

The finding of over 200 small oncocytomas in one of the kidneys has also been reported. Mostly, however, it occurs as a single tumour, as in the case of our three patients [25].

Reviewing our three cases seems worthy of note because oncocytomas are tumours of rare occurrence – approximately 400 cases have been reported in the world literature – their presence was only discovered during the course of studying the serial sections prepared after surgery [19].

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Patients and Methods

1. A 58-year-old female patient was admitted to our Department on November 23, 1991 because of a right-sided kidney tumour standing in the background of hypertonia.

Abdominal ultrasound study revealed a 70 mm solid mass in the central lower half of the right-sided kidney. This was confirmed by CT exam (Fig. 1). No lymph nodes were noted and the tumour showed no relationship with the large arteries. *I.v. urography* showed selection in both kidneys at 7'. The left kidney showed intact conditions, while on the right side a 70 mm sized soft shadow was observable in the lower part of the kidney, dislocating and compressing the upper calycular group.

Radical nephrectomy was performed and 10 days later the patient left the hospital with a healed wound. On the slide, the 7 cm sized tumour was seen to be of homogeneous structure and was ochre coloured. Six years after surgery the patient has no complaints and is free of any symptoms.

Histological study revealed kidney oncocytoma: the compact and tubular-structured tumour cells were slightly polygonal in general, their most striking feature was incorporated granulation detectable in their characteristically eosinophilic cytoplasm (Fig. 2).

Diagnosis: Oncocytoma renis.

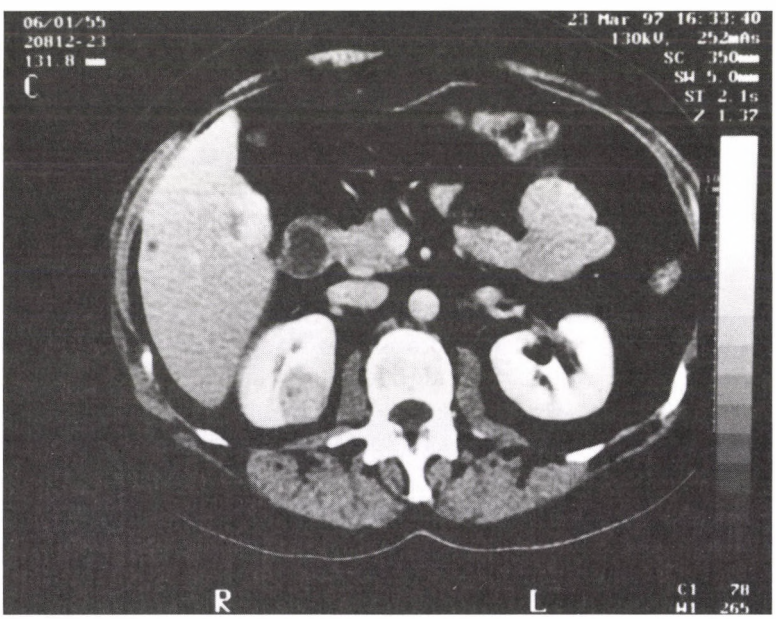

Fig. 1. CT: A sharp-edged, non-cystotic, solid formation, moderately accumulating the contrast material, can be seen on the inner contour of the right kidney, on the edge of the central-lower calyx-group. It is dislocating the central calyx-group

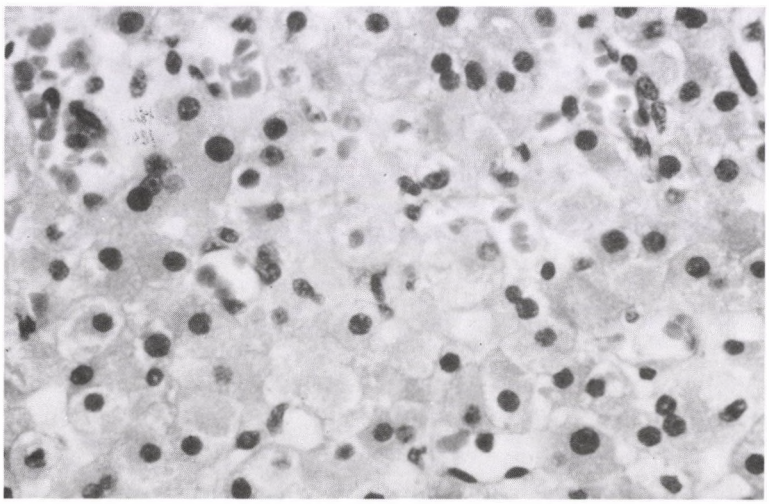

Fig. 2. The tumour cells are rounded or polygonal, with sharp boundaries. Eosinophilic granulation is observable in the cytoplasm. The cell nuclei are roundish, darkly stained, slight nuclear polymorphy can be seen, no dividing cells are visible (HE, magnification × 400)

2. A 64-year-old male patient was admitted to our Department on March 4, 1997 because of a kidney tumour which was discovered during exams for revealing the source of psoriasis.

From the results of the exams, the abdominal ultrasound showed normal sized, homogeneous liver. A large, ca. 16 mm sized stone was observable in the gall bladder. In the surroundings the mucous membrane was isolately more swollen, with a few smaller stones visible nearby. The gall bladder content was of average. A 20 mm solid formation was observable in the lower half of the right kidney.

The *CT exam* was in harmony with the above findings (Fig. 3).

Diagnosis: Tu. Renis l.d. Cholelithiasis.

Due to the signs referring to a tumour, as well as with regard to the bilestones, surgery was decided on: with a right-sided subcostal cut the kidney was retroperitoneally exposed, the lower part with the tumour was resected; organ-preserving surgery was performed.

After opening the peritoneum the thicker walled gall bladder was removed, together with the smaller, walnut sized stones.

The patient's condition was eventless following surgery. Ten days later he was allowed home with a healed wound.

Histology proved an adenomatoid type oncocytoma, and also confirmed the diagnosis of chronic cholecystitis with stones (Fig. 4).

3. The third patient was a 63-year-old female who was transferred to us from one of the Internal Medicine Departments, where a left-sided kidney tumour was found during the course of examination due to abdominal pain.

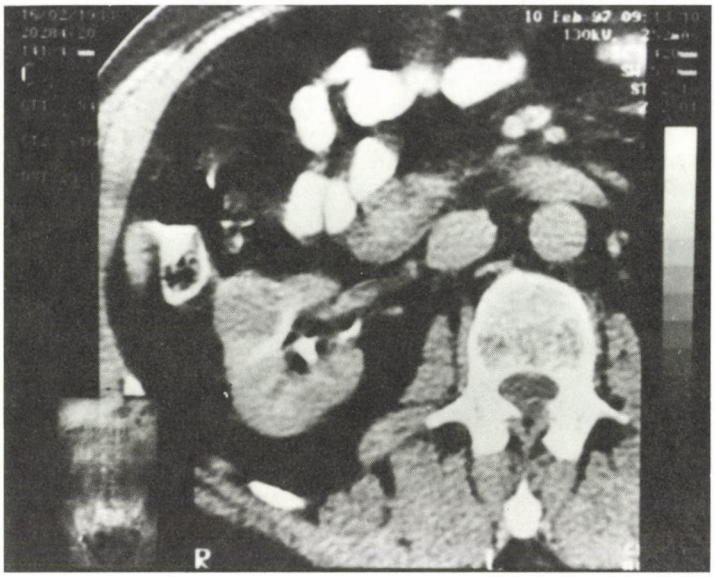

Fig. 3. CT: A 20 mm-sized solid formation is detectable in the lower part of the right kidney

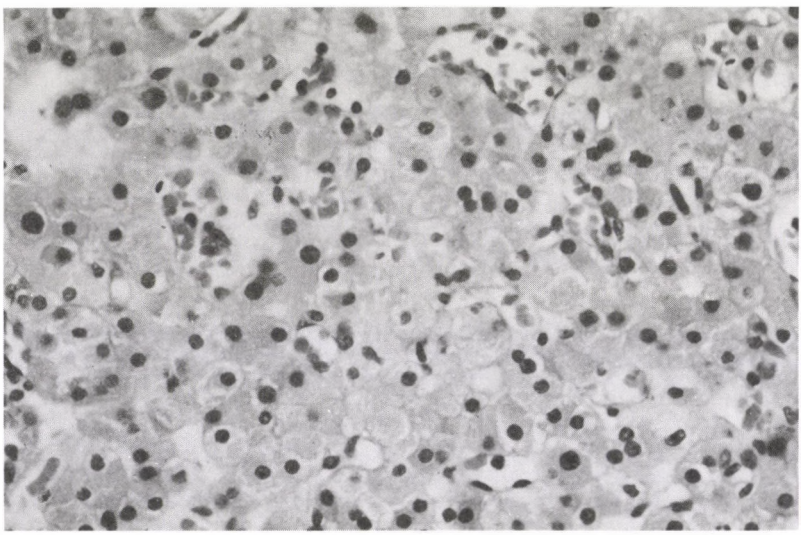

Fig. 4. A monomorph tumour cell field with eosinophilic cytoplasm is detectable. Capillaries are visible at places (HE, magnification × 200)

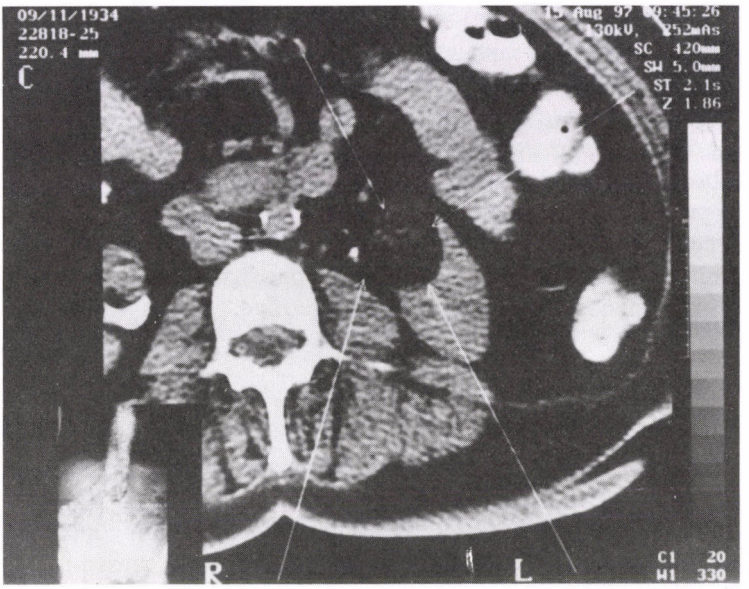

Fig. 5. CT: A solid formation, 35 × 40 mm in diameter can be seen in the middle third of the left kidney. No lymph nodes are observable

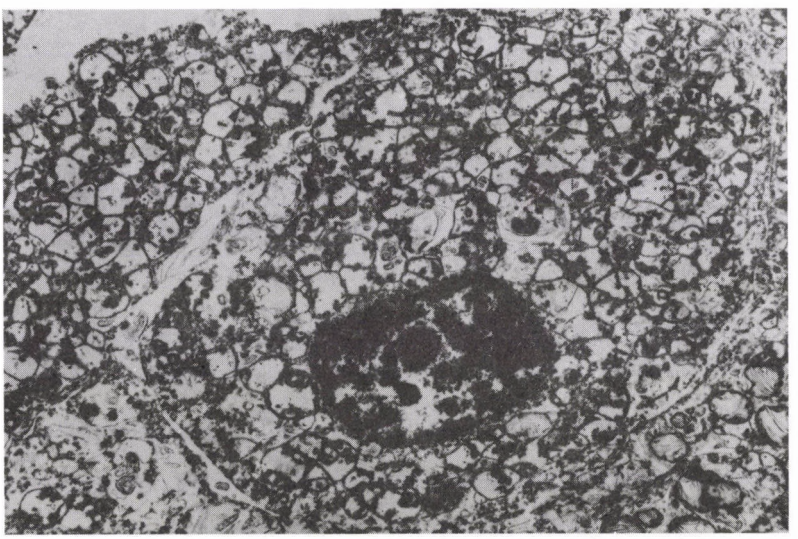

Fig. 6. Electronmicroscopic picture of a tumour cell. The cytoplasm is filled with mitochondria. Due to fixation problems the ultrastructure is less preserved, the mitochondrial cristae are only sporadically observable (magnification × 3800)

Her case history included a left-sided pyelotomy 25 years ago because of a stone. She had no other urological complaints.

The *ultrasound and CT exams* revealed a solid tumour 35 × 40 mm in diameter in the median third of the left kidney (Fig. 5).

Left-sided radical nephrectomy was performed, and on the 8th postoperative day the patient went home recovered.

Histology proved oncocytoma of tubular type.

In all three cases immunohistochemical and cytogenetic studies were also performed, as well as electronmicroscopic studies in one case (Fig. 6), by which means the light microscopic diagnosis of oncocytoma was verified.

Discussion

Oncocytomas occurring in the kidney are thought of as tumours of benign behaviour [10, 14, 15, 18].

The tumour cells are characterized by a high mitochondrium content [18–20]. According to electronmicroscopy, the cytoplasmic granulation is caused by swollen mitochondria [14–16].

Various authors give different ratios for the occurrence of oncocytomas, thus being 3.5–5.3–5.7% of the kidney tumours [8, 13, 17, 20].

They develop due to genetic disorder. Ultrasound, CT, MRI exams do not provide us with reliable possibilities for separation [14]. The earlier report of the so-called "wheel spoke" symptom is also questionable since the publication of Matmann, who has observed this alteration in kidney cancer as well [13, 17].

Preoperative kidney biopsies are also inconclusive, since oncocytoma islands may occur in kidney carcinomas, too [18].

It is most important to distinguish oncocytomas from chromophylic, eosinophilic kidney carcinomas because of their benign nature. Oncocytomas are well-circumscribed tumours; their macroscopic appearance being yellowish-brown, homogeneous, and mahogany in colour. The central part of a larger tumour may contain central scarring [9, 11, 12].

Kidney carcinomas with eosinophilic cells have infiltrating processes; haemorrhages, necroses can be seen on the cut surface [9, 12, 23, 24]. No mitoses are observable in oncocytomas microscopically, whereas large numbers can be seen in kidney carcinomas under the microscope. Reliable differential diagnosis can only be made by means of histological examination of the whole tumour [14]. In all our three cases the histological diagnosis was oncocytoma renis.

In all three cases the performed immunohistochemical studies showed the cytoplasms of the tumour cells to be only cytokeratin-positive; vimetine was not detectable in the cells (hypernephroma cells contain both cytokeratin and vimetine).

Electronmicroscopic studies were also carried out from the formalin-fixed material of our third case (Fig. 6). Furthermore, cytogenic studies were performed in all three cases at the Medical University of Pécs as well as at the Institute of Pathology, Univer-

sity of Heidelberg. Based on these, the diagnosis of oncocytoma was established in our case.

Even in case of a small tumour, the solution is its removal. Nephrectomy is recommended in case of a tumour bigger than 4 cm in size – and this is what performed in our first case [18, 20, 23]. Small tumours, located on the poles can easily be resected – which is what happened in our second case. Organ-preserving surgery may be a justified way to go in case of kidney carcinomas, too, if the tumour is smaller than 2.5 cm.

Between 1990 and 1997 a total of 150 nephrectomies were performed at our Department because of kidney carcinomas. From all these cases, three were oncocytomas.

In contrast to the literary data, we found the occurrence of this rare tumour to be around 1%. It is assumed that in the publications reporting an occurrence of 5–7%, one part of the tumours was not actually oncocytomas [6, 9, 10, 18, 21].

Our opinion of the above is that neither needle biopsy, nor intraoperative frozen-section histological studies are necessitated, in fact they are contra-indicated. These interventions might result in the dispersion of the tumour cells, at the same time the value of the study is uncertain and inconclusive.

Besides the high risk therefore, the diagnostic gain is negligible. According to our opinion, T1 tumours (2.5 cm in diameter) with intact opposite side kidneys can be resected by means of organ-preserving surgery.

According to the literature, routine adjuvant treatment is not necessary following surgery [12, 18]. Several authors recommend continuous follow-up of patients after surgery due to later metastasis-formation [19]. In our opinion, it is not impossible that these "malignant oncocytomas" were in fact chromophilic eosinophilic type kidney carcinomas.

Our first patient has been checked half yearly (laboratory studies, ultrasound, chest X-rays), and is currently symptom-free. Recurrence, later metastases have not been detected during the course of the control studies.

The diagnosis has also been confirmed by cytogenetic studies.

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PANCREAS, DIABETES MELLITUS AND PANCREATIC TRANSPLANTATION – A RETROSPECTIVE SURVEY

E. Adeghate[1] and T. Donáth[2]

[1]*Department of Human Anatomy, Faculty of Medicine and Health Sciences, United Arab Emirates University, P.O. Box 17666, Al Ain, United Arab Emirates and*
[2]*Department of Anatomy, Semmelweis University Medical School, H-1088 Budapest, Tűzoltó u. 58, Hungary*

The administration of exogenous insulin ameliorated the symptoms and increased the life expectancy of insulin dependent diabetic patients, but could not cure or prevent the devastating complications including retinopathy, nephropathy and angiopathy. It was recognised that despite insulin therapy, the severity and frequency of the degenerative late complications are still high in patients suffering from diabetes mellitus. The recognition of the increased frequency of and complications accompanying the disease has intensified efforts by scientists to find the form of pancreatic tissue to be transplanted and the suitable site in a bid to secure an insulin producing graft. This review presents an update in pancreatic organ and fragment transplantation. The history of the pancreas is also brought into limelight to show the long, hard and exciting path pancreas and diabetes mellitus have both gone through. An account is also given of experimental and clinical pancreatic whole organ/fragment transplantation including transplantation sites, the evaluation of the viability of pancreatic grafts and the complications of transplantation. Pancreatic islet transplantation is not discussed.

Introduction

Pancreas has been known to mankind since 300 B.C. Although several morphological and physiological experiments were performed on this organ before the 16th century, the association of pancreas with diabetes mellitus was not unveiled until 1889 when Joseph von Mering and Oscar Minkowski showed that extirpation of the pancreas of the dog caused diabetes mellitus. After the discovery of insulin by Banting and Best in 1922, exogenous insulin was made available. The administration of exogenous insulin ameliorated the symptoms and increased the life expectancy of insulin dependent diabetic patients, but could not cure or prevent the devastating complications including retinopathy, nephropathy, etc. It was recognised that despite insulin therapy, the severity and frequency of the degenerative late complications are still high in patients suffering from diabetes mellitus [14]. The recognition of the increased frequency of and complications accompanying the disease has intensified efforts by scientists to find the form of pancreatic tissue to be transplanted and the suitable site in a bid to secure an insulin producing graft. The present review updates pancreatic organ and fragment trans-

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plantation. The history of the pancreas is also brought into limelight, showing the long, hard and exciting path pancreas and diabetes mellitus have gone through. Experimental and clinical pancreatic whole organ/fragment transplantations are also discussed, including transplantation sites, the evaluation of the viability of pancreatic grafts and the complications associated with transplantation.

History of the pancreas

The first description of the organ pancreas was attributed to Herophilus of Chalcealon (circa 300 B.C.). Rufus Epheus (circa 100 A.D.) a well-known anatomist and physician named the organ pancreas (from the Greek word pan: all and kreas: flesh or meat) [39]. The pancreas literally, all flesh or meat, was likely named as such because of its soft, homogeneous consistency and the absence of cartilage or bone. Andreas Vesalius (1514–1564) who was born into a medical family in Brussels gave a spare description of the pancreas as a glandulous organ in the fifth volume of his book named the "Fabric of the human body". Vesalius knew nothing about the ductal system of the pancreas and attributed to pancreas a protective function for the stomach. The term pancreas did not appear in Vesalius description but an English translation gave the synonym "sweetbread". A later translation of the Latin anatomy book of Vesalius by the London astrologer Nicholas Culpepper in 1653 indicated that the lay term sweetbread was in common use at that time.

In 1642, Johann George Wirsung, the prosecutor to Vesalius in Padua described the main duct of the Human pancreas which bears his name. Up to this time, the significance of the pancreatic duct as a tool for physiological experiments was not realised. It was Regnier de Graaf (1641–1673) who demonstrated the importance of the pancreatic duct by its cannulation and by studies on the pancreatic juice [22]. Thomas Wharton (1610–1673) of York, a busy practitioner who found time to dissect, was the first to do a systemic study of the glands of the body. He noted the artificial similarity between the pancreas and the submandibular gland. Soemmering (1775–1830) a German anatomist was the first German author to employ the vernacular term Bauchspeicheldruse (abdominal salivary gland) in scientific literature. This terminology is still in use today in Germany and many countries in Europe. In the 18th century, Albert von Haller (1708–1777) a physiologist, observed that the pancreatic duct entered the duodenum in conjunction with the comon bile duct. In 1742 Santorini, an anatomist in Venice demonstrated the accessory pancreatic duct which bears his name.

Towards the end of the 19th century scientists unveiled the microscopic structure of the pancreas. This achievement was attributed to Paul Langerhans, who in 1869 while still a medical student, published a thesis entitled "Contributions to the microscopic anatomy of the pancreas". He was the first to describe the structure of the islet which Lauguesse (a French investigator) named the islets of Langerhans in 1893 (Table 1).

Table 1
Discoverers of the pancreas

Discoverer	Lived	Contribution
Chalcealon	circa 300 B.C.	Described the pancreas
Rufus Epheus	circa 100 A.D.	Named the organ pancreas from the Greek word (pan = all and kreas = flesh or meat)
Andreas Vesalius	1514–1564	Described the pancreas in his book the "Fabric of the Human Body"
Johann G. Wirsung	1600–1643	First to describe the main duct of the pancreas
Regnier de Graaf	1641–1673	Demonstrated the importance of the pancreatic duct
Thomas Wharton	1610–1673	Marked out the pancreas among other glands of the body
G. Santorini	1681–1737	Demonstrated the accessory pancreatic duct
Albert von Haller	1708–1777	Noted that the pancreatic duct entered the duodenum in conjunction with the common bille duct
S. Th. Soemmering	1755–1850	Named the pancreas the abdominal salivary gland
Paul Langerhans	1847–1888	Unveiled the microscopic structure of the pancreatic islets

Pancreas and diabetes mellitus

John Conrad Brunner, Swiss physician and anatomist, stated in 1682 that dogs could sustain pancreatectomy from three months to a year. No accurate estimation was possible of how much pancreas was actually excised. Brunner noticed that his animals suffered from polyuria, polydypsia and bulimia, he did not observe that the urine contained sugar and did not associate these symptoms with diabetes.

The association of pancreas with diabetes mellitus was first demonstrated by Joseph von Mering and Oscar Minkowski in 1889. They showed that extirpation of the pancreas of the dog caused diabetes. The experiment was the result of a debate between the two as to whether a dog could survive if the pancreas was totally removed. Their supervisor fold them not to argue but to try the experiment. The appearance of diabetes mellitus in the dog after total pancreatectomy was epochal [24].

These investigations opened way for a dramatic discovery in 1922. Frederic Banting (1891–1944), an orthopaedic surgeon who was experimentally inclined, – after reading an article by Dr. Moses Barron of the University of Minnesota on the relationship of pancreatic calculi to islet cell damage in the October, 1920 issue of *Surgery, Gynecology and Obstetrics* and without knowing that a previous attempt to extract the hormonal substance from the islet had failed – had gone to the physiology laboratory headed by Prof. McLeod at the University of Toronto and asked for space to carry out his experiments. A medical student Charles Best (1899–1978) was assigned to work with him. They obtained isletin (insulin) from the Ringer's solution of the pancreas of a dog that had its pancreatic duct ligated for 10 weeks previously. They injected a syringe full of

Table 2
Investigators who associated pancreas with diabetes mellitus

Investigator	Lived	Contribution
John C. Brunner	1653–1727	Observed that dogs could sustain pancreatectomy for more than three months in 1682
Joseph von Mering and Oscar Minkowski	1849–1908 1858–1931	First to associate pancreas to diabetes mellitus in 1889
Frederic Banting and Charles Best	1891–1944 1899–1978	Discovered insulin in 1922

isletin (insulin) into a dog with diabetic coma. The dog soon recovered and began to walk. In a matter of weeks the discovery was recognized throughout the world [92] (Table 2).

Pancreatic transplantation

After the association of pancreas with diabetes mellitus, attempts were constantly made to use pancreatic transplantation as a form of therapy. Pancreatic transplantation has a long history and can be divided into experimental and human transplantation.

Experimental transplantation

Minkowski [73] was the first to try pancreatic transplantation as far back as in 1892, in a bid to ameliorate the symptoms of diabetes mellitus. He transplanted pancreas into the subcutaneous region of the abdominal wall. The pioneer work on pancreatic transplantation could be divided into two main categories according to whether the experiments were short-term or long-term in type. In the successful short-term transplantation experiments of Gayett and Guillaume [41, 42] and Houssay et al. [52] pancreatic endocrine secretion was introduced into the carotido-jugular circulation by vascular anastomosis. These experiments were terminated after 6–8 hours and only Bottin [19] reported the survival of a dog 7 days after such a procedure. The long-term transplantation experiments could further be divided into two main groups, namely, pedicle grafting and pancreatic fragment transplantation techniques. Using the pedicle grafting technique, Banting and Gairn [16] and Simard [107] made successful subcutaneous grafts into the abdominal wall and mammary regions while Voronoff and Didry [132] and Tripodi and Sherwin [125] inserted pancreatic grafts into the wall of the intestine and stomach, respectively. The pedicle grafting technique was also applied by Pratt and Murphy [95] in an attempt to establish a functional pancreatic graft in the spleen. Using the pancreatic fragment technique, Browning and Resnik [21], Coupland [28], Adeghate and Donath [2, 3, 7, 10] and Donath and Adeghate [31, 32] reported the sur-

vival and growth of pancreatic fragments transplanted into the anterior eye-chamber of rats. Pancreatic fragments were also transplanted into the liver through the portal vein [77, 100] or into the renal subcapsular region in laboratory animals [137].

More recently, due to improvements in *organ procurement, preservation* and *surgical techniques,* whole organ [44, 47, 48, 55, 57, 82, 86, 101] or segmental [30, 56] transplantations have been widely employed to cure experimental diabetes in animals or to formulate a model for transplantation. For whole organ transplantation, pancreatico-duodenal grafts [82] are grafted into the renal, iliac or the splenic vessels of the host [48, 101]. The pancreatic ducts are either drained into the intestine [101] or into the urinary bladder [47, 48, 86, 101], the latter being the most common site of drainage of pancreatic secretion. In pancreatic fragment transplantation, pancreatic tissue is taken and implanted into different sites including the anterior eye chamber, kidney subcapsular space, peritoneal cavity, wall of the intestine, spleen, liver, testis, intramuscular area, fatty pads, spinal cord, or the brain parenchyma and ventricles (see Table 3 and transplantation sites).

Transplantation sites in experimental animals

Many different sites have been used for pancreatic transplantation in experimental animals especially in rodents, miniature pigs and dogs.

Subcutaneous region

This site was first used by Minkowski [73] and later by Banting and Gairn [16]. They introduced pancreas into the subcutaneous region of the anterior abdominal wall.

Table 3
Some contributors to pancreatic fragment transplantation

Author	Contribution
Oscar Minkowski [73]	First to transplant pancreas in a bid to ameliorate the symptoms of diabetes mellitus
Gayett and Guillaume [41, 42] Houssay et al. [52] Bottin [19]	Introduced pancreatic endocrine secretion into the carotido-jugular circulation
Pratt and Murphy [95]	Transplanted pancreas into the spleen
Voronoff and Didry [132] Tripodi and Sherwin [125]	Inserted pancreatic grafts into the wall of the intestine and stomach
Banting and Gairn [16] Simard [107]	Performed subcutaneous pancreatic transplantation
Browning and Resnik [21] Coupland [28] Adeghate and Donath [2, 3, 7, 10] Donath and Adeghate [31, 32]	Transplanted pancreas into the anterior eye chamber

The union between the normal and transplanted tissue was then severed at a later stage. Kramp and Renold [63] and Tuch et al. [126] successfully used this site to normalize blood sugar level in diabetic animals by transplanting pancreatic tissue into the axillary and mammary subcutaneous regions.

Blood vessels

Gayett and Guillaume [41, 42] and Houssay et al. [52] introduced whole pancreatic secretion into the carotido-jugular circulation by vascular anastomosis. The animals sur-vived 6–8 hours, but the sugar level was normalised.

The spleen

The proximity of the pancreas to the spleen might have wooed many investigators to transplant the pancreas into the spleen. Pratt and Murphy [95] and Voronoff and Didry [132] transplanted pancreas into the spleen but with little success in the treatment of diabetes mellitus.

The intestinal wall

This site, like the spleen is close to the pancreas and has been tried as a transplantation site by Voronoff and Didry [132] and Tripodi and Sherwin [125].

Skeletal muscle

Valente et al. [131] reported cases of pancreatic transplantation into the rectus abdominis muscle. The insulin requirement of the diabetic animal was decreased because of graft function.

The testis

The survival of pancreatic allografts in the testis of rodents was reported by Gonet and Renold [43].

Renal subcapsular space

This is one of the most common sites of pancreatic transplantation in animals. Brown et al. [20] were the first to transplant pancreas into the renal subcapsular region. Among others, McEnvoy and Hegre [70, 71] have successfully ameliorated experimental diabetes in animals by transplanting pancreatic tissue fragments into this site.

Liver

Pancreatic tissue fragments have been transplanted with success into the liver through the portal vein [76].

Table 4
Pioneers of human pancreatic transplantation

Investigator	Contribution
Kelly et al. [59]	Performed segmental transplantation in human beings
Lillehei et al. [65]	Adopted a technique for whole pancreatic transplantation in homo sapiens

Anterior eye chamber

The anterior eye chamber of rats has long been used as an experimental site to study different biological mechanisms because of the transparency of the cornea which enables microscopic changes to be seen, the rich vasculature and the innervation [2, 3, 7, 10], and because it is an immunologically privileged site [97, 135]. Browning and Resnik [21], Hultquist [54], Coupland [28] and Adeghate and Donath [1, 4, 8, 32] have also used this site to investigate the survival, growth and innervation of pieces of adult pancreatic tissue transplants. This site also makes provision for the escape of the exocrine secretion of the gland which Allen [13] and Simard [107] purported as important for the survival of pancreatic tissue transplants.

Human pancreatic transplantation

Since the early 1970s, diabetes mellitus has become one of the most frequent complications accompanying chronic disease with high morbidity and mortality. The increase in number of diabetic patients, the proliferation of severe complications (macro- and microangiopathy, neuropathy, nephropathy retinopathy, etc.) [14, 133] and the availability of modern equipments have motivated scientists to find new methods in their bid to achieve an insulin-secreting graft. Simultaneous kidney and pancreas transplantation is the accepted method of treatment in a selected group of type I diabetes mellitus with end-stage renal disease [114]. Human pancreatic transplantation can be divided into two groups, segmental and whole organ (Table 4).

Segmental pancreatic transplantation

This method of transplantation is employed in certain diseases of the pancreas that involve the destruction of pancreatic parenchyma, for example, carcinoma and pancreatitis. The procedure has been used to cure alcoholic and idiopathic pancreatitis associated with severe pain [120–122]. The grafts were usually autografts which are transplanted into the iliac fossa [29, 121] with the vessels tied either to the splenic or the iliac vessels. This is usually accompanied by pancreaticojejunostomy [29] or pancreaticocystostomy for draining pancreatic secretion. The method is not the common procedure used in the surgical treatment of type I diabetes mellitus.

Whole organ transplantation

The first systemic whole organ trial of pancreatic transplantation in human subjects began in December 1966 when Kelly et al. [59] performed a combined renal and segmental pancreatic transplantation. The body and the tail of the pancreas were transplanted retroperitoneally into the left iliac fossa of a 28-year-old woman who had diabetes for 19 years. The patient tolerated insulin withdrawal for 6 days before increasing blood glucose level required reinstitution of insulin therapy. In 1967, Lillehei et al. [65] adopted a technique of whole pancreatic transplantation in human subjects. Since then, numerous pancreas transplants has been performed [23, 45, 46, 78, 91, 99, 106, 111–113, 116, 118, 123].

From December 1966 to December 1997, more than 700 pancreas transplants were reported to the International Pancreas Registry located at the University of Minnesota, Minnesota, U.S.A. These include primary retransplants. Approximately half of the cases were reported from Europe and half from North America. Only a small fraction (2%) of the cases were from other continents [117].

These pancreas transplants were performed [99] either alone or in combination with kidney tranplants. Improvement in results has been achieved because of progress in procurement, preservation, transportation and transplantation techniques [81]. It must be realised, however, that rigorous immunosuppressive regimens including cyclosporin, prednisolone and azathioprine treatment were needed to attain these results. The general effects of these immunosuppressive agents are not negligible.

Procurement of pancreatic grafts

The pancreas is usually retrieved from a human subject who has suffered brain death resulting usually from a motor vehicle accident. The organ is then flushed *in situ* with the preserving solution, the most commonly used solutions are the Euro-Collins solution and the University of Wisconsin solution or silica-gel filtered plasma [85]. The exact time an organ could be removed from a "living" human being is still an issue of controversy. Unlike kidney grafts, pancreatic grafts must be removed relatively immediately after brain death because of possible cell and tissue autolysis by pancreatic digestive enzymes.

Pancreatic whole organ preservation in clinical transplantation

The grafts are usually reflushed in the preservative solution before cold storage in the same solution prior to transplantation. The preservative solutions employed in clinical pancreatic transplantation include, the Euro-Collins solution, University of Wisconsin (UW) solution (Viaspan, DuPont Phamaceuticals) and silica-gel filtered solution [75, 85, 119, 140].

The use of some other preservative solutions like Lactoboinate solution [130] and Histidine-tryptophan-ketoglutarate [129] are still in experimental stages. The most com-monly used preservatives are, however, the varieties of the Euro-Collins and UW solutions.

Transportation of retrieved or preserved pancreas

Pancreas transplantations do not only require surgeons and paramedical personnel to be on the alert to retrieve and preserve pancreatic grafts, when available. Effective transportation of these grafts also plays a very important role in the determination of the rate of survival of these grafts in the host. For example, better survival rate and lower transportation costs have been achieved when commercial airline transportation is used instead of chartered flight [90].

Transplantation techniques

Pancreatic organs perfused *in situ* and retrieved from brain-dead cadaveric donors are transplanted into the host by vascular anastomosis to either the iliac- [18, 36], splenic- [36], renal-, or the mesenteric vessels. The pancreatic duct is subsequently drained into one of the segments of the small intestine [127, 128] or into the urinary bladder [25, 51, 104, 110] to allow the passage of pancreatic secretion. The most common site of vascular anastomosis is, however, the iliac vessels. Because of the proximity of the urinary bladder to the iliac vessels, the urinary bladder is now the preferred site of pancreatic duct drainage.

Metabolic effects of pancreatic transplantation

Insulin dependent diabetic patients have been able to become normoglycaemic for up to seven years after transplantation [27, 40, 50, 74], with a halt in the progression of diabetic neuropathy [26, 78, 79, 83, 84, 87, 89, 115]. The Glycohaemoglobin levels also normalize soon after transplantation [109] and there is a decrease in the serum content of triglycerides after pancreatic transplantation [53, 64]. There is much controversy as to how effective pancreatic transplantation is in curing or reversing diabetic retinopathy. According to Scheider et al. [102], Bandello et al. [15] and Zech et al. [139] pancreatic transplantation is not effective on diabetic retinopathy. Some investigators [62], however, observed that the course of diabetic retinopathy is influenced positively by successful transplantation.

Evaluation of the viability of pancreatic grafts

A number of methods have been employed to test the function and survival of pancreatic transplants (Table 5). These methods include the followings:

1. Metabolic function

The most common parameters investigated include the plasma/serum and urinary insulin [57] and C-peptide levels, blood and urine glucose values [120], glucose tolerance test and glycosylated haemoglobin values.

Table 5
Methods used in the evaluation of the viability of pancreatic grafts

Method	Parameters evaluated
Metabolic	plasma/serum insulin C-peptide blood and urine glucose glucose and tolerance test glycosylated haemoglobin urine amylase
Immunological	phagocytosis antiinsular antibody insulin antibody pancreas specific protein C complex accumulation
Radiological	radionucleide technique ultrasonography magnetic resonance imaging computer tomography
Clinical	body weight decrease in insulin requirement polydypsia polyuria bulimia
Reversal of complication	decrease in diabetic cardiomyopathy, polyneuropathy and proteinuria, thickness of the renal glomerular basement membrane
Morphology	intactness of islet cells (using enzyme and immunohistochemical techniques and light and electron microscopy)

2. Enzymes

Serum anodal trypsinogen has been shown to correlate well with rejection occurring in pancreatic allografts [93]. Serum anodal trypsinogen is said to increase during pancreatic graft rejection. An increase in the serum levels of human pancreatic elastase I and an increase in urine amylase levels have also been shown to correlate well with exocrine graft damage [67].

3. Immunological parameters

The immunological values usually investigated are phagocytosis, antiinsular antibody, and insulin antibody. A new serum marker "pancreas specific protein" for graft rejection has been demonstrated by Fernstad et al. [37]. This protein is said to be elevated in graft rejection. The monitoring of plasma soluble interleukin-2-receptor (SIL-2R) concentrations has been proposed in organ transplantation to detect early manifestations of rejection. Increase in SIL-2R values predicts impending graft rejection or cytomegalovirus disease [61, 94, 124].

4. Radiological methods

Radionucleid, ultrasonography, computer tomography, Doppler flow and magnetic resonance imaging studies have been used by many investigators [35, 38, 49, 58, 72, 108, 136, 138] to test graft survival.

5. Clinical

The changes in body weight, decrease in insulin requirement, polydypsia, polyuria and bulimia are taken into account in assessing pancreatic graft function.

6. Reversal of complications

Decrease in diabetic cardiomyopathy, as well as proteinuria from patients suffering from diabetic nephropathy, polyneuropathy, glomerular basement membrane thickening and Complement 3 accumulation is usually measured in evaluating graft function.

7. Morphology

Before the 1960s the histological evaluation of pancreatic transplants was not common to come by. It was later in the 1960s that Coupland [28] performed a light microscopical investigation of the pancreatic tissue transplanted into the anterior eye chamber of rats. Afterwards Hultquist [54], McEnvoy and Hegre [70, 71], and Shah et al. [105], among others, performed morphological and immunohistochemical investigations on duct-ligated pancreatic tissue transplanted into the anterior eye chamber, renal subcapsular region and into the spleen, respectively. Most of these studies were only at the light microscopical level. It was only in the late 1980s that detailed ultrastructural work was done on transplanted pancreatic tissue [3, 7, 10, 31, 32, 68]. The endocrine cells and tubules of pancreatic tissue transplants were reported to survive and have intact light and electron microscopical structures after transplantation into the anterior eye chamber of rats [3, 7, 10, 31, 32, 68].

Innervation

Intrinsic nerves are undoubtedly very important in the regulation of hormone secretion in the pancreas. More so than the morphology the innervation of pancreatic tissue transplants has also been a neglected area. Detailed description of the surviving intrinsic nerves at both light and ultrastructural levels began in the late 1980s [5, 6, 9, 11, 12, 69]. The intrinsic nerves of the surviving pancreatic tissue transplants have been shown to be able to synthesize neurotransmitters necessary for pancreatic function [5, 6, 9, 11, 12].

Prevention of rejection

Immunosuppressive agents including antilymphatic serum, azathioprine and cyclosporin are widely administered to the host. Some others, however, indicated that immu-

nosuppression altered the Major Histocompatibility Complex (MHC) expression and prolonged host survival. Early graft thrombosis and rejection of the graft are purported to be the major causes of graft failure in pancreatic transplantation. Inclusion of the spleen in the pancreatic graft has been seen as a possible solution to both complications but severe graft failure has led investigators to abandon this technique. Instead, splenic, lymphoid tissue and peripheral lymphocyte irradiation by ultraviolet light have been shown to decrease the rate of graft rejection after pancreatic transplantation [134].

Complications and problems associated with pancreatic transplantation

The most common problems associated with pancreas transplantation include venous thrombosis [45, 47] infections of the respiratory system with cytomegalo-virus and pneumonia-causing microbes [34, 60]. Infections of the urinary bladder have become more common because pancreas secretion is frequently drained into the bladder and trypsin, a product of this secretion has been shown to promote infection [104]. Surgical complications like fistula [18], pancreas secretion leakage [88], carpal tunnel syndrome [80] and pseudoaneurysm of the graft were frequently observed in patients hosting pancreatic grafts. Dehydration and acidosis [17], haematuria [98], post-transplantation pancreatitis [66], recurrence of autoimmune diseases [96] and cardiovascular diseases are regular features following pancreatic transplantation (Table 6).

Table 6
Complications of pancreatic transplantation

Infections
– viral
– bacterial
Haematuria
Venous thrombosis
Post-transplantation pancreatitis
Leakage of exocrine secretion
Fistula
Dehydration and acidosis
Carpal tunnel syndrome
Recurrence of autoimmune diseases

Conclusion

The long history of and the enormous of investigations performed on the pancreas and pancreatic transplantation all go to show a how important and how crucial this area of science is to us. Some of the fruits of the labour put into the field of pancreatic transplantation is that insulin-dependent diabetic patients can now live without exogenous insulin for up to 7 years after pancreatic transplantation. Even though medical science has made tremendous achievements in the sphere of pancreatic diseases and pancreatic transplantation, the complete therapeutic cure and abolition and/or reversal of the complications of diabetes mellitus have not been completely abolished yet, nevertheless, there is hope of complete recovery if transplantation is done quickly before the onset of these fatal complications.

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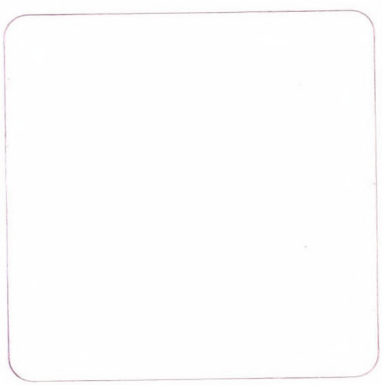

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FUSIONAL ANOMALIES OF THE TESTIS AND EPIDIDYMIS

M. Merksz

Department of Urological Surgery, Heim Pál Children's Hospital, H-1089 Budapest, Üllői út 86, Hungary

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Earlier, the cause of infertility in undescended testis (UT) had been widely accepted as a consequence of the higher temperature of the inguinal/abdominal region. Observations made in the past two decades, however, gave new evidences. The most important of these is that UT is often associated with the fusional anomalies (FA) of the testis and epididymis. FA is the consequence of pathological intrauterine hormonal processes and many authors believe FA to be the primary cause for infertility in UT. Since 80% of UT cases are of endocrine origin, it would be suspected that the very same factors are responsible for both UT and FA. FA and other anomalies of the epididymis often occur in testicular torsion (TT) as well. It is remarkable that infertility could follow the unilateral forms of UT and TT despite the presence of a "healthy" contralateral gonad. In both entities contralateral FA (probably associated with testicular dysgenesis) is suspected. These observations could influence the primary surgical treatment of patients with UT and TT, as well as the mode of further management of these cases.

Introduction

It is well known that higher than optimal temperature has a damaging effect on the testicular germ cells, as is also the fact that men whose testis is not in the scrotum are either infertile or have impaired fertility. This is because if the testis is not in the scrotum, the 2–3 °C cooler-scrotal-environment cannot develop, needed to ensure the optimal 34–35 °C for spermatogenesis. This heat effect has been generally (and by many authors exclusively) held responsible for the development of infertility in males with undescended testis. According to this so-called thermal theory, the noxa has a damaging effect on the testis not only in the case of grown men whose testes have differentiated tubulous epithelia, but also in case of young boys who are before puberty. At first, this heat effect was thought to exert its effect only around the age of puberty, then the age was believed to be around six, while nowadays this higher temperature is contemplated to cause degenerative alterations on the tubulous epithelium at the age of two- and even before the age of one according to certain authors. The theory, however, holds the alteration to be preventable if the scrotal position of the testis is ensured in time. Accordingly, the optimal time point for the surgical placement of the testis into the scrotum, i.e.

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Table 1
Occurrence of the fusional anomalies (review of the literature

Authors	No. of gonads	Rate of fusional anomalies
Marshall and Shermata	42	15 (35.7%)
Mininberg and Schlossberg	70	46 (65.7%)
Heath et al.	132	42 (31.8%)
Gill et al.	187	81 (43.3%)
Koff and Scaletscky	82	65 (79.3%)
Hazebroek et al.	181	88 (48.6%)
Johansen	148	59 (39.9%)
Rumlova	242	108 (44.6%)
Caterino et al.	750	377 (50.3%)
Herzog and Hadziselimovic	730	46 (6.3%)
Merksz and Tóth	1171	277 (23.6%)

orchiopexy has also been put to an earlier age. Even today the main indication of orchiopexy is the prevention of the thermal damage.

Many aspects of the thermal theory, however, show contradiction with the occurrence of infertility in the various groups of patients having undescended testes. It is known that part of the group of men with unilateral undescended testis are infertile, despite the fact that on the basis of the above theory – since the testis in the scrotum was not subjected to heat damage – they should all have intact fertility [41, 43]. Orchiopexy performed in infants and small children may also result several cases of infertility in the young age despite well-performed surgery, whereas what would be expected is for the early surgical procedure to successfully "prevent" the development of thermal damage [34, 53]. There are fertile cases also among men who have bilateral undescended testis not operated on [8]. According to the studies of Woodhead et al., those who in childhood had their unilateral undescended testis removed showed the same ratio of infertility as those who did not have their testis removed [55]. On the basis of this finding it became evident that other factors are also to be sought after in case of undescended testis (UT), regarding the cause of the associated infertility. In the late 1970s an apparently frequent detection among patients operated on because of UT was the fusional disturbance between the testis and epididymis. Based on this finding – following quite a number of publications (Table 1) and firstly built on the severe degree of total testis-epididymis dissociation – several authors raised the assumption that this anomaly should also be reckoned with in regard to the pathological factors causing infertility. These anomalies have been divided into more than one group (Figs 1 and 2) [20, 26].

Testicular torsion and undescended testis raise a number of similar problems: 1. In both entities, one can detect a considerable degree of growth disturbance of the epididymis as well as the fusional anomalies of the testis and epididymis. 2. In both forms of appearances – even if the form is unilateral – the vast majority of the patients become

infertile, despite the contralateral testis being seemingly intact. Mostly anatomical-morphological (growth!) disturbances are denoted among the factors leading to the development of TT. The most known of these are the lack of descent; non-closing vaginal process; lack of the gubernaculum; the narrow mesorchium; the dissociation of the testis and epididymis. The cause of the new-born – extravaginal – torsion is generally believed to be the lack of gubernaculum, or its being too long, furthermore, the lack of adhesion between the inner sheath of the scrotum and the lining membrane of the testis. The growth anomaly which is mostly held as the cause of torsion in adolescents and adults is when the tunica vaginalis covers too much of the testicular surface, letting the testis move too freely within the testicular lining membrane ("bell-clapper anomaly") [25, 46, 48]. There is not enough data, however, on the incidence of growth anomalies of the epididymis and testicular adnexum in TT cases, and on whether these anomalies can have causal role in the development of the torsion.

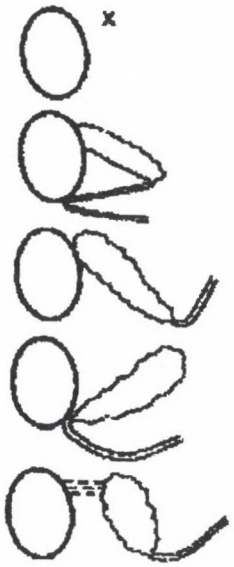

Fig. 1. Testicular-epididymal fusion abnormality types according to Heath

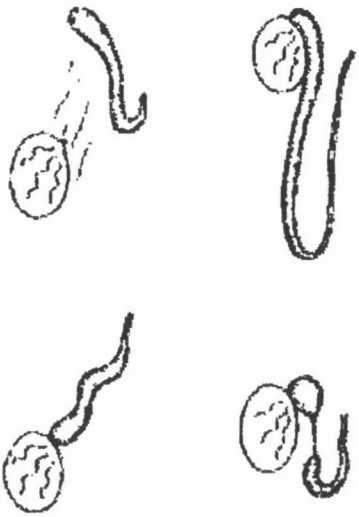

Fig. 2. Testicular-epididymal fusion abnormality types according to Johansen

Patients and Methods

Undescendes testis

A high number of operations are performed due to undescended on non-palpable testis (an annual amount of 110–120 surgeries) at the Department of Urological Surgery of the Heim Pál Children's Hospital. During the course of these surgeries – including orchiopexies – the possibility arises to observe those anomalies which could provide us with data in respect to both the lack of testicular descent and later fertility. The conditions of the testes and adnexes in these children were observed according to the following viewpoints, registering the observations after each surgery on a data sheet as well as in the surgical records: 1. condition of the testis prior to surgery, 2. the intact or not intact state of the fusion between testis and epididymis, 3. other malformations of the epididymis, 4. size of the testis, 5. turgor of the testis, 6. surgical possibilities and 7. state of the testis after surgery. A further point related to control studies was: 8. observation of postoperative results.

These examinations were performed in a total of 1195 surgeries in the case of 1071 boys. Bilateral surgery was necessitated in the case of 124 patients. The children were between the age of 1 to 15 years. Over 50% of the surgeries were carried out in boys under the age of 6. (In our opinion, the optimal time for surgery is around the age of 2, the older children had their operations at the time of their hospitalization, or following non-adequately effective hormone therapy.)

Testicular torsion

The newborns and older children treated at our Department because of testicular torsion were examined with the following purposes: 1. whether any fusional anomalies of

Table 2
Number of operations performed for undescended testis

Location of the testis		No. of patients	No. of operation
affected side	contralateral		
Abdominal	abdominal	6	12
Abdominal	inguinal	16	32
Abdominal	scrotal	80	80
Inguinal	inguinal	101	202
Inguinal	scrotal	845	845
Aplasia	aplasia	1	2
Aplasia	scrotal	16	16
Agenesia	scrotal	6	6
	Total	1071	1195

Table 3
Number of the abnormalities examined in undescended testis

Undescended testis	(n = 1171)	100.0%
Fusional anomalies	277	23.6%
Small testis	474	40.4%
(hypoplasia testis)	63	5.3%
Reduced testicular turgor	243	20.7%

the epididymis, as well as the testis and epididymis could be detected causing susceptibility to torsion, and respectively, 2. which could possibly present a basis for the origin of later infertility.

The examinations were carried out in a number of 24 children who were operated on due to testicular torsion. Unilateral testicular torsion was present in 22 of the cases, with bilateral testicular torsion in 2 patients. Supravaginal testicular torsion was detected in 5 infants, among whom this was observable simultaneously on both sides in 2 cases. In 19 children the testicular torsion was of the adult type. The age of the patients was between 5 days and weeks in case of supravaginal testicular torsion and between 1 and 18 years in case of infravaginal torsion, with the exception of two younger (1- and 4-year-old boys), the rest were between the age of 13 and 18 years. A total of 26 primary surgical procedures were performed on distorted testes; 20 distortions and 6 castrations. Later on, there were 4 further cases of castration due to testicular atrophy. The contralateral testis needed to be operated on in 13 cases. Testicular fixation was necessitated in 12 cases, while one patient was subjected to orchiopexy because of undescended testis years before the torsion. During the course of all surgical procedures, special note was taken of the followings: location and degree of torsion, state of the epididymis, intact or abnormal fusion of the testis and epididymis, as well as any presence of anomalies on the testicular adnexes or in the environs of the testis.

Results

Undescended testis

1. Location of the testis prior to surgery

A total of 132 surgical explorations were carried out in 125 children because of non-palpable testis (7 bilateral cases). The number of operations performed because of the inguinal location of the testis was 1063. In 102 children the testis was found in the abdominal cavity (Table 2), in 6 cases on both sides. In 16 cases the contralateral testis revealed inguinal palpation, while in 80 patients its was palpable in the scrotum. In case of 22 patients no testis or epididymis was found on one side – in 1 patient on either sides –

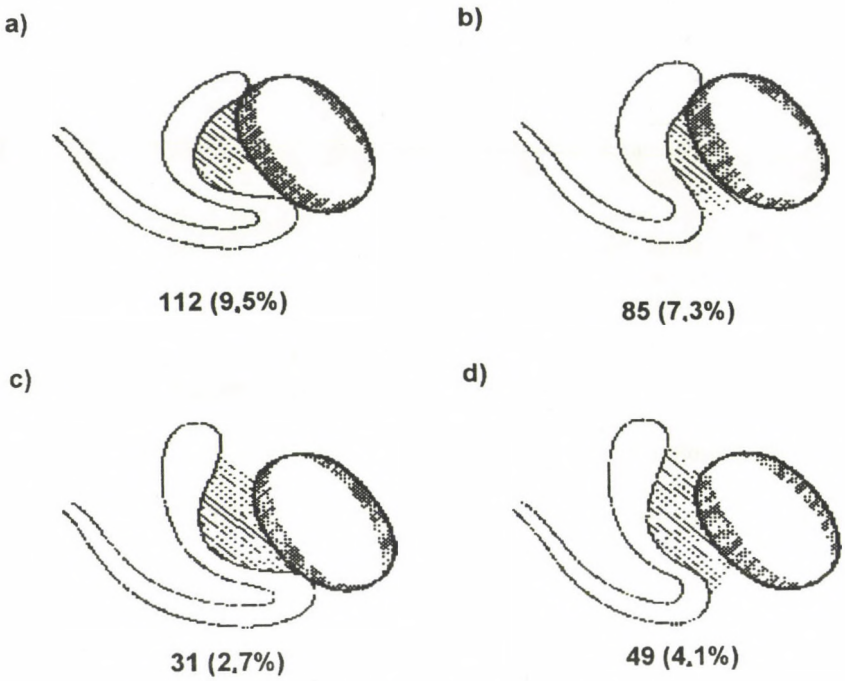

Fig. 3. Testicular-epididymal fusion abnormality types in our patients

however, in 16 cases a formation imposing a Wolff-tube origin was found in the inguinal canal, the shape resembling a deferent duct or an epididymis.

2., 3. Relationship between the testis and epididymis. Other malformations of the epididymis

The relationship between the testis and epididymis was considered to be adequate if at least two-thirds of the epididymis showed adherence to the testis (from the topmost part of the epididymis). Conditions other than this were observed during the course of examining 277 testes (23.6%, Table 3). Anomalies caused by fusional disturbances of the testis and epididymis were detectable in milder and severer forms (Fig. 3):

a) The epididymis located farther from the testis, with contact only by head and tail parts: in 112 cases (9.5%).

b) The epididymis having contact only with the head part: in 85 cases: 7.3%).

c) No contact with the head part, only with the tail part: in 31 cases (2.7%).

d) As the severest form of abnormality, when there was seemingly no contact at all between the testis and the epididymis: in 49 cases (4.1%).

There were 38 cases where the epididymis stood alone, having no contact with the testis. In a further 10 cases the testis was found in the abdominal cavity, the epididymis

in the inguinal canal, with a localization of the head part in the height of the inner, and the tail part in the height of the outer inguinal ring ("elongated epididymis"; "extended tail and vas"). In one patient there was a complete lack of the epididymis, with the thin and rudimentary deferent duct turning back near the testis towards the abdominal cavity in the shape of a loop. In this case, renal agenesis was proved in the same sided kidney.

4., 5. The size and turgor of the testis

Upon examining the size of the testis, a smaller size was detectable in 474 cases (40.4%) (Table 3). Among these, 63 (5.3%) were found to be rather small – the size of a rice grain, or a lentil. Decreased testicular turgor, floppy consistency was encountered during the course of 243 operations (20.7%). Upon studying those testes where the epididymis evidenced abnormal adherence, the testis was found to be of smaller size in 72.0% of the cases.

The above-observed and registered abnormalities occurred with the following frequency in the abdominal- and bilateral-retained testes:

Testes of abdominal location

During the course of 108 operations performed because of abdominal retained testes, fusional anomalies of the testis and epididymis were observed in 55.5%, smaller testes in 71.3%, and decreased testicular turgor in 38.0% of the cases (Table 4). All three abnormal conditions occurred in a significantly higher proportion as compared to the testes cases of non-abdominal location (using the chi-square probe $p < 0.0001$, $p < 0.001$, $p < 0.01$, respectively).

Bilateral testicular retention

Because of this anomaly, 248 surgeries were performed in a number of 124 children. Testes were found in a total of 246 operations. Among these, fusional anomalies of the testis and epididymis were found to occur in 23.8%, the smaller size of the testis in 41.1%, and decreased testicular turgor in 21.1% of the cases (Table 5). The observed pathological conditions showed no significant differences when compared with those found in the unilateral undescended testis cases (using the chi-square probe).

Table 4
Number of the abnormalities examined in abdominal testes

Abdominal testes	(n = 108)	100.0%
Fusional anomalies	60	55.5%
Small testis	77	71.3%
Reduced testicular turgor	41	38.0%

Table 5
Number of the abnormalities examined in bilateral undescended testes

Bilateral undescended testes	(n = 246)	100.0%
Fusional anomalies	59	23.8%
Small testis	101	41.1%
Reduced testicular turgor	52	21.1%

The most important finding was that in children born with undescended testes, *disturbances in the relationship between the testis and epididymis* and the defective development of this relationship, respectively, are frequently associated with disorders of the testicular descent. In the studied patients this anomaly was detectable in 23.6% of the cases, which can be regarded as a rather high incidence rate. Furthermore, it could be determined that the higher the location of the testis, the more frequent and severer the fusional anomalies of the testis and epididymis. This anomaly was observable in 23.6% in regard to all the studied testes, while the ratio was significantly higher in case of the testes found in the abdominal cavity (55.5%). The complete lack of any connection between the two organs – the severest of all fusional anomalies – was found in the case of 21 testes of abdominal location (21 from 108, corresponding to 19.4%) and in 28 testes of inguinal location (28 from 963, 2.9%). Considering the *testis size*, smaller testes were detectable in 40.4%, with extremely smaller testes manifest in 5.3%. It could therefore be determined that in comparison to the physiological size, the undescended testes showed smaller measurement in almost half the cases. Among the testes of abdominal location, the ratio of smaller ones amounted to 71.3%, thus nearly three quarters failed to reach the size of the intact testis. The finding of *limp testicular turgor* amounted to 20.7%, the figure being 38.0% in case of abdominal location. Considering these three studied factors, there were no significant differences between the unilateral and bilateral undescended testis cases. From the total 1171 surveyed gonads, 609 (52.0%) showed testes and epididymis, as well as fusion between the two organs which could be assessed as being intact. Abnormal state was found in the case of 562 gonads (48.0%) considering one, two or all three studied aspects.

Testicular torsion

During the course of 39 explorations of the testis (24 unilateral, 2 bilateral distorted testes, 13 contralateral explorations), growth malformations involving the epididymis, fusion of the testis and epididymis, the gubernaculum or the deferent duct were detected in 25 cases (64.1%). Growth disturbances related to the epididymis were verified during the course of 22 operations (56.4%) (Table 6). These anomalies were detected in 17 patients either on the side of the torsion, contralaterally, or on both sides. Among them, the severest was found to be the lack of the epididymis (in case of 3 testes – 7.6%) as well as the congenital lack of the epididymis head. In the case of 6 testes rudimentary,

Table 6
Epididymal and fusional anomalies observed in testicular torsion

Abnormality	No. of cases
Epididymal agenesia	3
Caput epiddiymitis agenesia	1
Maldeveloped (drop-shaped) epididymis	6
Fusional anomalies	12
Total	22

drop-shaped epididymis, while in 12 cases fusional anomaly of the testis and epididymis were encountered. It was found that in the children operated on earlier because of contralateral undescended testis, orchiopexy revealed the epididymis to be rudimentary, with adherence to the testis only with the head part, on a small surface. Deferent duct agenesis was found in 1 infant associated with epididymal agenesis, and the lack of the gubernaculum was detected during the course of 3 surgeries (the latter in one infant bilaterally). In 12 out of 26 torsions (46.2%) it could be proved that the development of the torsion was due to epididymal abnormalities. From the 2 bilateral testicular torsion cases, in one of them – a 6-week-old infant – we found an intact epididymis on one side, with epididymal and deferent duct agenesis on the other side. The other 10 epididymal anomalies were demonstrable contralaterally, in 76.9% of the total surveyed 13 contralateral gonads.

Discussion

In the first half of the 1900s, the fusional anomalies of the testis and epididymis were only rarely published by the physicians performing surgeries due to undescended testes. Campbell in his manual of 1951 entitled: "Clinical Pediatric Urology" makes mention of only 11 cases found in the literature [5]. In general, such a case was only reported on as a rarity. Up until 1961, only 29 case reports are to be found [18]. The growth malformations involving the epididymis were rare literary data. Molnár in his survey of 5203 infertile males found partial or total epididymal agenesis in 14 of the cases (2.7‰) [41]. Then from the end of the 70s, beginning of the 80s more and more cases became published. The frequency of occurrence of fusional anomalies showed great variation by the different authors, influenced not only by the number of related surgeries, but also by the way the physician performing the operation saw the condition of the testis and epididymis. A frequency of occurrence between 6.3% and 79.3% can be found in the literature. The number of gonads studied ranged from 42 (Marshall and Shermata) to 1171 (Merksz and Tóth) [35, 36] (Table 1). The fusional anomalies of the testis and epididymis show great variations of occurrence in the literature, explainable in part by the small number of cases studied. Marshall and Shermata, Heath et al., Koff and Scaletsky carried out their observations on less than one hundred patients, others

had cases ranging from 100 to 200 patients [20, 26, 30, 35]. On the other hand, certain authors only register the complete and apparent lack of fusion between the two organs. In these cases the testis and the epididymis are located far apart, with an obvious lack of any connection. This explains the incidence rate of 6.3% for fusional anomalies occurring in 730 studied gonads [22]. Our observations in respect to the undescended testis gonads are based on the largest number of cases in world literature (a total of 1171 during the course of 1195 surgeries performed because of undescended testes), thus the detection of the anomaly in a percentage of 23.6 can be regarded as factual data. How do these fusional anomalies develop? Can the cause be identical to the factors responsible for the lack of descent? From the descent-influencing effects, significance is attributed to the following 5 factors:

1. The differential growth of the embryonal body: a relative "descent" takes place with the longitudinal growth of the trunk.

2. The active and passive role of the gubernaculum in the testicular descent: the cranial gubernaculum attaches to the lower pole of the testis, the tail end of the epididymis, then later to the distal end of the developing vaginal process. On the caudal end, following the development of the scrotum, the fibers tend towards the scrotum, the os pubis, the inguinal ligament and the fascia lata. Physiologically, there is a scrotal tendency upon the testicular descent. When tendency is towards other gubernaculum fibers, the testis becomes ectopically positioned (perineal, suprapubic, femoral ectopy). The active contraction of the gubernaculum is attributed to the androgen: testosterone (T) effect, though no androgen receptors have been demonstrated so far in the gubernaculum. In animal experiments, repeated undescended testes have been successfully produced by cutting through the gubernaculum [12]. According to Hutson and Beasley, it is the branch of the genitofemoral nerve running in the gubernaculum – the ramus genitalis – which innervates the scrotum and the gubernaculum [24]. The androgen receptors can be found in the neural spinal cord cells at L I–II.

3. The development and role of the epididymis in testicular descent: The development of the epididymis is a lengthy and gradual process, requiring prolonged tissue T level (and accordingly, long-lasting T secretion [14, 15]. The process is called the "maturing" of the epididymis [15, 16]. It was published in the 1940s that the epididymis is located caudally from the testis during the course of testicular descent [56] and since then, others have also confirmed that it "precedes" the testis in descent [10, 35, 39]. It has been verified that in the early stage of embryonal life, the gubernaculum adheres to the cauda epididymitis and not to the lower pole of the testis [10, 18]. Then later, the gubernaculum fibers progress partly towards the lower pole of the testis and partly towards the tail end of the epididymis. Accordingly, it has been assumed that for the human organism, it is firstly the descent of the epididymis which is preferable rather than that of the testis [4]. This is because the tail part of the epididymis is the "storage" place of the sperms, therefore it is of prime importance for the organism to ensure their optimal-lower-temperature.

4. The role of abdominal cavity pressure in testicular descent: certain authors consider it fundamentally important to have proper intra-abdominal pressure for the testis to be able to pass through the inguinal canal [12, 13, 28]. Some authors even think this

to be the main promoting factor of testicular descent [13]. This theory has been supported by animal experimental data, as well as by observations on children with undescended testes [13, 38]. During the course of the latter, it has been detected that in children born with abdominal wall defects (omphalokele, gastroschisis, umbilical hernia, prune belly syndrome) – in which cases the abdominal cavity pressure is slighter – undescended testis is considerably more frequent than in children with intact abdominal walls [28].

5. The endocrine regulation of testicular descent: A well-functioning hypothalamo-hypophysial-gonadal hormonal chain is needed for the undisturbed descent of the testis [16, 27]. An error in the function of any of the chain-loops may lead to undescended testis.

The epididymal growth disturbances described in children are mostly associated with testicular retention. When looking for a cause and effect relationship between the two anomalies, several questions arise: Was the cause of testicular retention the abnormality of the epididymis? Was the fusional anomaly of the epididymis caused by the dysgenetic state of the testis? Were both anomalies caused by the same factor? Even today these questions cannot be answered with complete certainty. Nonetheless, the opinions agree on that the basic error is androgen hormone deficit – the consequences of which are the abnormal location, state and fusional anomaly of the testis.

The pathogenesis of infertility in undescended testis

As already mentioned in the introductory part, there is still a dispute as concerns the cause and effectivity of surgical procedure (orchiopexy) regarding infertility. Many authors believe surgery at the early age of 1–2 to be effective. Vincze et al. observed better results in relation to orchiopexy before the age of 2 as compared to surgery performed between the age of 8–10 [53]. Early orchiopexy, however, only partially improved the unfavourable fertility statistics. During the course of his studies, Madersbacher found no improvement in fertility results following orchiopexy [34]. Several extensive studies were carried out in Hungary, too, in connection with the later fertility results of orchiopexies [43, 44, 53]. According to the observations of Papp, surgery accomplished in late childhood did not improve spermatogenesis with certainty in 76% of his patients. Better results were only gained in 11.7% of the cases [43]. It remains unsolved why certain percentage of treated patients still have fertility problems. To answer these questions, it has become widespread to carry out histological studies on testicular tissue obtained from biopsies during the course of surgery. At first, the aim was to attempt demonstration of the harmful effect of the heat damage phase [21], later to confirm that in case of undescended testis, the testis shows pathological histological appearance even at birth [48]. In the period to follow, the histological studies aimed at demonstrating the numerical decrease in spermatogonia. The pathologically low S/T index (spermatogona/tubules) and low TFI (tubule fertility index – from 100 tubules in how many can spermatogonia be seen) proved the testicular damage in boys of different ages [17]. These studies were also expanded to the biopsy material gained from the scrotal contralateral testis of unilateral undescended testis cases [17, 29].

The following consequences could be drawn from the above studies:

A total of 30% of children with undescended testis – in whom germ cells could not be demonstrated at the time of orchiopexy – become infertile, independent of whether they have uni- or bilateral undescended testes [41]. Close correlation is manifest between the fertility index and testicular location – the higher the testis, the more unfavourable the fertility and the tubule fertility index. According to Kirby, in the scrotal testis the fertility index corresponds to that of healthy individuals, at the same time in the retained testis it shows pathological stagnation and not progression [29].

In accordance with the above, several, often contradictory theories have developed (sometimes showing contradictory practical conclusions):

1. *Thermal effect.* The cause of infertility is the heat damage to the testis situated in an environment of higher temperature [2]. The surgical procedure ensures lower temperature, therefore the damage can be reversed.

2. *Testicular dysgenesis.* There is a damage to the testis in its tissue structure, congenitally [48, 49]. Orchiopexy in these cases will not in all certainty improve fertility.

3. *Gradual numerical decrease in the amount of spermatogonia.* In the first year of life the spermatogonia are detectable in adequate number in the undescended testis. In the second year, their number starts to show dramatic decrease. The operation should be carried out before the age of 2.

4. *Intertubular fibrosis.* In infancy, fibrosis develops in the intertubular tissues of the testis, with massive collagen deposits [38]. Surgery should be performed prior to the age of 1.

5. *Dysgenesis in the contralateral testis of scrotal location.* Histological examination of the contralateral testis showing scrotal location refers to dysgenesis [21]. Accordingly, orchiopexy is to be performed on the undescended testis without any emergency.

6. *Autoimmune processes.* The testis of abnormal location sets of autoimmune processes, antibody formation, leading to the damage of the originally intact contralateral scrotal testis.

7. *Congenital anomalies of the epididymis.* The defective, abnormal fusion between the testis and the epididymis inhibits the sperms in getting into the epididymis.

Taking into account our own studies as well as those of others, together with the drawn conclusions, the opinion seems founded that the cause of infertility observable in the adulthood of children with undescended testis is not firstly due to the testis not reaching the scrotum in time (and thus exposed to thermal noxa), but lies in the damage to the testis and/or the epididymis in the course of their development. Inasmuch as there is no connection between the testis and the epididymis, the sperms are unable to get from the testis into the epididymis and respectively, in case of partial fusional damage, the passing of the sperms will become flawed. This condition was already in a congenitally present pathological state in 23.6% of our cases. If the anomaly if evidenced in both testes, infertility in these adults is obviously not brought off primarily by thermal damage, but is rather the consequence of fusional disturbances. Although the harmful effect of higher temperature on the germinal epithelium is indisputable, it is only a secondary damaging factor in case of the above congenital anomalies.

In these children, the small size of the testis refers to the underdevelopment of the testis, the limp turgor to disturbances in tissue structure. Observations on these pathological characteristics are in accord with earlier as well as the latest histological studies on undescended testes, proving the congenital damage, i.e. the dysgenesis of the tissue structure. The macroscopic morphological picture referring to testicular dysgenesis was observed in 474 of our studies cases (40.4%). Fusional anomaly of the testis and epididymis was accompanied by small testes and poor turgor in 72.2% of the cases. A total of 562 such testes (48.0%) were detectable which were small and/or showed testicular-epididymal fusion abnormalities – amounting to almost half of the studied testes. In accordance with the pathological findings of testicular biopsies performed by numerous authors [6, 7, 29, 48] it can be concluded from the joint occurrence of these two pathological conditions that the dysgenetic state of the testis and the fusional anomaly of the testis and epididymis are both responsible for the subsequent infertility – inasmuch as they occur simultaneously. As regards infertility, the development of these two congenial anomalies prior to exposure to thermal effect refers to their primary significance.

The fertility impairment accompanying the deviations in testicular size is confirmed by andrological studies as well. Based on the data of Molnár and Schirren, there is a directly proportional relationship between testicular size and degree of infertility, as these authors found that the smaller the testis, the severer the pathospermatogram [40].

Hypothesis to the pathogenesis of infertility associated with unilateral UT

Surgical observations on the scrotum-located testis of unilateral UT cases are either sporadical or there are none at all. (Just as there are no such observations on those retained testes which in infancy descend from their retained position either spontaneously or upon hormonal therapy.) There are cases when due to bilateral UT orchiopexy is performed on one side and the other side is operated on at a later time-point (because of the relatively favourable position of the testis or due to other causes) – and during this period the testis descends into the scrotum spontaneously. These patients also had bilateral undescended testis originally, where the testicular-epididymal fusion abnormalities may be present on the testis of scrotal location as well.

As regards the pathogenesis of UT, the defect of the hypothalamo-hypophysial-gonadal chain is held responsible for the entity. It is also this which causes the lack or damage of the testis-epididymis relationship. If in this chain the hypothalamic or hypophysial origin is established, obviously both gonads are involved in the hormonal insufficiency. Both show reaction to this insufficiency, even if not in the same manner. This reaction may manifest itself in the size of the testes, their reached location during the course of descent, their tissue structure, their fusion with the epididymis. In this manner, the scrotal testis may differ from its contralateral pair in only one of the above factors: its scrotal position, and despite this position, it may be dysgenetic or might show abnormal fusion with the epididymis. If the testis of scrotal location has an impaired connection with the epididymis similar to the undescended testis of the contralat-

eral side, the individual will become infertile. The joint occurrence of undescended testis, testicular-epididymal fusion abnormality and testicular hyperplasia refer to the fact that these are either factors inducing each other or can be traced back to the same common cause.

The significance of epididymal abnormalities observed in testicular torsion

These abnormalities were found to occur in rather high numbers – though in differing ratios – both on the distorted as well as contralateral sides.

On the torsion side: in 12 of the 26 torsions (46.2%). During the surgeries it could also be well determined that the epididymal anomaly was not only an accompanying phenomenon, but this pathological state also provided the possibility for torsion. These observations refer to the fact that these anomalies have a much greater causal significance in the development of the torsion than found in the literature and thought of by physicians. If the connection between testis and epididymis is loose, torsion between the two organs can easily develop; if the epididymis is rudimentary or missing, testicular suspension shows deviation from the intact testis – deficiency – and this is where torsion takes place. The fact is also of great importance that the rest of the factors leading to torsion are all developmental abnormalities as well – so whichever the cause, it is of congenital origin.

On the contralateral side, epididymal anomalies were found during the course of 10 explorations, from which 7 were of slighter degree and 3 were severer. (It is to be concluded from the above that contralateral epididymal anomalies were also found in the children where there was an intact testicular-epididymal fusion on the side of the torsion.) It can thus be determined that if an individual has an epididymal anomaly or fusional disturbance on one of the testes, there is a greater probability for a similar abnormality to occur on the contralateral side, than not to find such anomaly in case of the involved testis and epididymis.

Relationship between the factors leading to testicular torsion and the resulting infertility

Damage to fertility can be demonstrated in 50–95% of the cases. There are several explanations as to the origin. According to many, strong antigenic substances are released from the perished spermatides, inducing antibody formation. These antibodies reach the contralateral testis through the circulation, where they exert their damaging effect [3, 42]. This hypothesis suggests that early removal of the distorted testis may hinder or decrease the degree of antibody formation [9]. Others have not been successful in demonstrating antibody formation in their experimental studies [1, 51]. Several authors have revealed contralateral testicular damage by means of the histological examination of material obtained from biopsy of contralateral, scrotal testes [9, 17, 42]. Opinions vary as to whether the damage is the consequence of the torsion or has other causes. In 53% of their patients, Hadziselimovic et al. detected histological alterations in the contralateral testis, which they thought to be present prior to the torsion [42]. Upon studying contralateral testes, Laor et al. found such alterations in 60% of their

cases (inhibited maturation, germ cell degeneration, tubular hyalinization, presence of unmature tubules, focal thickening of the basal membrane) [33]. Dominguez et al. explain the alterations detectable in the contralateral testes with congenital dysgenesis [11]. It was Krarup who raised the possibility that following unilateral testicular torsion, the origin of infertility could be similar to that in the unilateral undescended testis [31]. In both entities the basis of infertility is a fundamental morphological – anatomical injury to the testis – which is present in the testis prior to the torsion as well [31].

Our observations have established that in case of testicular torsion, epididymal anomalies as well as fusional anomalies each occur on both sides. The cause of infertility following testicular torsion – grounded on our findings – is the contralaterally present congenital abnormalities of the epididymis, due to which the sperms are hindered in passing through the testis, towards the deferent duct.

Conclusions and practical clinical relations

Recognition of the significance of fusional anomalies implies numerous practical duties in respect to the management of both patients with undescended testis and those with testicular torsion. Among the tasks, the followings are of the greatest importance:

1. In the point of view of ensuring fertility, the theory of early as possible surgery only holds out in the reflection of our latest knowledge in those children with undescended testis whose testis is of appropriate size, well-developed and the adnexes are also intact. Nevertheless, orchiopexy is suggested in all children, to ensure undisturbed sperm maturation. Performance of the surgery is not advisable in infancy since on the one hand, it does not improve fertility and on the other hand, it is known that surgeries performed in infancy are frequently associated with complications (injuries to the deferent duct, testicular artery) which are less if the operation takes place after the age of 1. Based on these, the optimal time-point suggested for orchiopexy is around the age of 2.

2. It is essential for the surgeon performing orchiopexy to keep in mind the double function of the testis: the question of fertility as well as preservation of the testicular endocrine function are both to be considered. Based on our testosterone-stimulatory studies [37] it can be said that the male hormone secretion ability is present even in the testes where fertility cannot be expected. Accordingly, if the surgeon finds hypoplastic, dysplastic testes during the course of the operation, every attempt should be made to preserve the intactness of the Leydig-cell elements important for endocrine function. Thus, care should be taken not to damage the gracilis funiculus when placing the testis into the scrotum. In case there is a probability of damage to the testicular arteries, forcing of the testis into the scrotum should be avoided. If the procedure seems to require the straining of the testis due to a short funicle or there seems to be danger of funicle laceration, the testis should then be placed in the inguinal area where the surroundings are soft (not above the pubic bone) and physical as well as instrumental check-ups can easily be made.

3. In accordance with the above, bilateral undescended testis cases require even greater care since the danger of iatrogenic testicular atrophy affects both sided testes. If this should happen, the individual would become an eunuch. It is reasonable therefore

to perform the two operations separately in case of bilateral undescended testes, with performance of a second surgery only upon control studies verifying the viability, and not atrophy, of the firstly operated testis.

4. In the case of hypoplastic or pathologically small testes the thought of organ removal may seem justified during surgery. This could also be the way to go in case of intra-abdominal and rather short-funicled testes. Endocrine studies seem to verify the opinion according to which the testis should not be removed prior to puberty. In such cases the testis should be placed in the inguinal area. If this were not possible, it should be left in the abdominal cavity, since (till puberty!) the risk of tumor development is not greater than in boys who do not have undescended testes. After puberty, exposure and removal of the testis is recommended.

5. Besides placing the testis into the scrotum, one of the tasks of the surgeon performing orchiopexy is to carefully observe the condition of the testis and the epididymis, recording the findings in the surgical journal. Exact description and knowledge of the condition is of great help to the andrologist during the course of treatment in adulthood.

6. Fertility studies carried out in adults have been abundant in men born with undescended testis, but there have been only few studies pertaining to the comparison of the spermatogram with the childhood data. No studies are at hand in which a parallel has been drawn between the fusional state of the testis and epididymis and the spermatogram. If all cases were to be recorded in relation to the findings, the pathological role of the fusional anomalies in case of fertility disturbances could be confirmed.

7. As in testicular torsion cases the tendency to become distorted on the contralateral side is a generally known and accepted fact, surgical exploration and testicular fixation is recommended worldwide. During the course of contralateral testicular fixation, it is therefore advisable for the careful observation and registration of epididymal anomalies to become widespread practices, so as to contribute to the clarification of the cause of fertility disturbances.

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STUDIES ON TUMOUROUS AND OTHER UROGENTIAL PATIENTS WITH RESPECT TO ANTIGENS OF ONCOGENIC ADENOVIRUS

Gizella Kulcsár and J. Ongrádi

Department of Urology, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary

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The possible connection of viruses with tumours was investigated by serologic examinations. Concerning the presence of antibodies against adenoviruses, especially those against the early non-virion antigen of oncogenic adenovirus type 12, approximately 4000 tests were made with sera of 446 urogenital patients with and without tumours and 70 ones with internal diseases. It was found by complement fixation tests that antibodies against non-virion antigens of adenoviruses were present in 53% of urogenital patients suffering from malignant tumours and prostatic hypertrophy, in 18% of non-tumourous urological patients and in 4% of patients with internal diseases, respectively. The results suggest that adenoviruses may play a role in tumourous diseases of the urogenital organs.

Introduction

Since the beginning of this century over 60 viruses have been proved to have tumourigenic capacity. They can induce benign and malignant tumours in a wide variety of animal species [20–22]. One of the recent advances in tumour – virus research has been the finding that human adeno- and herpesviruses are also capable to induce malignant transformation of human and animal cells under experimental conditions [6, 14, 16, 17, 19, 23–25]. Though there are numerous observations and studies suggesting that the oncogenic feature of these viruses can also be effective in humans, no direct and unambiguous evidence has yet been found. The verification of virus etiology has only been successful so far in some human benign tumours, for example verruca vulgaris, condyloma acuminatum, molluscum contagiosum and certain papillomas. In case of malignant tumours one of the reasons for the lack of direct proof may be that obtaining infectious virus from human malignant tumours is usually without success, just as infectious virus particles cannot be found in cells that are made experimentally malignant by human adeno- and herpesviruses [22, 26]. In the latter cells, however, there are always substances of protein character present that evidence direct connection with the virus (T-antigens and early non-virion antigens that are meant to be virus "fingerprints"). This explains the effort to demonstrate in human tumours, too, the existence of

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such tumour-specific protein components or antibodies produced against them. Concerning herpesviruses such experiments have become almost conclusive in certain cases of tumours [7, 11, 12, 18, 27]. Similar data relating adenoviruses can hardly be found in the available literature.

For this reason studies have been performed as to whether antibodies against latent and oncogenic adenovirus types occur, and if so in what proportion, in sera of patients suffering from malignant or benignant urological tumours, prostatic hypertrophy and other urological diseases as well as in the relevant control sera. Furthermore, studies were carried out in search for antibodies against the early non-virion and tumour-specific antigens of viruses.

Results

The sera of over 500 patients and controls were tested; the majority with eight different antigens, thus about 4000 tests were performed. A total of 516 patients were grouped according to their diagnosis as follows: 253 cases of urogenital tumours, 193 cases of non-tumourous disease of the urogenital system, 70 cases with inflammatory internal diseases (control group).

The urogenital tumours consisted of 57 bladder, 32 prostate, 15 kidney and 23 other types of malignant tumours and regarding the benign tumours 22 urethra polyps and 89 prostatic hypertrophies completed the 253 cases.

Sera were examined with complement fixation (CF) test and the following viruses or early antigens were used: adenovirus types 1 and 5 (latent serotypes), 12 and 18 (oncogenic serotypes) as well as the early non-virion antigens of the same serotypes.

In the CF tests almost identical results were obtained with types 1 and 5 viruses of latent character; with the oncogenic types 12 and 18 we got very similar results.

In case of urogenital tumours the antibodies against the early non-virion antigens of the oncogenic adenovirus type 12 as well as adenovirus type 1 of latent character occurred in 53% and 56%, respectively. In case of the type 12 virus this frequency was 18% regarding the non-tumourous urogenital patients and 4% in case of the controls with internal diseases. In case of the type 1 adenovirus 23% of non-tumourous and 33% of the control patients had antibodies against the early antigens.

It deserves attention and supports the specificity of the studies that antibodies against the structural antigens of adenovirus type 12 were observable in only 13% of tumourous patients, in 6% of patients suffering from non-tumourous diseases of the urogenital system and in 2% of patients with internal diseases. Antibodies against the structural antigens of adenovirus type 1 were found in 34% of the non-tumourous patients. This can be explained partly by the tendency for latency of this virus and partly by the fact that these patients were younger than those with tumours. The same may also relate to the occurrence of antibodies to early type 1 antigens in case of control patients suffering from inflammatory diseases.

Discussion

The possible connections of benign and/or malignant tumours with viruses have been approached by means of manifold investigations [13–15, 18, 21].

Viruses and their antigens, nucleic acid fragments or genes, enzymes related to the viruses in the tumours and antibodies against the virus or its components have been searched for. The early non-virion antigens produced in the infected cell but not identical with the structural elements of the virus, as well as the antibodies against the latter have also been studied. Connections between several kinds of human tumours and viruses could have been demonstrated by means of the above-mentioned methods. Thus, connections in tumourous cases of the urogenital tract with herpes simplex, cytomegalia, papova viruses and and C-type virus particles have also been observed [9, 10]. Viral nucleic acid sequences have been consistently observed *in vitro* in prostate cells cultivated for longer periods [21]. Concerning the herpes simplex virus there are data available according to which antibodies against the non-virion viral antigens can be found almost in 100% of patients suffering from tumourous diseases of the urogenital tract and the oral region [1–3, 10, 14]. It has also been investigated to what organs or organic systems the oncogenic viruses have greater affinity. Accordingly, it has been found that herpesviruses occur frequently in the male urogenital organs [12]. Persistence of cytomegalovirus for quite a long period has been observed in the human semen [4, 5]. There are many observations indicating that adenoviruses have affinity to the urogenital organs, but no specific data are known as yet. Our former investigations have suggested a connection between the female genital organs and adenoviruses. While studies on the cervix epithelial cells by immunofluorescent technique indicated that in addition to herpesvirus antigens adenovirus antigens might be present in 7% of otherwise clinically healthy women, the occurrence of virus antigens in the malignant cervix epithelial cells could reach more than 20% [13–15]. Latent adenoviruses have, however, been discovered in 14% of patients with irregular haemorrhage, during the examination of epithelial cells of curettage. It has been observed in animal experiments that the virus in case of pregnant mice infected with human adenovirus can transplacentally permeate into the embryo and persist in the ovaries of the pregnant animals [8].

According to these results, antibody against the non-virion antigen of oncogenic adenovirus type 12 can be observed in more than 50% of the tumourous cases of the urogenital system, contrary to the 18% of non-tumourous urogenital patients and to the 4% of the internal disease cases.

The data suggest that the defective form of oncogenic adenovirus or its genes is present and functions in the organism of quite a high percentage of patients with tumours in the urogenital system, since only non-virion antigens can be induced by them. Furthermore the presence of non-virion antigens is proved by the specific antibodies produced against them.

Based on the results obtained from over 400 tests it seems that – besides other already tested viruses – adenoviruses may also play a role in tumourous urological diseases.

It may also be noteworthy that while during our recent investigations the antibodies against the non-virion antigens of oncogenic adenoviruses were primarily and with a high percentage found in patients suffering from tumourous diseases, the antibodies against the non-virion antigens of latent adenoviruses were observed mainly in the sera of patients with internal diseases, namely in 33% of the selected controls. The diseases of the controls were of inflammatory character and in such clinical cases antibodies may always occur or latent adenoviruses may be present in the organism [25].

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COMPARISON OF PROPOFOL-FENTANYL OR MIDAZOLAM-FENTANYL INTRAVENOUS ANAESTHESIA FOR CAROTID ENDARTERECTOMY

E. Dárdai and L. Szeredi

Department of Anaesthesiology and Intensive Therapy, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary

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Carotid endarterectomy has become a standard surgical operation in the therapy of cerebrovascular insufficiency. The cardiovascular status of the patients needs special attention, since the long-term prognosis is predominantly influenced by concomitant coronary artery disease. General anesthesia techniques are raising the challenge of maintaining cardiovascular stability and establishing adequate cerebral monitoring. Randomly selected 30 patients gave informed consent to this approved study. Fifteen patients were anaesthetised with propofol-fentanyl or midazolam-fentanyl combined with N_2O–O_2. Haemodynamic parameters (mean arterial pressure, heart rate) showed not significant changes during anaesthesia. Recovery profil proved to be significantly better after propofol-fentanyl compared to midazolam-fentanyl anaesthesia.

Introduction

Transient ischaemic attack, reversible ischaemic neurological deficit are the leading symptoms of atherosclerosis and stenosis of the carotid artery [1, 3]. Atherosclerotic involvement of the major extracranial carotid arteries can produce cerebral ischaemia by the reduction of blood flow to certain regions of the brain secondary to stenosis or occlusion of the vessel, by the embolisation of atheromatous debris released from the exulcerated plaque or by diversion of blood away from the brain to other part of the body creating a steal syndrome [3, 8, 10, 12].

The removal of the atheromatous plaque and restitution of the cerebral circulation is the aim of surgical reconstruction of the carotid artery. The result of surgery should be a smooth arterial wall thereby preventing future embolic phenomena [4, 6].

It is important to take all risks to the patient into account and assess them against the advantages of the successful operation [2, 8, 12, 14, 16, 19]. If the operation is to be undertaken, the ultimate goal of surgery and anaesthesia is the maintenance of improvement of oxygen delivery to potentially ischaemic brain tissue [10, 11, 14].

Patients presenting for carotid artery surgery are frequently elderly and may be expected to have coexisting medical problems common to patients with vascular disease: hypertension, the presence of cardiac disease, chronic obstructive airway disease and

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diabetes. The adequate control of arterial pressure and an optimal general medical status should be obtained as far as possible before elective carotid surgery [10, 14, 17].

Great care should be taken to alleviete preoperative anxiety in patients. The preoperative anxiety are potentially dangerous for patients with cerebrovascular disease because it is often associated with hypertension, increased heart rate, systemic vascular resistance and an increase in myocardial oxygen consumption. It is equally important to evoid pharmacologic oversedation and respiratory depression. The primary objective of premedication before carotid endarterectomy is to produce a calm and tranquil patient [10, 17].

Adequate monitoring is of crucial importance to allow early intervention to prevent potential neurological or cardiovascular mishaps are vital functions performed by the anaesthetist [7]. Any anaesthetic technique should attempt to protect the brain from hypoxic damage [5]. This may be achieved under general anaesthesia maintaining normocapnia, normotension or slight hypertension, mild-anticoagulation and normovolaemia by careful choice of anaesthetic agents, technique to allow a smooth rapid awakening for evaluation of neurological status [11, 14].

Present study compares the haemodynamic parameters and recovery of patients operated with carotid endarterectomy and anaesthetized with propofol-fentanyl (P+F) or with midazolam-fentanyl (M+F).

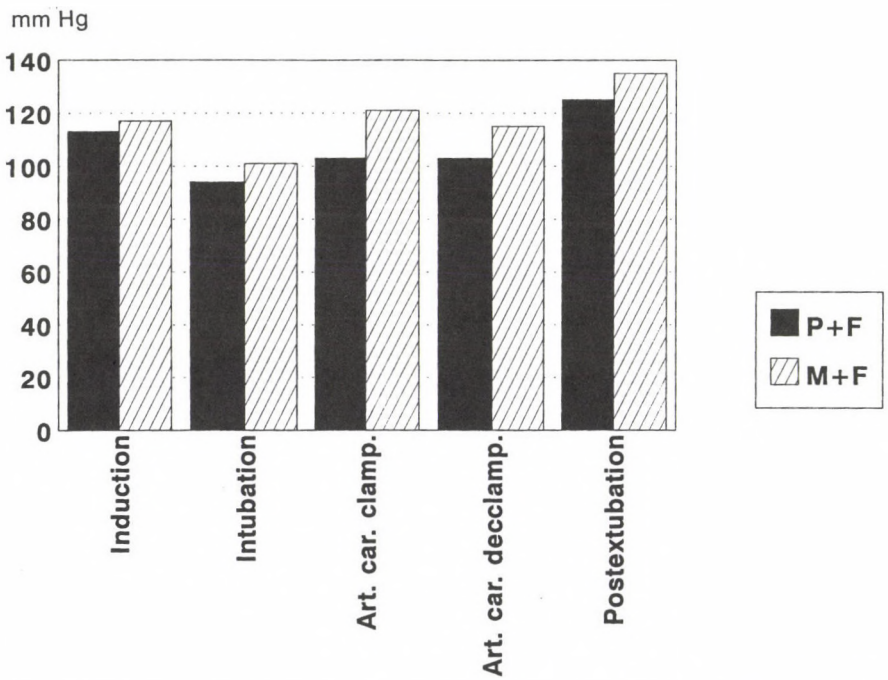

Fig. 1. MAP changes during carotis endarterectomy anaesthesia with the intravenous techniques

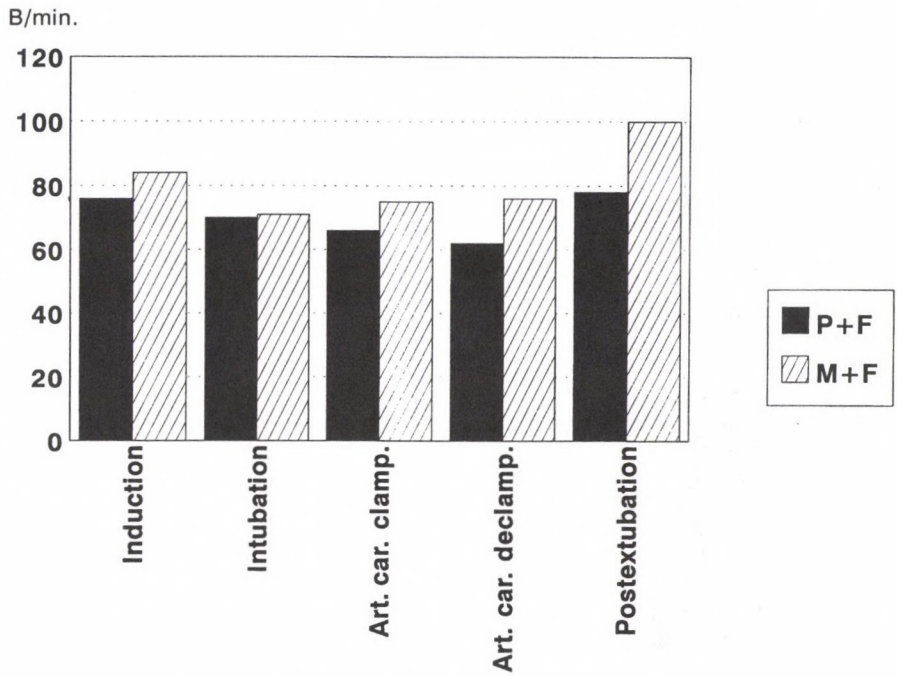

Fig. 2. HR changes during carotid endarterectomy anaesthesia

Patients and Methods

Thirty ASA (American Society of Anesthesiologists Physical Status Classification) physical status II–III patients scheduled for elective carotid endarterectomy were studied. The protocol was approved by the Local Ethical Committee, and written informed consent was obtained from each patient.

The patients were randomly devided into two groups according to the anaesthesia protocol. Group 1 received propofol-fentanyl anaesthesia (15 patients: 2 women, 13 men; ages 63 ± 5 years) and group 2 was anaesthetized with midazolam-fentanyl (15 patients: 3 women, 12 men; ages 61 ± 5 years).

Premedication for all patients consisted of oral midazolam 7.5 mg, fentanyl 0.1 mg and atropin 0.25 mg intravenously prior induction. In group 1 propofol 1.5 kg/kg, in group 2 midazolam 0.25 mg/kg were used for induction. Intubation was facilitated with vecuronium 0.1 mg/kg. General anaesthesia was based on nitrous oxide 60% in oxygen. In group 1 propofol 10–6 mg/kg/h and fentanyl 0.0025 mg/kg/h with infusion pump, in group 2 supplementary doses of midazolan 2.5 mg and fentanyl 0.1 mg were administered. Normocapnic ($ETCO_2$: 37 ± 3 mm Hg), artificial ventilation was maintained during anaesthesia. Heart rate (HR), mean arterial pressure (MAP) and puls oximetry (SO_2) were monitored continuously, and data after induction, intubation, cross-clamping

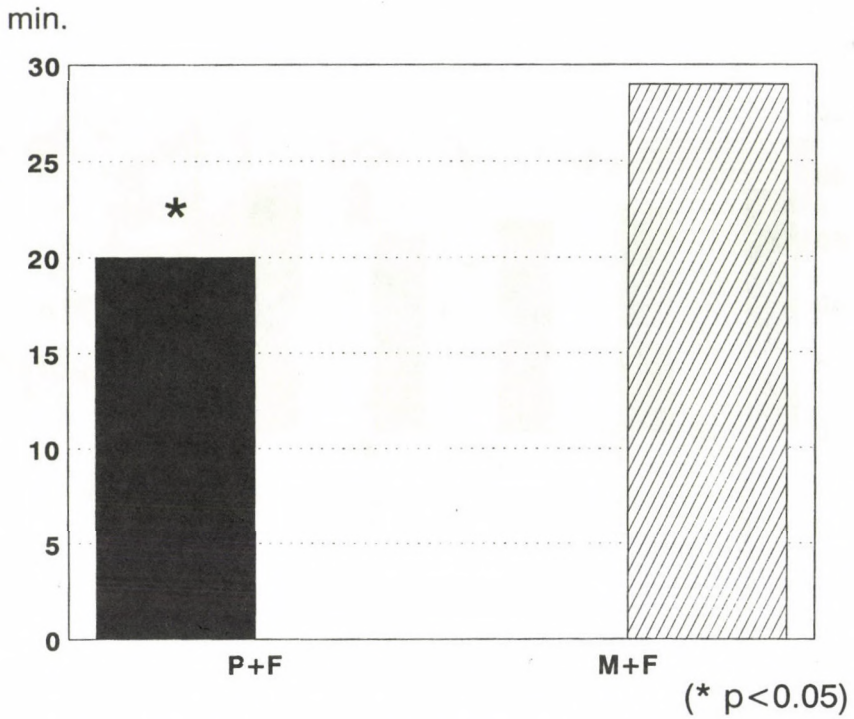

Fig. 3. Steward Recovery Score No. 6 optimal time after general anaesthesia

clamping of carotid artery (Car. clamp), after release of clamping (Car. de-clamp) and after extubation were evaluated statistically. Recovery data were assessed by Steward Recovery Score (SRS): 6 optimal time (min) [18].

Data of the two groups were compared using a paired *t*-test. A p-value < 0.05 was considered statistically significant.

Results

Stable circulation of the patients could be maintained by both intravenous anaesthesia techniques during carotid endarterectomy. Non-significant MAP depression was observed at the intratracheal intubation in patients anaesthetized with P+F (Fig. 1). The HR of the patients appeared stable showing increasing tendency during M+F narcosis probably due to a lighter anaesthesia level (Fig. 2).

The recovery time after operation and general anaesthesia was significantly shorter using P+F anaesthesia measured by SCR (Fig. 3).

Discussion

In patients operated carotid endarterectomy and anaesthetized with intravenous agents supplemented with N_2O–O_2 there seemed to be the best solution to achieve proper oxygenation, blood carbon dioxide tension and systemic arterial pressure, to maintain the adequate cerebral and coronary blood flows [17].

The volatile anaesthetics halothane and enflurane are not recommended for carotid surgery. There are known to increase cerebral blood flow in man and to be a poor suppressor of cerebral metabolic rate and oxygen consumption [13]. Isoflurane less than 1.0 minimum alveolar concentration (MAC) combined with opioids has some cerebroprotective effects. It is the inhalation agent of choice [10, 13, 17]. The inhalational agent has certain disadvantage that is the slow recovery.

Recently intravenous anaesthetics combined with supplementary opioids have been introduced for carotid endarterectomy [9, 11, 15, 20]. In this study propofol or bezodiazepine (midazolam) provided a rapid, smooth and pleasant loss of consciousness. The pattern of haemodynamic response to tracheal intubation was similar for propofol and midazolam. However, propofol more effectively attenuated the blood pressure response, decreasing the HR and MAP. It is probably due to direct myocardial depression and a decrease in systemic vascular resistance. That can be avoided by careful tailoring of the dosage [9, 20].

During maintenance of anaesthesia propofol produced haemodynamic effects similar to those produced with midazolam. Both provided satisfactory anaesthetic conditions haemodynamic values were steadily reached the pre-induction values. The haemodynamic responses to the stress of surgical stimulation was more observable under midazolam-fentanyl anaesthesia.

Compared with young adults, elderly patients are more sensitive to doses of propofol. A decreased propofol clearens rate has also been obsrved in patients over 65 years of age. In agreement with these studies, we noted an age-related decrease in the mean propofol infusion rate [9, 10, 17, 20].

The recovery profile was significantly more rapid with propofol than midazolam. There was less nausea and vomiting after propofol-fentanyl-N_2O–O_2 anaesthesia. The rapid recovery profile for propofol following its use during carotid reconstructive surgery makes it a useful tool in situations in which a rapid and complete recovery from general anaesthesia may be of benefit.

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NON-SURGICAL TREATMENT OF ERECTILE DYSFUNCTION

Gy. Papp and Zs. Kopa

Clinic of Urology Center of Andrology, Semmelweis Medical School, H-1082 Budapest, Üllői út 78/b, Hungary

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Authors survey the conservative treatment possibilities of erectile dysfunction. With the increase in interest, they estimate the new oral- and intracavernosal drugs, giving a review of their experiences with the treatment. A perspective prognosis is given of the important role of NO (nitric oxide) donors and PHD (phosphodiesterase) inhibitor drugs in the field of conservative therapy, while intracavernosal and intraurethral prostaglandin therapies are still important ingredients in the therapeutic arsenal, as is hormone substitution in indicated cases.

Introduction

The abundance of pathophysiological knowledge has led to development regarding treatment of erectile dysfunction. Detailed exploration of the mechanism of erection (compression of the arterio-lacunar dilatation – filling – venous efferent system to the tunica albuginea) as well as clarification of the role of relaxation mediators essential for the process [acetylcholine, nitrogen monoxide, VIP (vasoactive intestinal polypeptide)] have opened new paths concerning therapeutic possibilities [34], to which, no doubt the expansion of modern testing methods has also contributed (color duplex Doppler, dynamic- and pharmaco-cavernosographs, cavernosometry, vasoactive tests). Accordingly, a goal-directed approach and therapy may take shape in medical practice, which in usage often means invasive therapy. At the same time, there is a worldwide view which, according to the possibilities, prefers *the primary application of conservative treatment* – keeping in mind the extremely complicated neuroendocrine regulation of erection. Justification of this trend seems to be proved by the large number of patients requiring – as a first step by all means conservative – medical treatment because of erectile dysfunction (being around 79% according to certain literary data) [41]. There is no doubt that the quality and severity of the cause of sexual dysfunction greatly limit what is to be done, nevertheless, it is our opinion that the grounds for conservative treatment is unquestionable in the majority of the cases. On our part, we do not find stereotyped treatment the best of modes (therapeutic protocols mostly go through complete changes every 2–3 years), therefore, with the exception of evident surgical cases

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(arterial impotency, venous leak, traumas), we think the primary application of constantly developing and renewing conservative treatment is justified. Naturally, the failures in this regard (resistance to therapy, vacuum therapy without results, unadjustable vasoactive self-injection) can be followed by more invasive methods. While earlier, conservative therapy mostly meant the use of aphrodisiacs, nowadays there is a wide variety of modern hormone and vasoactive products at hand to help in the elaboration of the therapeutic schedule.

Theoretical grounds for conservative treatment

Modern medicine describes erection as a haemodynamic event. The physiological background is provided by the relaxation of the corpus cavernous erectile tissues as well as of the arterial smooth muscle elements playing role in the blood supply of the penis. An essential condition of smooth muscle relaxation is the decrease of the intracellular free Ca level. It ensues from this that enhancement and inhibition of the effect of the proerectile and antierectile neurotransmitters important in stimulus transmission are the main aims of conservative therapy. In knowledge of the mechanism of muscle relaxation at the cellular level, pursuit is therefore on the successful influence of the regulation. Several participants of this process – firstly guanyl cyclase, adenyl cyclase, cAMP and cGMP, and the biologically rather active NO (nitric monoxide) and phosphodiesterases – mean distinguished targets for conservative therapy.

Another possibility is to inhibit the flow of the Ca ions into the arterial smooth muscle cells.

The paths of conservative treatment

The drugs inducing erection may reach the organism by several means (Table 1). Currently, oral- as well as intracavernosal intakes are regarded as the most widespread from the listing. There have also been quite encouraging results with the administration of buccal (phentolamine, apomorphine) and transurethral (prostaglandin) substances.

Table 1
Modes of intake of vasoactive agents

– oral
– buccal
– transdermal
– intraurethral
– intracavernosal
– intraspongious
– transrectal

Though attempts made with transdermal hormone patches are not new, their widespread use has not yet followed, which could also be said about iontophoretic intake. Intraspongious (glans) vasoactive therapy is usually applied in helping the muscle phase of erection, on occasions as a supplement to intracavernosal therapy. Up until now, transrectal intake is the least elaborated method, rather being a theoretical possibility.

The possibilities of conservative therapy

I. Oral therapy

This is the main line of conservative therapy, with the availability of a wide variety nowadays. Hormone treatment, the different aphrodisiacs, alpha adrenoreceptor antagonists, the phosphodiesterase inhibitor drugs comprise the main practical possibilities.

A) Hormone treatment

In respect to erectile dysfunction, hormone treatment is either a substitution or a stimulation (transitional) therapy.

Substitution therapy involves the previously diagnosed forms of hypogonadisms, where – depending on age – improvement of sexual disturbances is no the only purpose.

In case of *stimulation* therapy, hormonal assistance is temporary, helping the patient through the negative phase of climax or sexual disturbance [10, 18–20, 24, 26, 36]. In Hungary, the most frequently used drugs are Andriol (Organon) and Proviron (Schering). The formerly used Androral of methyltestosterone content has been taken off the therapeutic palette.

The Andriol capsule containing 40 mg of Testosterone undecanoate is usually taken in an introductory dose of 120–160 mg/day for a period of 2–3 weeks, followed by an average maintaining dose of 2 × 1 capsule/day throughout a minimum of 1–2 months. The first signs of effectiveness appear after 15–20 days of treatment, usually manifest in an increase of libido, and an increased number of morning erections. It should be noted that due to its few by-effects and good tolerance, the drug gives excellent results in the treatment of sexual complaints. Another fine agent in the Hungarian conservative therapy is the 25 mg mesterolone-containing Proviron 25 tablet. The commencing dose is 3 × 1 for 2–3 weeks, with a maintaining dose of daily 2 × 1 tablet. For long-lasting effect, a minimum of two months' treatment is required. In respect to both drugs, attention should be called to prostate cancer (application in the elderly!) and breast carcinoma, which are among the counter-indications. Concerning the male hormone-containing agents, the period of indication in this regard is the early climax phase between the age of 45 and 55.

B) Aphrodisiacs

The traditional aphrodisiac treatment in Hungary has always been influenced by the possibilities of our drug supply. Modest experiences were obtained earlier in treatments with Fortisex, containing animal testis and pituitary gland extract, vitamin as well as Muira-puma. Inprovement in libido, rather than erection was detectable with this drug in patient groups mainly having psychic and moderate potency complaints [25].

On the contrary, the formerly imported but by now locally available Afrodor 2000 drug-combination (Farcopharma) is regarded as fundamental medication in slight and moderate degree erectile dysfunction on non-organic origin, as well as in the male climax. This slightly sedative combination of Quebracho extract and vitamin E can practically be used without any side-effects at all. It can be recommended as a supplementation with other drugs used in the treatment of erectile dysfunction, in a dose of 3×1 tablet daily for a minimum of 40 days [1].

It should be mentioned here that bromocriptine therapy is justified in hyperprolactinaemia-associated hypogonadism and the resulting erectile dysfunction.

C) Alpha-adrenoreceptor antagonists

Further possibilities of oral treatment are given by the alpha-adrenoreceptor antagonists. The yohimbine hydrochloride (Yohistrin) formerly also available in Hungary was mostly the only means of therapy in this category. The present analogs of this substance (Yocon, Yohimbin) mean a renaissance in therapy. They have central and peripheral alpha II-adrenoreceptor antagonist effect, and although literary data have not verified their statistically significant positive efficacy, they are in widespread use. The daily dose is an average of 15 mg (3×1 tablet). The side-effects to be mentioned are nausea, trembling, and elevation in diastolic blood pressure value [18, 20, 27, 37, 40].

Lately, phentolamine well-known in intracavernosal therapy is being used in buccal form as well [2, 42]. The average dose is 20–40 mg, to be taken 15–30 minutes prior to planned coitus. The data of placebo-controlled, multicenter studies have shown erections in 32% as opposed to the 13% observable in patients receiving placebo [42, 46].

D) Neurotransmitter agonists

Erection can also be expressed as the resultant of the proerectile and antierectile neurotransmitter effects. It is understandable that the agonists of these substances also play important role in the development of erection.

1. Dopamine agonists

The dopamine agonist apomorphine has peripheral vasodilatory, as well as direct receptor stimulatory effect (hypothalamus D-1 receptor), thus its effects in erection is easily understood. It is used in a dose of 3–4 mg/day in sublingual form, firstly in psy-

chic impotency cases. Side-effects can be vomiting, nausea, hypertension, however, a positive effect of around 70% has been observed by some authors [11].

2. Serotonin agonists

Serotonin is known to have double effect on erection, depending on the type and localization of the receptor: stimulatory and inhibitory effect. Trazodon used as an antidepressant is a central serotonin agonist, with a peripheral alpha-adrenergic antagonistic effect as well.

The usual dose is 50–200 mg/day prior to bedtime, and according to certain data it has an effectiveness exceeding 60%, with priapism occurring in a ratio of 1:10 000–20 000 [41].

E) Phosphodiesterase inhibitor drugs

The phosphodiesterases play role in the hydrolisation of cAMP. By means of hindering this process, their effect of inhibition leads to smooth muscle relaxation and the resultant erection.

Sildenafil (Viagra TM)

This inhibitory drug is specific to the type 5 phosphodiesterase having an especially important role in the relaxation of the corpus cavernous smooth muscle.

This "to be taken before action" tablet is one of future's big promises, which was coded for quite a while at international congresses (UK 92480). Its registration is in process throughout the world, to commence shortly in Hungary as well. Worldwide multicenter studies have been carried out to judge its effectiveness, according to which the efficacy of the tablet taken ½–1 hour before the activity is around 87.1% [4, 7, 31]. Side-effects could be headache, dyspepsia, flush, and muscular aches. Its application is mainly in the field of neurogenic and psychic impotence.

F) NO-donors

According to our present knowledge, *nitric oxide* (NO) is the number one erectogenetic neurotransmitter. L-arginine precursor of NO. NO develops from the precursor on the effect of nitric oxide synthetase (NOS). These physiological facts supplied the idea to use L-arginine in the therapy of erectile dysfunction [5, 26, 31, 45]. Placebo controlled studies have proved large doses of L-arginine (2.8 g daily) to show improvement of erection in 50% of the studied population. Authors have obtained positive results with a daily L-arginine capsule (California Fitness) dose of 2–4 g taken throughout a period of one month (Papp and Kopa, 1996, Int. Androl. Symp., Cyprus). Based on their experiences, they find the oral administration of L-arginine to be useful in their everyday andrological practice.

G) Further conservative possibilities

The conservative therapy of erectile dysfunction shows constant development. In the followings, without aiming at completeness, mention is made of a few drugs with which certain experience has been gained and which may have role in future therapy.

Such are *pentoxiphyllin* known as a vasodilator (for improving local circulation in the corpus cavernosa), *melatonin* (applied subcutaneously in psychic impotence, but presently also being evaluated in respect to its oral use), as well as *naltrexon* (an opiate antagonist), only being found to have primarily significant effect in morning erections [41].

II. Intracavernosal therapy

If conservative treatment is fruitless – or when the diagnostic results indicate this form of therapy – the next step is intracavernosal self-injection therapy. *The essence of the method is to inject vasoactive substance into the corpus cavernosa to induce artificial erection.* This form of therapy is one of the most widespread methods used around the world nowadays. Its advantage is in the patient being able to self-administer at the desired time and place, following the determination of the required amount by the physician. In the last 15 years a wide variety of vasoactive substances have been used in this respect, and since quite frequently they enhance or supplement each others effect, drug combinations are not rare (BI-MIX, TRI-MIX) [3, 6, 8, 17, 39, 40]. Products automatically prepared in the BI-MIX form are also known (Androscat).

A) Papaverine

Earlier, the main course of intracavernosal therapy involved papaverine. Apart from its non-specific phosphodiesterase inhibitory effect, it has Ca antagonist effect as well. The average dose is 20–80 mg. Due to its frequent side-effects it is rarely used on its own [8, 31, 40].

From the side-effects, noteworthy are the formation of nodules in the penis as well as prolonged erection, priapism. The method was the first to be introduced by authors in Hungary in 1986. In one of their earlier studies from 1993, they had successful adjustments in 752 out of 888 patients, besides an erectile period of 30–180 minutes. Due to the spontaneous return of erection ability, 14 individuals stopped the treatment after 4–6 injections. Prolonged erection was detectable in 31 cases, from which corpus cavernosal puncture adjusted the occurrence in 16, and Metaraminol administration (2 mg) in 15 of the cases. The feeling of discomfort, nausea, changes in tension were found in 24, nodular formation in 27 cases [26]. When possible, authors do not use intracavernosal papaverine as primary choice in today's practice. The latest possibilities are provided by papaverine in topical gel form [13].

B) Prostaglandin E-1

The prostaglandin E-1 of adenyl cyclase activating, noradrenaline release inhibiting effect is no doubt today's *most widely used intracavernosal vasoactive agent worldwide* [14, 16, 24]. Its popularity is due to its reliability that is combines well with other agents and that it has good erectile-genetic features [9, 17, 28, 30, 40, 43]. Upon being introduced in Hungary, 145 out of 154 patients showed success in neurogenic, psychogenic, and erectile dysfunction cases of mixed etiology. The therapeutic doses were as follows: 5 μg or less for 20 patients, between 5 and 10 μg for 62 patients, between 10–20 μg for 53 patients, 30 μg for 8 patients and 40 μg for 3 patients. (The majority of the patients can therefore be adjusted between the dose of 5–20 μg!) The encountered side-effects were pain in 8 cases, and 1 case each of penis oedema, nodular formation and testicular pain. There were no occurrences of priapism as a complication [28].

These data are in accordance with the averages found in the literature. It should be noted that the pain associated with the injection was never of such degree that adjustment would have had to be stopped. The patients showed good tolerance and found the drug to be safe.

Authors recommend this drug – readily available in Hungary today as Caverject 10 μ or 20 μ – as a first choice in intracavernosal therapy.

C) Phentolamine

This non-specific alpha-receptor blocking agent, which was a well-established vasoactive agent earlier, is nowadays rarely administered on its own due to its slight erectile-genetic effect. It is used, however, in combination, firstly with papaverine, and sometimes with PGE 1, in an average dose of 0.5–1.0 mg. Since it is difficult to obtain, it is becoming more and more ousted from the Hungarian practice [26, 27].

D) Phenoxybenzamine

This agent which irreversibly binds to alpha-receptors was also widely used in earlier years, but by now it has been taken off the therapeutic palette because of the great likelihood of priapism [40].

E) Lisindomine (Sin 1)

This non-enzymatic NO donor belongs to the group of drugs which are used in combination. It is cheap, has few side-effects, although little erectile-genetic effect. It has undergone comparative studies and is used in 1–2 mg dosages [30, 38, 40, 43].

F) Moxisylate

The competitive receptor blocking moxisylate has erection facilitating effect, and is usually administered in combination. Its fibrotic effect, however, cannot be left unmentioned [6].

G) VIP (vasoactive intestinal polypeptide)

Similarly to alprostadil, VIP has adenyl-cyclase stimulatory effect, and is a non-adrenergic, non-cholinergic neurotransmitter. Not causing rigid erection on its own, it is used in combination [12, 33, 40].

H) Forskolin

This substance gained from the root of the Indian coleus shrub, has direct adenyl-cyclase stimulatory effect. Its usual dose is 80–100 mg. Muhall et al. have used Forskolin with success after the inefficiency of other vasoactive drug combinations (TRI-MIX) [21].

I) CGRP (calcitonin gene-related peptide)

The presence of CGRP in the nerve endings of the corpus cavernosa has already been proved. The substance is an adenyl-cyclase activator, with proven smooth muscle relaxing effect in animal experiments, and erectile-genetic effect manifest in the form of intracavernosal injection in combination with PGE-1 [39].

J) Verapamil

This substance known from cardiotherapy as having Ca influx inhibitory and peripheral vasodilatory effect is not used on its own any more. In general, it is combined with papaverine and prostaglandin, the usual dose being 5 mg [3].

Intraurethral therapy

This is an alternative to intracavernosal therapy, with indication primarily being the treatment of erectile dysfunction in patients receiving anticoagulant therapy, hemodialysis, etc. Prostaglandin (PGE-1) is the most widespreadly used, in the dosage of 125–1000 mg. Padma-Nathan et al. have reported on good results regarding the intraurethral administration of 500 mg [22]. A special system has been developed for the urethral administration (MUSE – Medical Urethral System for Erection).

Dinoproston (Prostaglandin E-2 cream, suppository – 20–40 mg) and Prasosin have also recently been introduced as intraurethral modes [31, 44].

There is no question about the acceptance of this therapy form, although there are patients who will rather opt for puncture treatment.

Vacuum therapy

The essence of the method is to produce vacuum in a plastic cup, whereas erection is induced by the pressure of the surface veins. This type of erection can be maintained for a period of half an hour on average, by means of sliding a tightening rubber ring from the

cup onto the penis root. The area of indication is firstly among the elderly "risk patient" group, where hormonal therapy or invasive intervention cannot be taken into account [15, 23, 26, 27, 32, 35]. This non-invasive method is not really popular in Hungary, being more preferred in other parts of the world, e.g. in the Arabian countries. Vacuum erection can be induced by means of several devices, the most frequently in use are the Erec-Aid (Osbon) or the Inno Vital System (Innotec) – with Hungarian devices also available.

Discussion

Today, the conservative treatment of erectile dysfunction is an accepted and applied medical activity throughout the world. Its priority as opposed to other modes of treatment lies in its less invasive nature, simpler applicability and the better acceptance on behalf of the patient. With the ever increasing amount of medical products on this topic becoming known worldwide, it is not hard to predict the future headway of this therapy form. *From the drugs in use, male hormones, NO donors and phosphodiesterase inhibitors seem to have an ensured place on the therapeutic palette, both today and tomorrow; furthermore, the intraurethral administration of prostaglandin also seems to have a developed area of indication besides the intracavernosal vasoactive substances (PGE-1) already used with success.* In Hungary today, there is a wide variety of medication available regarding andrological treatment, and the range is ever increasing, providing this groups of patients – who owing to the topic are more sensitive anyway – even better and more reassuring possibilities.

With the development of diagnostic methods, the opportunity is there in our days to divide patients with erectile dysfunctions of various origin into different groups in order to establish a more "targeted" therapy.

Possibilities of the future

The natural demand of patients regarding conservative treatment of impotence has led to the broader scope of therapies as well as a wider choice of drug availability. *Among the intake modes of vasoactive substances, besides the presently applied oral and intracavernosal forms, the buccal and intraurethral administrations seem likely to become of large-scale proportions.* From the vasoactive drugs, the PGE-1 (Caverject), with its extremely good erectile-genetic character and few side-effects will possibly stay one of the most reliable weapons in the hands of the andrologist for quite some time to come, nevertheless, development is to be expected in regard to combinable drugs as well, like lizindomine and forskolin. Oral administration is a great future prospect, in which field – apart from hormone therapy – the appearance of the phosphodiesterase inhibitor Sildenafil (Viagra) will revolutionize the therapy of erectile dysfunction. According to authors, however, it is extremely important to keep selection of the individually tailored form of therapy in the hands of the specialist, *otherwise the effect of the various drugs will not be able to be judged as the consequence of indication-related confusion.*

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TESTICULAR SPERM ASPIRATION (FIRST HUNGARIAN RESULTS)

Gy. Papp[1], Klára Rajczy[2], A. Bernard[2] and Zs. Kopa[1]

Semmelweis Medical University, Clinic of Urology Center of Andrology,
[1]Semmelweis Medical School, H-1082 Budapest, Üllői út 78/b, Hungary
[2]Kaáli Institute, H-1125 Budapest, Istenhegyi út 54/A, Hungary

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Authors summarize the first results with the use of spermatozoas retrieved with direct surgical method in intracytoplasmic injection in Hungary (1995–1997).

Eighty-nine procedures were performed in 65 patients and 84 cases were successful. Out of 84 cases 23 clinical pregnancies could be achieved (27.3%). Thirteen children were born, including one case of twins and one triplets.

Introduction

In cases of maximal or almost maximal defect of sperm number the only solution in the past was donor insemination or adoption, except in case of microsurgical solution of obliterative azoospermias. Although the initial opposition against donor insemination decreased gradually, there is continuous effort for developing new methods in such sperm conditions, which would allow genetic fatherhood. On the other side, the fact that adoption is still not completely accepted way of founding a family in Hungary, it also supports these efforts.

Introduction of *in vitro* fertilization and micro-manipulating methods meant a new approach and possible solution for the problem. The new knowledge about sperms became useful in practice, when it was cleared, that micro-manipulating techniques can help to penetrate the covers of the ovum mechanically, instead of the classical "by sperm itself" way.

After the intracytoplasmic injection became practice (in Hungary: 1994, Kaáli Institute) it was obvious that 1 or 2 sperms are enough for fertilization [1]. For andrology to help the azoospermic patient was still a task, doubly so as, the passage surgery of the ductus deferens not always successful. (The average success rate of vaso-vasostomy is around 80%, in case of VEA it is 35–40%.)

This was the reason, why direct sperm aspiration arisen and in the everyday practice testicular, epididymal and deferental sperm aspiration cold have been achieved (TESA – Testicular Sperm Aspiration, MESA – Microsurgical Epididymal Sperm Aspiration, DESA – Deferental Sperm Aspiration). The above-mentioned methods (including the

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needle biopsy methods) are summarized in andrology nomenclature as SMART (Sperm Micro Aspiration Retrieval Technique). The first Hungarian sperm aspiration was done in 18 January, 1995, and the first SMART+ICSI baby was born in 24 November, 1996 [10].

Patients and Methods

Between 1 January, 1995 and 31 December, 1997 89 direct sperm aspirations were done in 65 patients in the Urology Clinic of Semmelweis Medical University and Urology Department of Szent István Hospital, in scientific cooperation with Kaáli Institute. The andrological examination of the males was started in different out-patient offices and judgement of suitability for assisted reproduction was carried out in Kaáli Institute. Prior to sperm aspiration, the follicular stimulation and punching was done here, as well as the fertilization with the retrieved sperm and the embryo-transfer. Obtaining the required andrological instrumentation (Pomerol microaspiration instrument, Goldstein microsurgical ASSI set), high power operating microscope and personal study tours preceded the Hungarian introduction of the method.

Summary of the Method

Pieces of parenchyma were always acquired by open biopsy method and were put in sperm medium (Medi-Cult, Denmark). It was followed by micro-cutting in sterile conditions and 24-hour incubation (in medium of 5% CO_2). It is followed by washing, mixing (albuminised HAM F.10-GIBCO), centrifugation and sperm isolation from the sediment (Fig. 1). The next step is with the ICSI and 48 h after ICSI the embryo transfer.

According to the tasks of the biologist and methods of *in vitro* fertilization and assisted reproduction we refer to related articles [2, 8, 12].

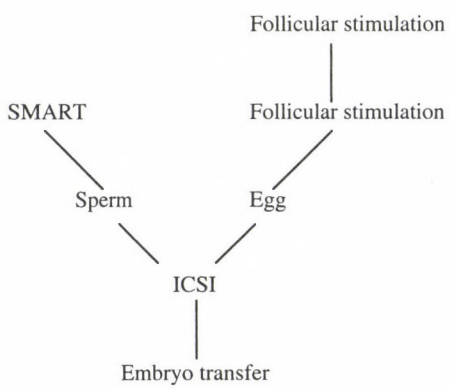

Fig. 1. SMART + ICSI Scheme

Indication and Results

Between 1995–1997 89 sperm aspirations were carried out in 65 patients, and 84 were successful. Our results are summarized in Table 1.

Table 1
SMART results

Number of patients	65
Number of interventions	89
Number of successful sperms	84
Number of interventions per patient	5 × 1 patient 4 × 1 patient 3 × 1 patient

The maximal number of interventions carried out in one patient was five. Five and 4 interventions were carried out in one patient, and in both cases the procedures resulted in delivery. In 3 cases 3 procedures were carried out, and in the rest of the cases 1 or 2 procedures were done. Table 2 shows the success rate in reproduction.

Table 2
SMART results II

8/23 Clinical pregnancies	(27.3%)
10 births	1 set of twins 1 set of triplets 8 single births
Advanced pregnancies	8
Extra-uterine gravidity	1
Spontaneous abortions	4

Twenty-three clinical pregnancies were reached in 84 patients, which equals 27.3%. Out of 10 deliveries one twin and one triplet were born (13 children).

We noticed 8 cases of advanced pregnancies, 1 case of extra-uterine gravidity, and 4 spontaneous abortions.

Different andrological status was the indication of the procedure. These are summarized in Table 3.

Developmental disorders (mainly deferens and epididymis, which result in sperm passage obliteration were the main reason for the procedure. The other group was the azoospermic state, after unsuccessful passage surgery (VEA, vaso-vasostomy, Coll. sem. tur.). In cases of retrograde ejaculation surgical sperm aspiration is still the safest was although in some cases conservative therapy can be successful or sperm can be gained from postcoital urine.

Table 3
Indications for SMART

Agenesia D. Deferentis	16
Agenesia Epididymis	5
Obliteration D.Def.	16
Insuff. Recanalisation (unsuccessful vaso-vasostomy)	5
Insuff. VEA	5
OM (1-1 SP/LT)	4
Insuff. TUR (Coll. Sem.)	2
Retrograde ejaculation	3
Aspermia (spinal unjury)	3
Insuff. Allopl. Sp. Cele Impl.	2
Sp. Arrest (Spermatida)	2
Cryptozoospermia	65

Further indication can be the unsuccessful implantation of alloplastic spermatocele or azoospermia and aspermia after bone marrow injury. Cryptozoospermia and very bad quality (1–1 sperm/visual field) oligozoospermia (when sperm from testis tissue can be added to the ejaculated sperms) can mean relative indication for the procedure. Another relative indication can be developmental disorders of spermatogenesis (spermatogenetic arrest), and even spermatide can cause pregnancy with this kind of procedure, as seen in the literature [3]. Above-mentioned results and indications well-correspond to the general data in the international literature.

Discussion

Development of assisted reproduction cannot happen without the development in the knowledge about reproductive quality of sperms.

ISCI is a big step ahead in the treatment of infertility compared to IVF [12]. Since the first results [8] the indication fields expanded, the technical knowledge related to the procedure developed, and it was compared with other methods correctly. By 1993 it was clear that the results are better with intracytoplasmic injection compared to other micromanipulating methods (e.g. SUZI) [15]. The method was successfully applied in immunological infertility and CAVD (congenital agenesia of vas deferens) [7, 14]. It was also cleared that immobile sperms and spermatide can also be used for the procedure [3, 4]. The classical spermatogram parameters are not very informative in the new method [6]. Intracytoplasmic injection with deep-frozen sperms was also a new possibility [11]. Summary of 3 years results of the method was also very successful [16].

Above-mentioned steps helped that application of surgical sperm aspiration and intracytoplasmic injection is accepted in human reproduction. During this process, the

androlgist have a very significant role, in setting up the indication, in clearing up the reasons for male infertility, in optimizing the fertility status, and in the procedure of surgical sperm aspiration [9]. Hungarian results in this field are well-known and recognized abroad and it guarantees the progress, too.

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LAPAROSCOPIC VARICOCELE OPERATION: A CHANCE TO PREVENT THE RECURRENCE

P. Nyirády[1], L. Pirót[1], Á. Altorjay[2], A. Pelényi[3], M. Merksz[1], A. Kiss[1] and Á. Csontai[1]

[1]*Department of Urology, Heim Pál Children's Hospital,* [2]*Department of General Surgery, Haynal Imre Medical University, H-1089 Budapest, Üllői út 86, Hungary*
[3]*Department of Surgery, Heim Pál Children's Hospital, H-1135 Budapest, Szabolcs u. 33–35, Hungary*

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There are recurrences and postoperative hydrocele of varicocele after any kind of surgical treatment. Laparoscopic clipping and dissection of internal spermatic vessels was performed without any complication in 73 children to treat varicocele in our department between 1995 and 1998. We have used a new method to detect etiological factors at laparoscopic surgery. The well-known Linton and Trendelenburg test was adapted to detect incidental collateral veins in 73 patients. Using these test, collateral veins were detected in 16 boys. The testicular artery identified in most of the cases as a pulsatile vessel. The operating time was 10–25 minutes. Laparoscopic varicocelectomy is a safe, effective treatment causing minimal discomfort and allowing patients an early to return to activity. These results suggest this technique a viable alternative to open ligation in paediatric urological practice.

Introduction

After Nitze's development of the incandescent cystoscope in 1875 to Kelling's report in 1901 on endoscopic examination of the peritoneal contents of a dog called 'celioscopy' [7]. Jacobeus performed [10] examination first in human abdomen in 1911 and this procedure known today as laparoscopy. Operative laparoscopy/pelviscopy was introduced in the 1960s by gynaecologists. Urological laparoscopy was reported in 1976 by Cortesi et al. [2] for the identification of a nonpalpable testis. With the introduction of laparoscopic cholecystectomy in 1985 by Eric Mühe, many laparoscopic surgical applications were performed in the field of urology. Such as testicle varix ligation, nephrectomy, hemynephrectomy pyeloplasty and pelvic lymphadenectomy. In paediatric urology ligation of the clinical varicocele, diagnosis and treatment of nonpalpable testes and total or partial nephrectomy has been applied predominantly [5, 6, 9]. The advantages of laparoscopy compared to the open surgical approach appear to be the excellent identification of the anatomical structures, shorter hospitalisation, rapid convalescence of young and active patients and less need for postoperative narcotic pain medication. The earliest description of a surgical treatment for a varicocele was made in 1885 by Barwell [1]. The ideal method of spermatic vein ligation for varicocele is still a matter of controversy [17]. Methods such as high ligation are associated with signifi-

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cant postoperative discomfort, while transvenous percutaneous immobilisation of the internal spermatic vein [15] has a failure rate of up to 15% and risks migration of the occlusion device and vessel wall perforation. Laparoscopic varix ligation was first reported in 1988 by Sanchez De Badajoz et al.

Patients and Methods

Between 1995 and 1998 73 boys underwent laparoscopic treatment for varicocele in the department of Urology of Heim Pál Children's Hospital. The ages of the patients ranged between 7 and 18 years (average 12.5 years) with idiopathic varicoceles of grades II and III (grading system of Dubin and Amelar, 1971). In all patients, the varicocele was on the left side. The diagnosis was based on physical examination (positive Vasalva manoeuvre), scrotal ultrasound and colour Doppler examination which were performed on the Department of Radiology Heim Pál Children's Hospital. Alternatively, varicocele may result from extrinsic compression of the venous drainage of the spermatic veins. Abdominal ultrasound was performed in all children preoperatively. Abdominal masses such as tumours or systemic diseases, should lead to further evaluation [11]. However, extrinsic compression had never diagnosed.

All patients received a general anaesthetic administered via endotracheal intubation and muscle relaxation [12]. Children were never catheterised but invited to empty their bladder. Pneumoperitoneum was created by inserting a Veress needle [18] through an infra-umbilical incision. An automatic insufflator was used to maintain an intraperitoneal pressure at 12 mm Hg. After the primary 5 mm telescopic trocar sheath was introduced in the same incision (Olympus S 5 laparoscope) was inserted. First an inspection was performed to exclude any intra-abdominal injury. Two other trocars were inserted under laparoscopic guidance.

Ten mm port was placed on the right, 5 mm port on the left side of midpoint halfway between umbilicus and anterior superior iliac spine. The larger port has been required for the insertion of the clip applicator. The patient was placed in Trendelenburg position. The spermatic vessels can be early identified. Small bowel and colon adhesions by the sigmoid colon covered the internal inguinal ring had to be. The left internal inguinal ring had been identified the dorsal abdominal wall was incised, 2–3 cm above the internal inguinal ring. The incision was made from medial to lateral direction. The wound on the posterior parietal peritoneum has to be big enough to mobile the vascular structures. The vessels were isolated and removed from the psoas major. The spermatic artery was separated from the venous plexus by nontraumatic dissectors. The child was placed anti-Trendelenburg position and waited varices were dilated. The main spermatic vein was grasped atraumatically and then the blood was pressed out manually from the scrotum. This manoeuvre could detect the existing collateral vein (veins) because they are filled up with blood. If there was no collateral, the vein was clipped. Two titanium clips were applied distal and one proximal. The vessels were dissected in all cases and were taken a part of them to be send hystological examination. Collateral veins were prepared, clipped and transacted similarly. Small size collaterals were elec-

trocoagulated. The small retroperitoneal incision was not closed. After inspection for haemostasis and visceral integrity by low intra-abdominal pressure (5–6 mm Hg) the working parts were withdrawn under direct endoscopic vision. Before removal of the last, subumbilical port, all the gas was expelled.

Results

In 73 children laparoscopic ligation of spermatic vessels were performed. Our adapted test were used in all cases. Using this method collateral veins were easily detected and ligated. Collateral vessels were found in 16 patients. The testicular artery was identified in most of the operations as a pulsatile vessel. At a minimum 2 months follow up there were recurrences in 2 children and in one patient developed hydrocele postoperatively. The improvement in the intratesticular arterial circulation and the emptied varices were visualised by 2 months after surgery performed control colour Doppler ultrasound.

The total operative time was between 10 and 25 minutes. There was no convertion to open surgery. Postoperative complication were subcutan emphysema in 4 children and pneumoscrotum in 1 boy. All patients were discharged from the hospital on the first postoperative day.

Discussion

In children the anterior peritoneal membrane is less fixed to overlying rectus muscle and fascial layers [5], it tends to tent in front of the introduced Veress needle less room for error. However, we never performed Hasson open laparoscopy approach.

There are recurrences of varicocele and postoperative hydrocele after any kind of surgical treatment [3]. In some cases the recurrence is caused by underlying angiological variations, e.g. insufficiency of the left-testiculorenal valve or collateral veins between the left-vena testicularis and the veins of the lower extremity. We have used new methods to detect etiological factors at laparoscopic surgery. The well-known Linton and Trendelenburg test was adapted to detect incidental collateral veins to the lower extremity in our patients. While the main testiculorenal trunk was occluded the pressed blood were indicated the incidental collaterals and laparoscope gave an excellent identification of small veins.

Although in our paediatric urological experience surgical routes of Palomo and Bernardi gave a good result a recurrence rate of 5–6%, hydrocele developed in more than third of the cases postoperatively. Varicocele operation according to Narrat technique (scrotal incision) a good result and no postoperative hydrocele was given. However, sometimes scrotal discomfort and pain were appeared postoperatively.

Although laparoscopic varicocele operations require general anaesthesia, we believe that it is a simple, safe, effective method and excellent identification of anatomic structures like collateral spermatic vessels [4] and it is superior for preserving the spermatic artery.

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OUR EXPERIENCE WITH THE THERAPY OF BLEEDING PEPTIC ULCERS

J. Regős, A. Sárospataki, Edit Harasta and Z. Kökény

Department of Surgery, Weiss Manfred Hospital of the Budapest Municipal Authority
H-1211 Budapest, Déli u. 11, Hungary

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Authors present their clinical experience gained in the therapy of bleeding peptic ulcers. The modified Baylor Bleeding Score has proved to be a reliable tool for assessing the risk of recurrent hemorrhage. Early introduction of H_2-receptor blocker therapy is justified both in conservative as well as in surgical management of bleeding peptic ulcers.

Introduction

The several decades long dispute between surgeons over the optimum surgical therapy of peptic ulcer seems to be approaching a final consensus.

The advent of H_2-receptor blockers and proton-pump inhibitors as well as the elucidation of the etiologic importance of *Heliobacter pylori* infection have changed the clinical approach to peptic ulcer disease dramatically. Nowadays, this condition is regarded a chronic infection and consequently, the number of elective operations for peptic ulcer disease has decreased substantially worldwide. Nevertheless, surgical intervention is still indicated when the ulcer persists and no symptomatic improvement occurs despite appropriate conservative therapy. Most authors recommend Billroth I resection for gastric, and proximal selective vagotomy for duodenal ulcers [1].

Despite the availability of effective medical treatment the incidence of complications – especially bleeding from peptic ulcers – has not shown significant decrease. This can partly be attributed to gastrointestinal ulceration induced by drugs, particularly nonsteroidal anti-inflammatory agents.

H_2-receptor blockers and proton-pump inhibitors seem only to delay onset of the complications of peptic ulcer disease, and not prevent it [14].

A similar change is apparent regarding the principles of surgical treatment for the complications (i.e. bleeding or perforation) of gastroduodenal ulcers [11]. 'Definitive solution', i.e. radical resection is no longer considered pertinent. The primary objective of the operation is to avert acute, life-threatening complications and thereby provide a chance for subsequent – and expectedly successful – medical treatment.

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Patients, Methods and Results

During the years 1996 and 1997, 44 patients with peptic ulcer disease were treated at our department for acute, massive gastrointestinal hemorrhage (Table 1).

In two patients with hypovolemic shock, urgent endoscopy identified Forrest 1/a stage ulcers as the source of gastrointestinal bleeding, immediate surgery was performed in both cases (endoscopic coagulation was not yet available in our department during the study period).

Medical management included the early institution of intravenous, then oral famotidine therapy. Conservative management of bleeding peptic ulcer was successful in 60% of the cases. Immediate surgery was performed on 17 patients (Table 2).

According to the Forrest-classification, surgical intervention is almost inevitably required to stop bleeding in cases of stage I/a–b and II/a lesions (Table 3).

Stratification of cases according to the Baylor Bleeding Score leads to the same conclusions (Table 4).

Table 1

No. and age of patients		Localization of ulcers	
Males	23	Gastric	13
Females	17	Duodenal	27
Mean age	57.1 years		

Table 2

	No. of patients	Fatal outcome
Conservative therapy:		
Definitely successful	23	0
Temporarily successful	4	0
Surgical therapy		
Immediate surgery (within 6 hours)	10	3
Early elective surgery	7	0
Total:	44	3

Table 3
Forrest staging classification

	I/a	I/b	II/a	II/b	II/c	III
No. of patients	2	6	6	13	6	7
Surgery	2	5	5	3	1	1

Table 4
The modified Baylor Bleeding Score

	Total number of patients	Surgical patients
Low risk (>7)	5	0
Moderate risk (8–11)	8	2
High risk (<12)	27	15
Total:	40	17

Table 5
Surgical intervention

Gastrectomy (Billroth I–II)	10
Vagotomy + ligation	2
Ligation	4
Ulcer excision	1
Total:	17

The types of surgical procedures performed for massive ulcer bleeding are summarized in Table 5.

Four patients were considered high-risk cases owing to recurrent gastrointestinal hemorrhage.

Discussion

Currently, referrals for acute, massive gastrointestinal bleeding account for 1 to 2% of hospital admissions. The most common sources of bleeding include ruptured esophageal varices, gastrointestinal erosions induced by drugs (particularly NSAIDs), Mallory–Weiss syndrome, as well as gastric and duodenal ulcers.

Although the absolute number of cases with acute ulcer bleeding has decreased during the last few years, no such improvement has been observed in the percentage of patients requiring surgical intervention [7].

The changes in the clinical approach to the management of ulcer disease have influenced the therapeutic strategy of complicated cases as well. In particular, an increasing number of publications report on laparoscopic interventions as substitutes for primary resection.

The medical history of patients undergoing surgery for gastrointestinal bleeding is usually short, most of these patients had not received appropriate therapy previously. Consequently, there is a good chance for successful medical treatment, provided that potential life-threatening complications are averted promptly. When surgery is unavoid-

able, recommended procedures include vagotomy, pyloroplasty, extra- or intraluminal ligation as well as excision of the lesion. Resection is seldom performed, e.g. when a giant, or stenosing ulcer is the source of bleeding [1].

Sixty to eighty % of ulcer hemorrhages resolve spontaneously, or respond to drug therapy. In the remaining proportion of cases, however, immediate or early elective surgery is necessary.

Endoscopic coagulation has reduced the morbidity and mortality of ulcer bleeding significantly. Several modalities of this procedure have been developed. Although laser-photo-coagulation is preferred by many authors, its efficacy is not superior to that of endoscopic thermocoagulation or sclerotherapy. Endoscopic sclerotherapy enjoys wide popularity owing to its cost-effectiveness and ready availability. Local tissue destruction interferes with ulcer healing; this is a drawback common to all endoscopic methods [6, 14].

While the mortality of acute gastrointestinal hemorrhage is 10%, this increases to 30 or even 40% in early recurrent bleeding. Importantly, this increase in mortality does not occur when recurrent hemorrhage is prevented by early surgical intervention. The subset of patients at high risk of recurrent bleeding is identified through the simultaneous evaluation of several factors. Forrest's classification is the most widely used system for the assessment of the risk of recurrent hemorrhage.

Ell reported a 31% incidence of recurrent bleeding (and 21% mortality) in patients with Forrest I/a stage disease [2]. Forrest I/b to II/a stages are associated with a 14 to 17% risk of recurrent hemorrhages, proving to be fatal in a similar proportion (10 to 13%) of patients.

In addition to the Forrest stage of the disease, the localization and size of bleeding ulcers also carry prognostic significance. The Baylor Bleeding Score published by Saeed et al. [12] evaluates 5 attributes. This scoring system has been further improved by Ondrejka et al. [9], its practical usefulness having also been confirmed by our experience. The algorithm of the recommended therapeutic strategy is depicted in Fig. 1 [11].

Patients at risk of recurrent bleeding should undergo surgery within 6 to 8 hours, i.e. following successful endoscopic coagulation and hemodynamic stabilization [13, 16]. Vigorous medical treatment of peptic ulcer disease is also essential in the therapy of hemorrhagic complications. Neither H_2-receptor blockers nor proton-pump inhibitors should be expected to stop active bleeding; however, the administration of these agents is justified by several reasons [10]. Although these drugs do not control bleeding directly, they enhance the regeneration of the mucosa and thereby facilitate spontaneous hemostasis.

Furthermore, while the administration of H_2-receptor blockers of proton-pump inhibitors is regarded adjuvant treatment in surgical patients, these drugs should be considered as etiologic conservative therapy in cases when there is a good chance for the bleeding to stops spontaneously. Fullatron et al. have emphasized the efficacy of intravenous famotidine [4]. This agent does not interfere with the activity of gastric alcohol dehydrogenase, thus consequently being particularly suitable for the treatment of patients who consume alcohol regularly [3, 5, 8]. Patients undergoing surgery can also benefit from this property of famotidine, because in this case, the primary objective of surgical intervention is to eliminate the risk of a potentially fatal outcome.

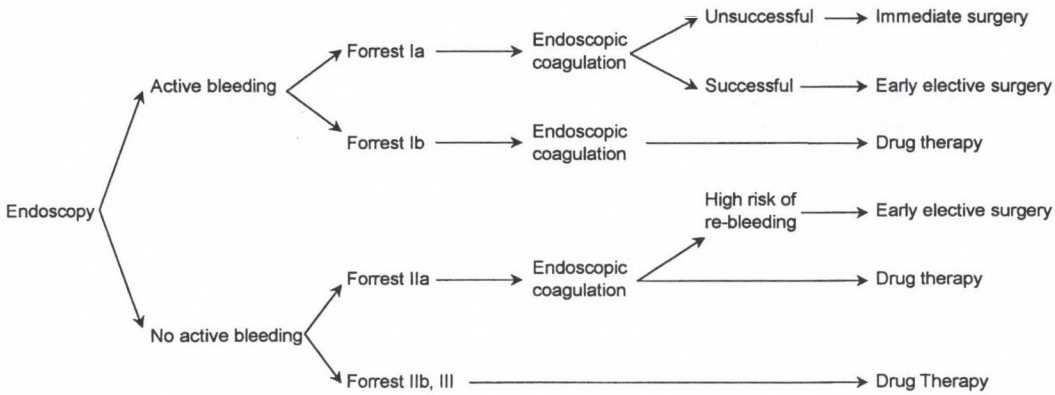

Fig. 1. Recommended therapeutic strategy for acute peptic ulcer bleeding

Finally, it seems reasonable to supplement drug therapy with antibiotics in all cases. In surgical cases this option can be exploited for antibiotic prophylaxis; whereas in conservatively treated patients, properly selected antibiotics are useful for the eradication of *H. pylori.*

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REFERRAL PATTERNS AND MOTIVATION FOR ANTI-REFLUX SURGERY OF PATIENTS SUFFERING FROM GASTROESOPHAGEAL REFLUX DISEASE

A. Bálint[1], H. J. Stein[2], W. K. H. Kauer[2], H. Feussner[2] and R. J. Siewert[2]

[1]*3rd Department of Surgery, Semmelweis University Medical School, H-1096 Budapest, Nagyvárad tér 1, Hungary*
[2]*Department of Surgery, Klinikum rechts der Isar der TU München, München, Germany*

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Due to a better understanding of the pathophysiology of gastroesophageal reflux disease (GERD), as well as the improvements in surgical technique, the number of anti-reflux procedures has increased worldwide during the last decade. This trend has been facilitated by the advent of minimally invasive surgery. Although a great number of publications deal with the indications or selection of patients for surgery, only a few discuss the motivation of patients for choosing surgery rather than long-term medical treatment.

In order to evaluate the different elements of motivation of patients suffering from primary gastroesophageal reflux disease, the data of 115 patients who had undergone anti-reflux surgery between January 1990 and June 1997 at the Department of Surgery, Technical University, Munich, were evaluated. As laparoscopic anti-reflux surgery has only been regularly performed since 1994 in our Department, the study period was divided and the two periods (1990–1993 and 1994–1997) were analyzed separately. The data were evaluated according to the referral pattern and the motivation of patients with GERD who chose surgery.

In the period from 1990 to 1993, 38.5% of the patients were referred to surgery by general practitioners, 38.5% by internists, 10% by practicing surgeons and 8% by gastroenterologists. In 5% of the cases the patients themselves initiated surgery. The corresponding results for the period from 1994 to 1997 were 29%, 38%, 12%, 8% and 13%, respectively.

The most common reason for a patient to choose surgery was moderate or only short-term response to appropriate conservative treatment, which accounted for 98% and 92% of the patients, respectively, during the study periods. This was followed by avoidance of life-long medical therapy and its potential risks in 77% and 85% of the patients. Fear of cancer was reported in 10% and 25%, respectively. In the second period, the option of a minimally invasive procedure was reported as an important factor in 45% of the patients.

Although the number of anti-reflux procedures performed per year is increasing and there is also an increasing tendency regarding the application of minimally invasive procedures, the factors leading to referral failed to show significant differences in the two periods. The motivation of patients, however, clearly changed in favour of surgical therapy, mainly because of the availability of a minimally invasive approach.

Introduction

There are two treatment options for the long-term management of primary gastroesophageal reflux disease: conservative treatment and surgical management. By application of potent anti-secretory drugs (proton-pump inhibitors) and prokinetic agents, healing of esophageal mucosal injury can be achieved in nearly 100% of patients, how-

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ever, up to 50% of patients require permanent maintenance therapy to remain in remission [10]. The severity of esophagitis on initial endoscopy, a defective lower esophageal sphincter on manometry and the presence of duodenal contents in the refluxate are predictors of a chronic or recurrent course of the disease [19]. In these patients anti-reflux surgery is a rational treatment option [9, 16, 24].

The fundoplication, first performed by Rudolf Nissen in 1955, became the standard surgical procedure to prevent the reflux of gastric contents [12, 13]. Recently, however, new technologic advances in laparoscopic surgery have resulted in a renaissance of the Nissen fundoplication [3–5]. A cost-effectiveness study comparing initial surgery versus adequate medical treatment has shown surgery to be the superior option for men 48 years old or younger and for women aged 55 or under [1]. More recent studies have confirmed this finding, showing a break-even point between the costs of anti-reflux surgery and continuous medical management after 1.4–10 years of treatment [7, 23]. Another rational justification for surgery is that it definitively treats the disease prior to the development of possible complications such as Barrett's esophagus or strictures.

Besides pathophysiologic and morphologic elements, the psychological background of the patient and the attitude of the involved physicians are also of importance in selection of the treatment strategy. While the indications and patient selection for fundoplication have been extensively discussed in earlier literature, publications analyzing the patient's point of view are rare [14, 18, 20].

Patients and Methods

Data from 120 consecutive patients with primary GERD (median age = 47 years, range: 16–84, male:female ratio: 89/31) who had undergone a fundoplication as an anti-reflux procedure between January 1, 1990 and June 30, 1997 were prospectively collected and analyzed. The indications for anti-reflux surgery were in accordance with the previously published criteria [14, 18, 19], i.e. (i) recurrent or persistent symptoms or esophagitis despite at least one 12-week course of intensive medical acid suppression therapy (usually proton-pump inhibitors) or (ii) manifest side-effects of medical therapy in patients with GERD proved by 24-hour pH-monitoring and (iii) no severe medical risk factors related to the planned surgical procedure. Patients who had undergone a redo operation or had a paraesophageal or mixed-type hiatal hernia were excluded from the study, since both their motivation as well as the indication for surgery are quite different from those with primary gastroesophageal reflux disease. In order to determine the influence of laparoscopic surgery, the period from 1994 to 1997 was analyzed separately because laparoscopic anti-reflux surgery had only been regularly applied in our Department since 1994. The data were collected by personal interviews of the patients prior to treatment according to a standardized questionnaire. The database was complete in 98.6% of patients (115/120), in 5 cases a comprehensive interview was not possible. The questionnaire consisted of two parts, one concerning the referral patterns, the other the patient's reasons for choosing surgery rather than continuous medical therapy.

The first part contained a list as follows regarding the person who sent the patient to surgery: 1. general practitioner, 2. internist, 3. gastroenterologist, 4. surgeon, 5. patient him/herself influenced by family, friends, or media. The second part described the elements of motivation: 1. lack of long-lasting response or moderate response to adequate medical therapy, 2. avoidance of long-term medical therapy and its potential risks, 3. fear of developing cancer, 4. side-effects of medical therapy, 5. option of a minimal invasive approach.

Statistics

The evaluated parameters were compared between the two study periods using standard statistical tests for nonparametric data sets. A p-level of < 0.05 was considered significant.

Results

The patient groups of the two study periods were comparable concerning their demographic data and the length of history of reflux symptoms. The first study group consisted of 39 patients with median age of 47 years (20–76), the second group consisted of 76 patients with median age of 47 years (16–84). The male:female ratio was 30/9 in the first group and 55/21 in the second group. The median length of the history of GERD was 6 (range 1–40) years in the first period, 10 (range 1–40) years in the second period. The difference between the two groups was not significant.

During the first period, 8% of the patients were referred to surgery by gastroenterologists. In the second period this proportion of patients was 12%. General practitioners were responsible for 38.5% and 29% of referrals during the two periods, respectively. 38.5% of the patients in the first period and 38% of the patients in the second period were sent by internists. Practicing surgeons contributed to 10% and 8% of referrals in the two periods. In 5% of the cases in the first, and in 13% of the cases in the second period, the patients themselves initiated surgery (Figs 1a and 1b).

The most common element of patient motivation was a dissatisfying response to appropriate conservative treatment, with 97% and 92% of patients, respectively, reporting this factor in the two periods. The second most frequent component was avoidance of life-long medical therapy and its potential risks. A total of 77% and 84% of patients listed this factor in the two groups, respectively. In the second period the possibility of minimal invasive approach was reported as an important factor by 45% of patients. Fear of developing cancer was reported in 10% and 25%, respectively, during the two study periods (Figs 2a and 2b).

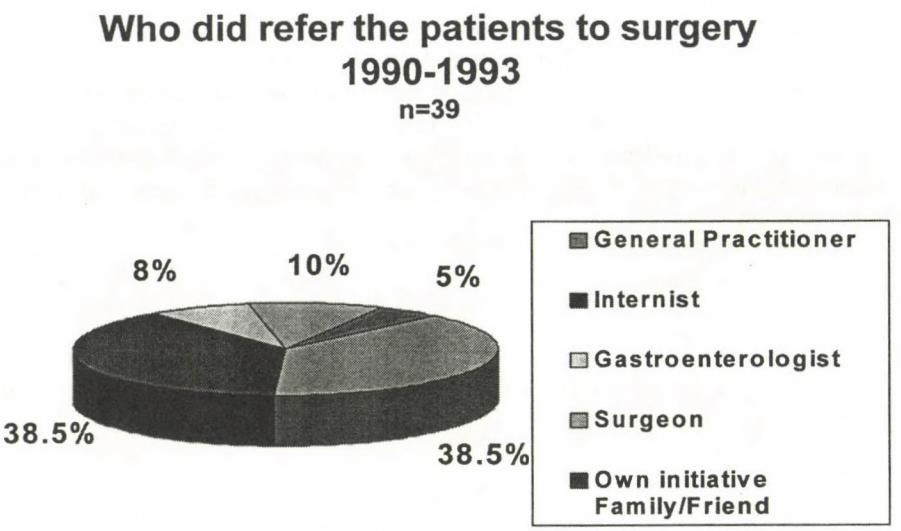

Fig. 1a. The referral patterns of patients for anti-reflux surgery in the first study period

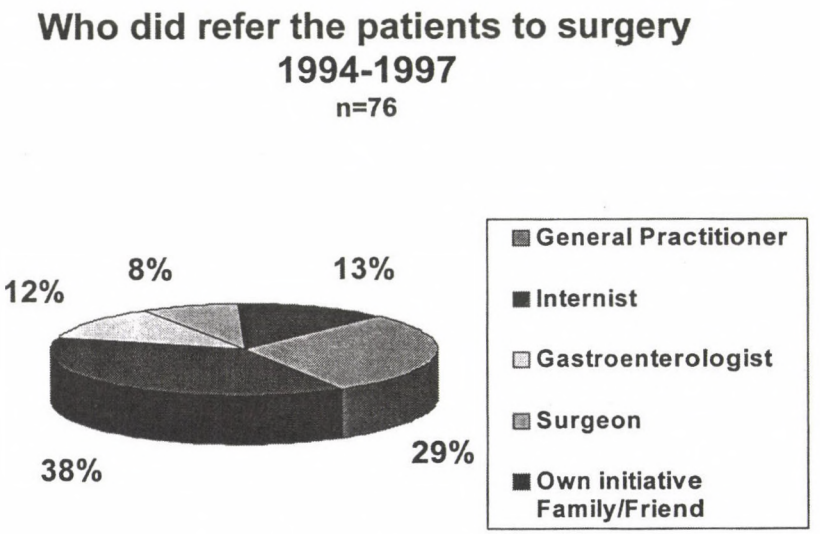

Fig. 1b. The referral patterns of patients for anti-reflux surgery in the second study period

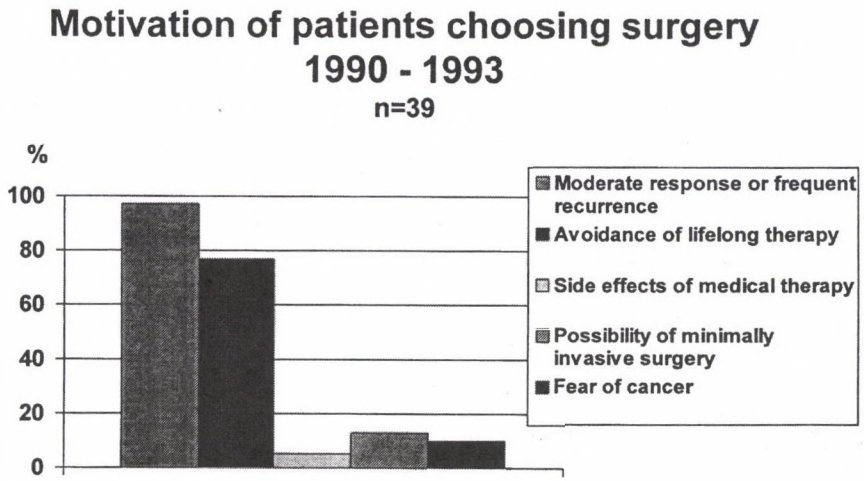

Fig. 2a. Motivation of patients for anti-reflux surgery in the first study period

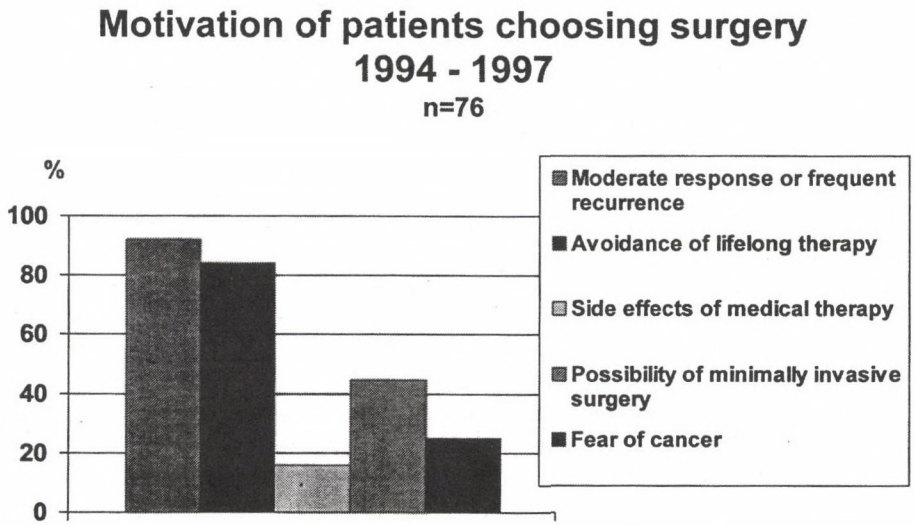

Fig. 2b. Motivation of patients for anti-reflux surgery in the second study period

Discussion

The motivation of patients choosing surgery for gastroesophageal reflux disease rather than life-long medical therapy is influenced by various factors. Besides the psychological characteristics of the patients, the importance of giving the patient adequate information in respect to the possible treatment options must be emphasized. Potential risks as well as potential benefits of each treatment option should be communicated [15, 17, 21]. To find the optimal treatment option for each individual GERD patient, a close cooperation among involved physicians should be considered to be the key element. The patient must make the final decision, but the physicians are responsible for providing the patient with objective information. This is especially true for cases that can be treated by alternative methods, in other words, in cases of facultative indications for surgery. The guidelines of the health insurance system concerning the prescription of drugs used in the treatment of gastroesophageal reflux disease should also be taken into consideration when evaluating the attitude of medical personnel in this process. These rules may influence and modify the behavior of physicians.

The referral patterns of patients showed no significant differences in the two study periods. This fact underlines the importance of continuous medical education of general practitioners as well as gastroenterologists about alternative treatment options for GERD. Primary care physicians and gastroenterologists take care of the vast majority of GERD patients, including the potential candidates for anti-reflux surgery. The data are suggestive of the fact that gastroenterologists are in particular reluctant to offer their patients the benefits of minimally invasive anti-reflux surgery. Contrary to the practice of involved medical personnel, the tendency of the patients to initiate a request for surgery has increased. This can probably be explained by the growing interest of the population regarding the management options for their individual health problems and the great volume of information available from various media sources.

Regarding the motivation of patients for surgery, the two most frequently reported elements in both groups were the merely moderate response to appropriate medical therapy and avoidance of potentially life-long medical therapy. Long-term or maintenance therapy may be inconvenient for the patient and the financial aspects (cost of drugs) also appear to be important. Two additional elements showed different incidence in the two groups. The option of minimally invasive anti-reflux surgery played an important role in the choice of therapy during the second time period. This can be explained by the evident advantages of minimally invasive anti-reflux procedure, i.e. less pain, faster recovery, and earlier return to work [2, 6, 22].

Interestingly, more patients reported the fear of developing cancer in the second period than in the first, a reflection of the population's growing fear of developing cancer. However, it must be mentioned that according to the available literary data, anti-reflux surgery does not reliably prevent esophageal adenocarcinoma once a Barrett's esophagus is present. It is evident that fear of cancer alone cannot therefore be an indication for anti-reflux surgery. Patients with Barrett's esophagus must also be followed up after a successful surgical intervention [11].

Surgery, especially minimally invasive surgery, plays an increasing role in the management of primary gastroesophageal reflux disease, but prospective follow-up studies are needed to confirm its clinical value and reliability. The minimally invasive antireflux surgery has been accepted by the patients, however, this was not reflected in the practice of physicians taking care of GERD patients.

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DEVELOPMENT OF A SURFACE MODIFIED SILICONE-KERATOPROSTHESIS WITH SCLERAL FIXATION

Tatjana von Fischern[1], Stéphanie Langefeld[1], Liya Yuan[2], N. Völcker[3], M. Reim[2], B. Kirchhof[2] and N. F. Schrage[2]

[1]*Interdisciplinary Centre of Clinical Research (IZKF) BIOMAT, Technical University of Aachen, Paulwelsstr. 30, D-52057 Aachen, Germany*
[2]*Department of Ophthalmology, Technical University of Aachen, Pauwelsstr. 30, D-52057 Aachen, Germany*
[3]*Department of Textile and Macromolecular Chemistry, Technical University of Aachen, Veltmanplatz 8, D-52062 Aachen, Germany*

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Background: Many attempts have been made to create artificial corneas. The keratoprostheses currently available do not allow measurements of the intraocular pressure (IOP) and restrict the visual field. The main problem is extrusion due to an insufficient connection between implant and surrounding tissue. It is our aim to create a flexible keratoprosthesis with a wide field optic allowing measurements of the IOP. Surface modification will improve cell adhesion and therefore stability between implant and tissue.

Methods: The keratoprosthesis is made of silicone rubber. The optical zone is 11 mm in diameter with a thickness of 0.3 mm. The surface modified haptic consists of a scleral rim and 8 branches for scleral fixation. Optical and mechanical qualities were tested by tensile tests, spectrophotometry and topography.

Results: A method to produce one-piece silicone keratoprostheses was established. Submicron lathing of the mould led to an excellent optical quality. Spectrophotometry showed high degree of visible and ultraviolet light transmission of the silicone. Mechanical tests revealed high tensile strength and elongation at break which were not impaired by surface modification.

Conclusion: The production of a flexible silicone keratoprosthesis with high optical and mechanical properties was accomplished, with possible use as both permanent and temporary keratoprosthesis.

Introduction

In the past, a large number of different types of keratoprostheses have been developed for the treatment of corneal blindness. Currently, there are several models in clinical use. Most of them consist of a rigid optical cylinder and a rigid or flexible flange for corneal fixation [3, 8, 11, 12]. Although some of these keratoprostheses have been implanted successfully in humans with a sufficient visual outcome [1, 11], there still remain major disadvantages:

1. Glaucoma is a frequent complication after keratoprosthesis implantation [5, 10]. All currently available keratoprostheses do not allow measurements of the intraocular pressure (IOP). Diagnosis of glaucoma is restricted to digital assessment of the IOP and funduscopic observation of the optic nerve head. As the patients' visual fields are con-

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siderably reduced by the length and diameters of the optical cylinders [14], perimetry survey is limited to late stages of glaucoma.

2. Funduscopy of the peripheral retina is difficult or even impossible. Therefore retinal detachment is not easy to discover and treat.

3. Cosmetical restitution remains unsatisfactory, especially in case of through-the-eye-lid-keratoprostheses [7].

4. The main problem after keratoprosthesis surgery is still extrusion of the implant [2, 4, 9, 13].

Considering these aspects, a flexible one-piece keratoprosthesis with a large optical zone similar to the human cornea was developed. A chemical surface modification of the haptic would improve cell growth across the polymer/tissue interface and thereby stability between implant and surrounding tissue. In addition, a scleral fixation would prevent extrusion.

Properties of the "Aachen" keratoprosthesis

I. Design

The one-piece keratoprosthesis (Fig. 1) is made from a polydimethyl-siloxane free of phenyl-groups.

The optical zone is 11 mm in diameter and is 0.3 mm thick. The spherical anterior surface has a radius of curvature of 7.8 mm.

The surface modified haptic consists of a scleral rim and 8 branches being sutured to the sclera. The haptic is to be covered by conjunctiva leaving the optical zone uncovered.

A ridge at the back of the keratoprosthesis fitting into the corneal trephination hole similar to the Eckhardt-Keratoprosthesis is incorporated as an aid to prevent the adherence of a retroprosthetic membrane and to avoid leakage.

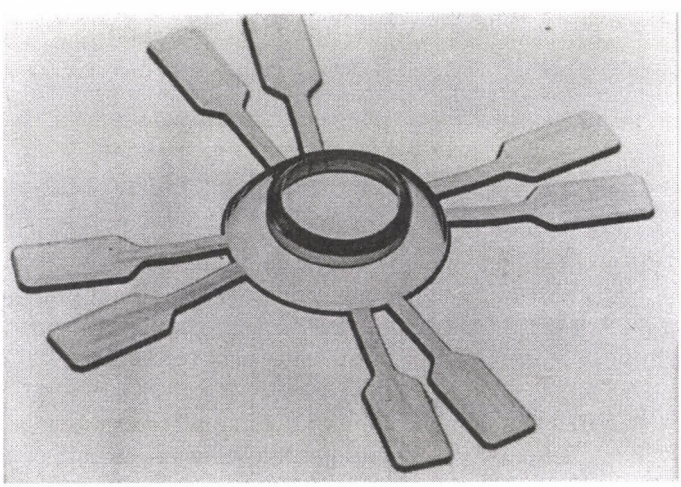
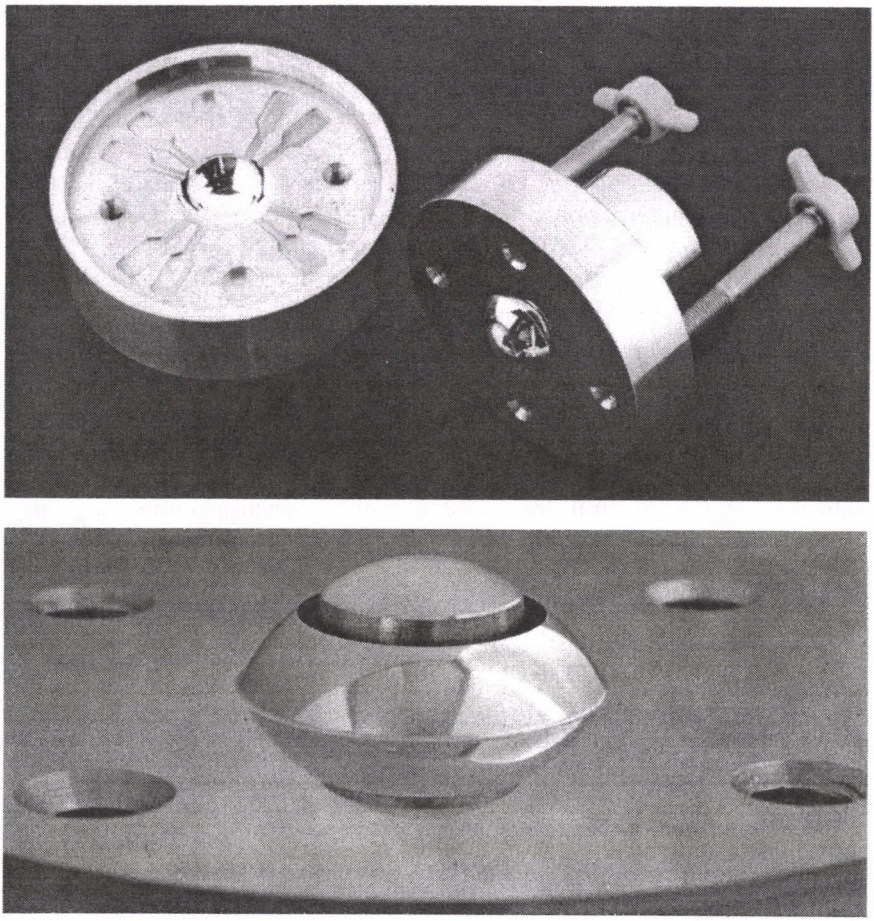


Fig. 1. The "Aachen" keratoprosthesis



Figs 2 and 3. Aluminum-mould, the central part treated with submicron lathing technique

II. Production

The keratoprosthesis can be manufactured in the laboratory apart from the surface modification requiring special technical equipment. The haptic surface is modified by argon-plasma-etching and graft-copolymerisation of polyacrylic acid. Afterwards, the cell adhesion protein fibronectin can be bound covalently to the modified surface.

III. Optical system

The optical quality of the keratoprosthesis is excellent due to the treatment of the mould (Fig. 2) using a submicron lathing technique. Even fine concentric ridges do not occur usually observable after conventional lathing of the mould (Fig. 3).

The calculated refractive power of the optical system after implantation in the aphacic eye is 42.79 diopters (Gullstrand's eye, refractive index of silicone = 1.415, refractive index of aqueous = 1.336, assumed axial length = 23.3 mm).

For topography, a keratoprosthesis is placed in a water-filled pressure chamber. The chamber is connected to a pressure trans-ducer (Menuet, Dantec). Topography (C-Scan, Technomed, Germany) is assessed at chamber pressures varying between 0 and 200 mm Hg. Elevation of the pressure in the water-filled chamber decreases the radius of curvature considerably (Fig. 4). The initial central radius of curvature is 7.72 mm at 0 mm Hg, with a decrease to 6.03 at 200 mm Hg. This steeping is completely reversable. In-between 0 and 80 mm Hg there is a linear dependence of pressure and anterior curvature ($R^2 = 0.9515$). With a pressure rise of 10 mm Hg the anterior curvature decreases about 0.1 mm.

IV. Spectral transmission

Evaluation of the spectral transmission with a spectrophotometer [Cary(1)UV-visible spectrophotometer, Varian] shows a high degree of ultraviolet and visible-light transmission for silicone. Surface modification does not influence the light transmission of the silicone. Storage of the silicone in silicone oil for intraocular tamponade (adato ®Sil-ol 100 and 5000, Adato-med ®GmbH, Germany) for six months shows only slight alteration of the spectral transmission (Fig. 5).

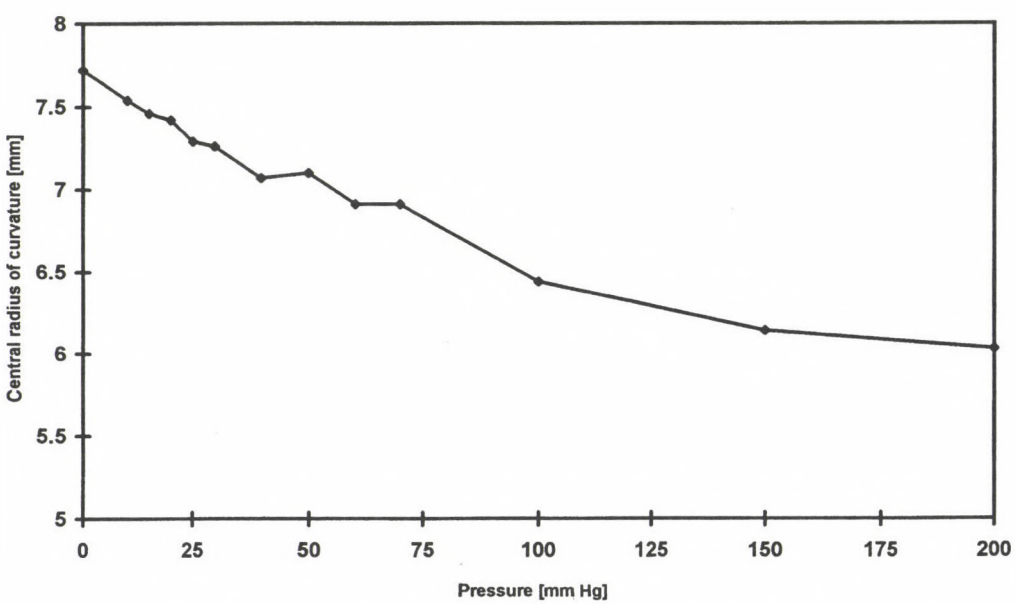


Fig. 4. Topography of the keratoprosthesis at various pressures in the pressure chamber

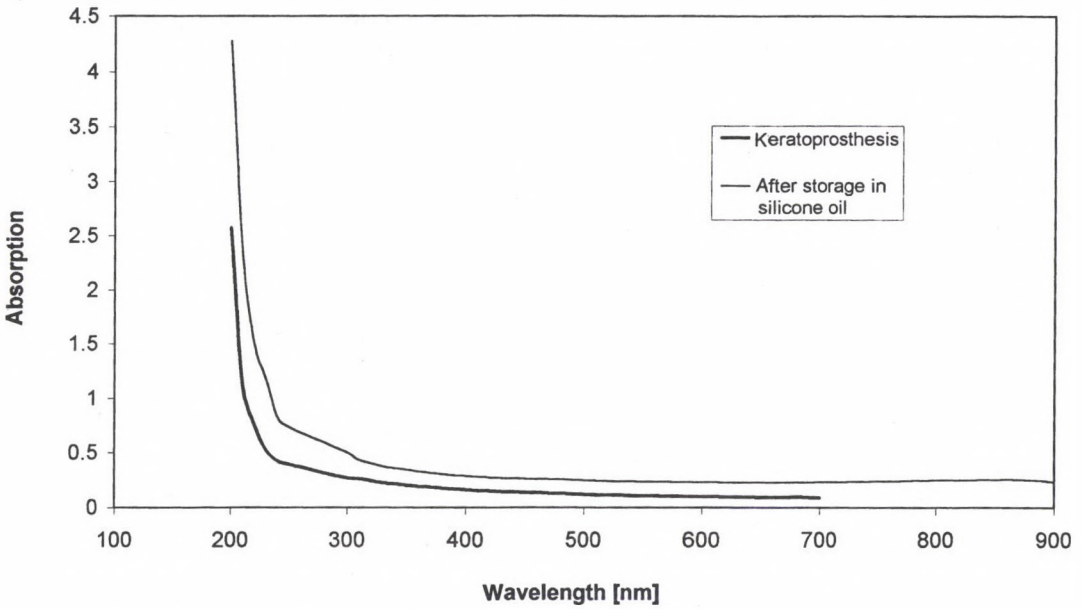


Fig. 5. Spectral transmission of the keratoprosthesis before and after storage in silicone oil for intraocular tamponade

V. Mechanical properties

Tensile tests are conducted according to DIN 53504. Testing and conditioning of the samples are performed at 24 °C and 45% relative humidity. Type S2 shaped specimens with a mean thickness of 1.87 mm are tested. Tensile strength and percentage elongation at break are measured with a Zwick® testing machine (Zwick 1456 UPM 14×6, Germany) equipped with an automatic multisense extensometer, the grips set to the standard length of 20 mm. The samples are elongated at a constant strain rate of 200 mm/min as recommended for type S2 specimens.

Table 1
Mechanical tests of silicone samples (mean value of n = 11) and surface modified silicone samples (mean value of n = 8)

Material	Elongation at break (%)	Tensile strength (N/mm^2)
Silicone	403	10.05
Silicone with polyacrylic acid	475	8.125

Mechanical tests at 11 unmodified and 8 surface-modified silicone test pieces reveal high tensile strength and elongation at break for both the pure silicone and the surface modified silicone (Table 1). Even after perforation in the centre of the test piece with a surgical needle the elongation at break is still high with a mean value of 233% (mean value of n = 4).

Discussion

Among all keratoprotheses, which have been implanted successfully in the past, the Strampelli-Osteo-Odonto-keratoprosthesis seems to have the lowest extrusion rate and the best long-term results. Biocompatibility of the material especially in the haptic region obviously plays an important role as far as extrusion of the implant is concerned. For this reason we tried to find a material which promotes cell adhesion on its surface. The silicone rubber chosen has mechanical properties similar to the human cornea and good optical qualities. The hydrophobicity of silicone rubber leads to poor cell growth. We consider these properties to be ideal for the optical part of the keratoprosthesis where cell growth is not desired. In order to improve cell growth on the haptic region, this part of the keratoprostheses is hydrophilised and surface modified as described above. Covalent binding of cell adhesion protein on the silicone's surface will accelerate cell adhesion and proliferation. By this means, a permanent and tight fusion of the keratoprosthesis with the host tissue is assumed. Downgrowth of epithelium into the anterior chamber will hopefully be prevented by the design and surface modification of the keratoprosthesis.

Hydrogel sponges, used by the Australian keratoprosthesis research group for corneal fixation of the implant, are reported to have a high tendency to tear [6]. Suturing of the "Aachen" keratoprosthesis to the sclera is possible due to the excellent mechanical properties of the silicone rubber. As described above, a perforated test specimen can be extended up to 233% of its original length before it bursts.

Topography showed that a pressure rise in the eye leads to changes in the curvature of the keratoprosthesis optical zone. This effect might be helpful in the diagnosis of glaucoma, in which case the patient becomes more myopic. Assuming a refractive change for the keratoprosthesis of +0.7 diopters/–0.1 mm change of anterior curvature, we can conclude that a pressure rise of 10 mm Hg causes a refractive change of about +0.7 diopters. In these special cases refraction and topography might be additional diagnostic tools for the detection of glaucoma.

The "Aachen" keratoprosthesis is very flexible due to its slight thickness of only 0.3 mm and the material properties of the silicone. Preliminary yet unpublished investigations have shown that pressure measurements can be carried out with standard ophthalmological tonometers. Different kinds of tonometry are to be tested and the adequate method is to be found for keratoprosthesis-tonometry.

Ultraviolet radiation transmission of the silicone rubber has been demonstrated to be high. This will cause problems especially in aphacic patients and regarding eyes which are filled with silicone oil for intraocular tamponade. Retinal damage by UV-light is likely. For this reason, a UV-absorbing agent has to be integrated into the silicone. Until

such UV-protection is not realized, patients will have to wear laterally closed sunglasses while staying outside. The need for an aphakia correction might warrant the sufficient glass wearing for UV-protection.

Conclusion

Authors accomplished the production of a flexible one-piece keratoprosthesis having high optical and mechanical qualities, with recent first clinical applications as temporary keratoprosthesis in vitreous and retinal surgery as well as permanent keratoprosthesis. The results of these are soon to be reported.

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ASYMPTOTIC PARATHYROID CYST – DIAGNOSTIC DIFFICULTIES (A CASE REPORT)

S. Jaroszewicz[1], L. Cyryłowski[2], Maria Chosia[3], P. Szlarb[1], Maria H. Listewnik[4] and Anna Walecka[2]

[1]Department of General Surgery and Surgery of the Hand, [2]First Department of Radiology, [3]Department of Pathology, [4]Department of Radioisotope Diagnostics, Pomeranian Medical Academy, Unii Lubelskiej 1, P-71-252 Szczecin, Poland

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The case of a 70-year-old female with asymptotic parathyroid cyst is presented. It was not possible to make a proper diagnosis preoperatively. The correct diagnosis was based on the result of the postoperative microscopic examination of the resected tissues. The diagnostic difficulties are discussed.

Introduction

The parathyroid cyst is a very rare entity. After the first report by Swedish medical student Sandstrom in 1880 and the first resection of this lesion by Goris in 1905, 239 cases of parathyroid cysts were reported in the literature [2, 8, 12, 14, 16, 17]; with 15% of the cases accompanied by hyperparathyroidism [3, 4, 7, 18]. The neck is the most common localization of the cyst, but it is also found in the mediastinum, reported by de Quervain for the first time in 1925, and as many as 21 cases of this localization have been observed until 1993 [2, 9, 14, 19]. The last report in the Polish literature concerning the cyst and hyperparathyroidism was published in 1980 [20]. Usually, the cyst are small-sized (the diameter of several cm) and filled with clear liquid. They are 2-3 times more frequent in females [3, 7, 10, 14, 18, 20] aged between 30 and 50, with the cysts in males more frequently accompanied by hyperparathyroidism [14, 17, 18, 20, 22]. The aetiology of the parathyroid cyst is still unknown. Its formation is attributed to developmental disorders – pertaining to the 3-4th brachial cleft, secrete retention, fusion of small cysts, infarction or degeneration of adenoma. A multiplicity of hypotheses may evidence a heterogeneous mechanism for the formation [4, 6, 7, 11, 14, 16–18, 20, 25]. A case of a patient subjected to parathyroid cyst resection, as well as the difficulties related to preoperative diagnostics are presented below.

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Case Report

A 70-year-old female (case record No. 140/1260/97) was admitted to the Clinic of General Surgery and Surgery of the Hand on January 20, 1997 with a diagnosis of thyreotoxic goitre and a presence of a tumour on the left side of the neck. Before that, she was treated with thiamazole since January 1996, and euthyreosis had been achieved. She was also treated because of hypertension (II WHO) since 1979, and because of diabetes (with talbutamide) since 1995. In April 1996 she was diagnosed with thyreotoxic thyroid gland enlargement, and beside the enlarged and unsymmetrical thyroid gland, a cystic lesion near the left carotid vascular bundle was discovered. Radioisotope examination performed in June 1996, confirmed the state of euthyroidism (TSH – 0.32 mIU/l, FT4 – 13.63 pmol/l, FT3 – 4.54 pmol/l). The patient was admitted to the First Department of Radiology of the Pomeranian Medical Academy on June 17, 1996 (case record no. 759/7317/96) for continuing preoperative diagnostics. Ultrasound examination of the neck raised suspicion of aneurysm on the left common carotid artery the size of 4.4 × 2.7 cm (Fig. 1); Doppler sonography showed maintained blood flow in common, external and internal carotid arteries. The diameters of the arteries were of normal size. A cyst the size of 43 × 22 × 17 mm could be seen in the left supraclavicular region. The

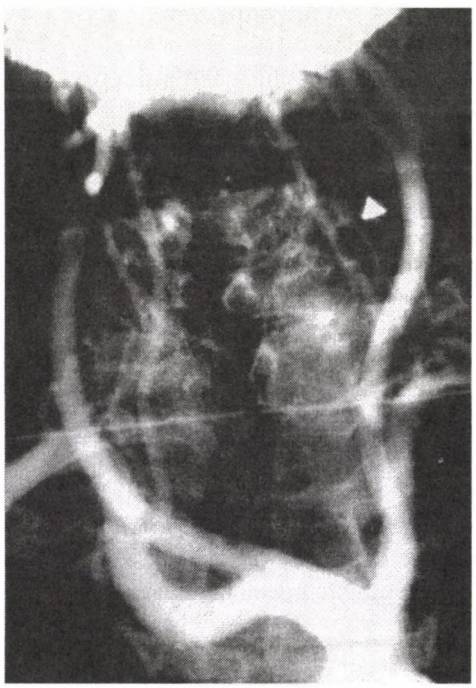

Fig. 1. Ultrasound imaging of the lesion: fluid lesion behind the thyroid; involvement of the internal carotid artery could not be excluded

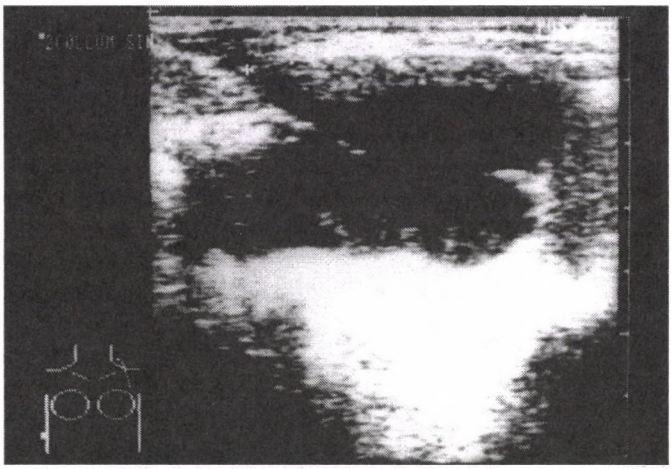

Fig. 2. Aortography: no connection between the lesion and the carotid arteries could be found

patient could not be operated on because of subendocardial infarction. Upon recovery she was discharged from the hospital, and re-admitted on January 20, 1997. The follow-up ultrasound examination (January 27, 1997) revealed a large fluid-filled lesion the size of 2.3 × 5 cm in the left supraclavicular region. It was not possible to determine unambiguously whether the lesion was in contact with a vessel, therefore, aortic arch arteriography was performed using the classic Seldinger technique. No pathologic vessel was detected on the neck. Only moderate modeling with lateral shift of the left common carotid artery was observable (Fig. 2). In addition, left selective vertebral arteriography was performed, with no lesion found. Other preoperative laboratory analyses included RBC 4.2, HGB 11.0, HT 33.4, WBC 6.6; ions: Na 140 mm/l, K 3.98 mmol/l, Ca 2.58 mmol/l, P 0.92 mmol/l, Cl 103.25 mmol/l; serum total cholesterol 193 mg/dl, serum total proteins 71.5 g/l; circadian glycemia profile: 6^{00} – 130.6, 10^{30} – 196.6, 16^{30} – 107.4, 21^{30} – 162.0. With the diagnosis of thyreotoxic goitre and tumour of the neck, the patient was submitted to surgery, performed under general anaesthesia. Almost total, bilateral resection of the thyroid lobes was performed in the typical manner, during the course of which a 60 × 50 × 50 mm sized cyst localized behind and loosely accreted to the left lobe (Fig. 3) was totally resected. Histological examination of the resected tissues (No. N-4340-5/97) revealed nodulous goitre and a thin-walled cyst with a diameter of around 5 cm, filled with clear fluid with the parathyroid tissue in the cyst wall. Postoperative laboratory analyses showed: RBC 4.29, HGB 12.4, HT 36.1, WBC 7.9; ions: Na 144 mm/l, K 4.24 mmol/l, Ca 2.18 mmol/l, ionised Ca 1.16 mmol/l, P 0.91 mmol/l, Cl 103.25 mmol/l; serum total proteins 71.5 g/l; circadian glycemia profile: 6^{00} – 124.0, 10^{30} – 160.0, 16^{30} – 155.0, 21^{30} – 138.8.

No complications occurred during the postoperative period and the patient was discharged on the 8th postoperative day.

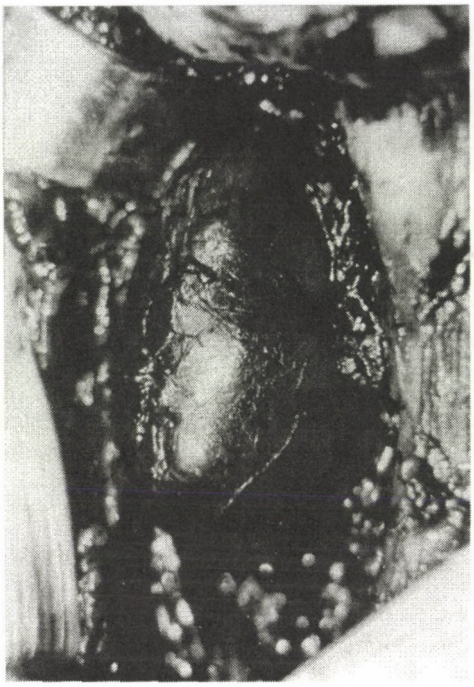

Fig. 3. Intraoperative picture and localization of the cyst

Discussion

Parathyroid cysts are seldom occurrences, although being more frequent than so-called true cysts, i.e. without functional disorders [6, 10, 14–16]. It is very difficult to make a preoperative diagnosis of an asymptotic parathyroid cyst due to its rare occurrence [3, 4, 18, 20]. When diagnosed in the early stage, it can be emptied by means of fluid withdrawal during the fine needle biopsy of the "tumour" [3, 6, 7, 14, 18]. The symptoms of hyperparathyroidism were undetected in our patient before the surgery; she was diagnosed to exclude aneurysm of the carotid artery, according to the ultrasound findings. Nies et al. [17] describes similar difficulties in differentiation between the parathyroid lesion and the innominate artery aneurysm. Most often, the lesion is described as a "cold nodule" in the scintigraphy of the thyroid, and complementary ultrasound examination of the thyroid gives more precise description of a fluid cistern – a cyst, usually located in the thyroid [3, 6, 16, 18, 21, 23]. If ine needle biopsy is performed, clear and colourless fluid is usually obtained [1, 3, 4, 7, 13, 14]. Intraoperatively, the parathyroid cyst is usually separated from the thyroid, and has a thin, unvascularized capsule, filled with water-coloured fluid [4, 16, 18, 22, 25, 26]. It is usually located on the left side, below the thyroid. This is emphasized in reports by Asfar and other investigators [1, 21], who encountered such localization in 95% of their patients, as

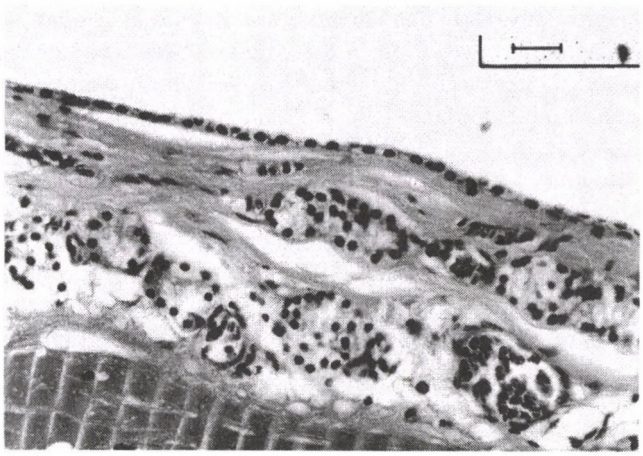

Fig. 4. The fibrous cyst wall is visible, with nests of parathyroid tissue, lined by a single layer of epithelium. Hematoxylin and eosin staining, magn. ×400

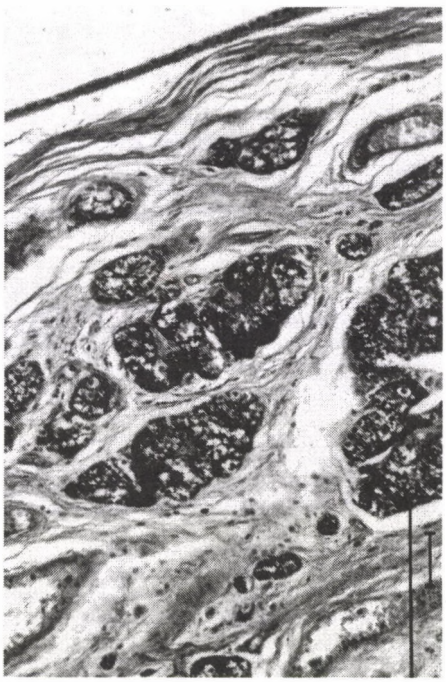

Fig. 5. The cyst wall can be seen glycogen in the parathyroid principal cells and lining epithelial cell. PAS method, magn. ×200

was the case in the present report. The correct diagnosis of our patient was based on the results of the microscopic examination of the resected tissues, which revealed a thin-walled, unilocular cyst, lined with simple cuboid epithelium composed of clear cells, containing glycogen in the cytoplasm (Fig. 4). Scattered clusters of normal parathyroid tissue could be found in the cyst wall. The principal cells with clear cytoplasm containing glycogen dominated in the clusters; fewer cells with eosinophilic, granular cytoplasm and pycnotic nuclei could be seen among these cells (Fig. 5). Similar microscopic images have been reported by other authors as well [5, 10, 13, 24]. The present case has been reported on because of the difficulties pertaining to the preoperative differentiation of tumours of the neck. In case of a "cold nodule" in the thyroid region, one should always bear in mind the possibility of the existence of a parathyroid lesion.

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EXPERIENCES OF 25 ORTHOTOPIC ILEAL NEOBLADDERS

D. L. Répássy, S. Csata, Gy. Tamás, A. Bécsi and T. Weninger

Department of Urology, Szent István Hospital,
H-1096 Budapest, Nagyvárad tér 1, Hungary

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Authors report on their results obtained from orthotopic ileal neobladders following 25 cases of radical cystectomy. Analysis is given of the possible complications, their prevention, as well as of surgical techniques. It is determined that orthotopic ileal neobladder is one of the best bladder substitution methods, giving the patient a chance for a high quality of life.

Introduction

Removal of the bladder necessitates one of the methods of urine conduit or bladder substitution. Cystectomy due to infiltrative, malignant bladder tumor is from oncological point of view a curative and therapeutic step determining prognosis. For the purposes of health, reconstruction and rehabilitation, however, it is important that urine conduit, bladder substitution be as flawless as possible. The variety of methods have differing complications and risks, in certain cases even leading to life-threatening conditions and death. Upon considering these, selection of the optimal diversion method as well as surgical success are both basic determining factors in the patients' later quality of life.

There is no doubt that the best quality of life is provided by orthotopic ileal neobladder [1, 2]. Several methods of bladder substitution have been elaborated in the past decade, but none of them are complication-free solutions. One of the best substitute bladders is the Hautmann-type 'ileum neoblase' [3–5]. We used this method for operating 25 patients between the period of 1st January, 1996 and 1st June, 1998. The obtained results are summarized in the followings.

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Patients and Method

Between 1st January, 1996 and 1st June, 1998 a total of 25 radical cystectomies were performed due to infiltrative bladder carcinomas at the Department of Urology of the Szent István Hospital in Budapest. The average age of the patients was 63 years (48–80). The indication of surgery by means of transurethral resection was infiltrative bladder tumor, proved histologically. Details of indication have been reported on in a previous paper.

Bladder substitution was carried out in accordance with the ileal neobladder method described by Hautmann [1–5] – applying minor modifications. Within the above period, only those patients received urine conduit with a method other than the Hautmann-type, who showed the following contraindications or one of them:

– chronic kidney failure,
– chronic intestinal disease, inflammation, growth disturbances,
– tumorous infiltration of the urethra.

Our present study of the 25 cases does not include these patients.

Lymph node positivity manifest during surgery, easily attendable damage to the rectum, as well as old age of the patient were not considered contraindicative factors. A natural contraindication was, however, the patients' general biological state, which would have meant a direct life-threatening risk even anaesthesiologically in performing such an operation and in the hazardous postoperative period, respectively.

The patients were checked at least fortnightly in the first three months following surgery (UH, routine laboratory tests, ASTRUP, uriculture). In case of complications, the control studies were performed as frequently as necessitated, but all patients were regularly checked every three months.

Tables 1 and 2 demonstrate the complications which typically arise from the direct nature of the operation. Table 1 shows the continence, incontinence, hypercontinence data related to urethral anastomosis, Table 2 demonstrates the occurrence of reflux and obstruction arising as a consequence of ureteral implantation.

The general complications which may arise in case of any large-scale abdominal operations – thus bladder substitution as well – are shown in Table 3.

Table 1
Complications related to urethral anastomosis (n = 25)

Continence	17
Incontinence	
– complete	1
– nightly	3
– slight, periodical	2
Hypercontinence	
– total retention	2

Table 2
Complications related to ureter implantation
(n = 25)

1. Reflux	–/25
2. Ureteral disturbance	4/25
– anastomosis obstruction	2/25
– ureteral strangulation	2/25

Table 3
General abdominal and consequential complications

Complications	Case No. (n = 21)
Preoperative death	–
Urinary wetting	14
Intestinal anastomosis stitch insufficiency	1*
Ileus	–
Abscessus	–
Bleeding	–
Wound parting	2*
Lymphokele	–
Pneumonia	3
Pulmonary embolism	1
Thrombosis	–

*Reoperation was needed in these 3 cases.

Results

Table 1 summarizes the data on continence, incontinence and hypercontinence. These can firstly be brought into connection with the error of urethral anastomosis, although other factors may also play role. We have divided the symptom of incontinence into three categories:

– complete incontinence: meaning that the patient has to be put into diapers,

– night incontinence: the patient is continent during the day, but slight incontinence appears during the night, possibly necessitating diapers,

– periodical incontinence: when the patient is continent in general, with the occasional occurrence of incontinence for one or two days.

By hypercontinence we mean a disturbance in urination, residues or total retention. These two categories are shown in the Table.

Table 2 comprises the data on VUR and ureter passage disturbance-obstruction, fibrosis.

Stagnation was manifest in four cases, in one case the cause was anastomosis obstruction, in the other three cases ureter strangulation or periureteritis. There was no occurrence of VUR in our patients.

In 14 cases urinary wetting occurred in the postoperative period lasting for 3 to 14 days (Table 3) the source of which was not verified according to each case. Sooner or later the urine seepage ceased in all of the cases, there was no need for another operation.

Table 3 lists further general complications, including such complications for the sake of completeness which did not occur in our material, but have been noted in world literature. Another operation was necessitated in three cases: two because the wounds opened and one due to ileum-suture insufficiency.

Ileus and subileus, respectively, were experienced in 7 cases, the causes of which were partly on mechanical and paralytical grounds. In all cases the solution was medicinal treatment, with no need for surgical exploration.

Pneumonia, atelectasia occurring in the postoperative period was found to be less frequent in our material as compared to the literary data (4 cases).

We had no cases of preoperative death.

During the course of the controls, 16 patients were found to have slight hyperchloraemic acidosis, which could easily be kept in balance by giving bicarbonate of soda per os [22, 23].

Discussion

Continence–incontinence

Almost 50 years have passed since Bricker [7] first used the small intestines for the purpose of urinary diversion. His method is still in use worldwide. This type of incontinence conduit has gone through many modification, and a variety of continence conduits, 'pouches' have been constructed, all of which have greatly improved the patients' quality of life [8–12]. The greatest leap in development has been the use of orthotopic, bladder substitution techniques introduced 10–12 years ago [1–5, 13–15], providing the patient with the best possible rehabilitation, continence and voluntary urination.

Continence is ensured by two conditions:

1. intact sphincter (outer sphincter, rhabdosphincter) and its innervation,
2. appropriate reservoir (ileal neobladder).

ad 1: The procedure in case of cystoprostatectomy is similar to that of the nerve sparing radical prostatectomy [16]. It is important that no dissector is led beneath the urethra instead, the urethra should be resected as far proximal as possible, by means of the prostate pulled back with the catheter. In such manner most part of the rectourethral muscle fibres also remain intact. Another important step is that there is no anastomosis-stitch at six o'clock. For the purpose of nerve sparing, the neurovascular bundle running on both sides of the rectum is preserved, therefore ensuring innervation [16].

ad 2: In order to ensure undisturbed urine conduit from the kidneys, as well as good capability of urine continence and voluntary urination, the followings should characterize an orthotopic ileal neobladder:

a) Appropriate degree of capacity

A capacity of at least 1000 ml is obtained by means of a spherical cut performed on a 60 cm long ileal segment. This allows for urination to be suffiecient 4–5 times during the day [1, 2].

b) Low intravesical pressure

This is one of the conditions for continence, since only the outer sphincter is functioning, which is uncapable of keeping too great a pressure in balance. The other essential role lies in reflux hindrance, even if there is no antireflux ureterimplantation.

Appropriate capacity and low pressure are provided by the geometric shape and regular spherical configuration of the ileal neobladder. A 60 cm long ileal segment has less capacity than a similar length of detubularized, spherically cut small intestine. It is the W or M forms that ensure the spherical-like shape. Besides these, however, there is another important factor, being the dilatation capability of the bladder wall which arises partly from the physical characteristics of the wall, and partly from the contractility of the motor innervation.

During the course of urine collection, the pressure only starts to rise with the growth in volume when the bladder wall has reached this dilatation limit. At the time of urination, the patient voluntarily raises the intravesical pressure by applying abdominal pressure. In ideal cases there is no stress incontinence, since the sphincter keeps in balance with the pressure brought about by coughing.

It is the small intestines which have the best contractility and dilatation ability befitting the afore-mentioned conditions. According to the studies of Martins [17], the small intestines are thus more suitable for the preparation of reservoirs than the large intestines. According to Hautmann [1, 2] continence during the day can be reached in 90 with this method. Our results (Table 1) are in accordance with this ratio.

On rare occasions hypercontinence may occur, with a large amount of residue, total retention and possible overflowing incontinence. Most of the time, the cause is urethra stricture, a weak abdominal wall, powerless abdominal press, the patient's insufficient collaboration. The latter factor is of great importance since there is no stimulation to urinate; this is substituted by the patient's feeling of abdominal fullness. All these, as well as the action of urination have to be learnt by the patient – which sometimes taking weeks, even months.

Ureteroileal stricture, questions of reflux-antireflux

One of the most problematic steps in any urinary diversion technique is the implantation of the ureter(s) into the small or large intestines, conduit, or ileal neobladder. The two most important, most frequent complications are reflux and anastomosis obstruction, or other passage disturbances. Many methods have been applied in order to prevent reflux Leadbetter [18], Bricker [7], Slpit-cuff nipple [19, 21], le Duc [6].

No reflux was experienced in any of our 25 cases (49 ureters, 1 solitary kidney), in which a simplified, pulling in and fixing technique was used with lengthy spatulated, open ureters. According to our experiences with these cases, it is our opinion that in the instance of low pressure ileal neobladder there is no need for any antireflux operative manouvering. By means of the ileal neobladder's low pressure, balance is kept by the ureter's peristaltic tone.

In two of our cases, however, we noted dilatation due to anastomosis obstruction.

Besides the above-mentioned two complications, passage disturbance is quite worthy of note. This can develop as the consequence of the ureter's unsuccessful transposition, localization or fixation, or because of periureteritis, retroperitoneal fibrosis. Both ureters should be well mobilized quite lengthily upwards so as to ensure their adequate length for tension-free implantation. For this purpose, the left ureter has often to be led through the mesosigma in medial direction. If the retroperitoneal tunnel is not wide enough or there is a fracture on the ureter because of the arteria sigmoidea, a passage disturbance may develop. Further two of our cases showed such complications.

Hyperchloraemic acidosis is a nonsurgical-technical, but an ileal neobladder-related complication. It develops mainly in cases of insufficient kidney function and/or significant residue. The slight degree of acidosis occurring in 16 of our patients could easily be kept in balance with medical treatment [22, 23].

General abdominal surgical complications

Compilation of the literary data [1, 2, 20] showed that in 15% of cases reoperation is necessitated due to abdominal complications, and the most frequent cause was found to be ileus.

Mechanical ileus develops mostly because of strangulation: an intestinal loop may slip under the ileal neobladder's mesenterium-peduncle or under the too highly fixated ureter. Inner hernation is also possible through the improperly closed opening of the reconstructed mesenterium, or under the parietal peritoneum turned up for the *infra*peritonization of the ileal neobladder. It is our experience that surgical exploration is rarely needed because of postoperative subileus, ileus. Most of the time the strangulated intestinal loop can be freed with bowel-moving medication, following which the passage is restored. Reoperation was only necessitated in one of our cases because of bowel anastomosis insufficiency.

In two cases secondary reconstruction was required due to wound parting.

A frequent phenomenon is urinary wetting – in 15–20% of cases according to the literature [1–5], more often in our material (Table 3: 14/25). Urine leaking may have a number of causes: urethral anastomosis, implanted ureters, long rows of stitches on the ileal neobladder. In our opinion surgical exploration should be avoided here as well, even in cases of peritoneal excitement symptoms.

Urinary wetting mostly leads to benign peritonitis, which heals relatively well upon ceasing the cause. The most important task is to ensure drainage; that is, the urethral catheter should be periodically washed through.

Indirect complications

This lengthy operation putting a big burden on the patient, as well as the postoperative period, mean further complication risks. Circulatory and respiratory problems, pneumonia, atelectasia, sepsis may develop, which might also endanger the patient's life. The risk of thrombosis is also high, with consequential pulmonary embolism.

Table 3 comprises these data as well, since they occur in the literature [1–5] – although such complications were only rare in the course of our cases.

Conclusions

The Hauptmann-type ileal neobladder is one of the simplest, most successful methods of bladder substitution following radical cystectomy. This is not a complication-free technique either, none the less, it provides for excellent low pressure, continence and in the long run a better quality of life for the patient. The procedure does not involve more complications than any other orthotopic bladder substitution method [1–5] and the advantages are beyond argument. Nevertheless, it is our opinion that the simplicity of this surgical procedure is only relative. Several unforeseeable difficulties, critical phases have to be reckoned with. Success depends on chosing the appropriate method for the given patient and on professionally accomplishing the surgical-technical steps of key importance.

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EXPERIENCES ON 25 CASES OF RADICAL CYSTECTOMY

D. L. Répássy, S. Csata, Gy. Tamás, A. Bécsi and T. Weninger

Department of Urology, Szent István Hospital,
H-1096 Budapest, Nagyvárad tér 1, Hungary

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Authors review their early experiences and the oncopathological relations in respect to 25 cases of radical cystectomy involving orthotopic bladder substitution. The difficulties of diagnostics and indication are discussed. Attention is drawn to the fact that pathological "staging", "grading" are not entirely exact and reliable, though surgical indication is positioned on these. It is the opinion of authors that in case of TIG3 radical surgery is indicated. Due to the shortness of the follow-up periods, no studies on survival were performed.

It remains an open question whether radical cystectomy is indicated as opposed to the possible choice of organ-preserving surgery.

Introduction

Radical cystectomy is indicated in the event of invasive, infiltrative bladder carcinoma. In male patients, this means total removal of the bladder, the covering peritoneum sheath, the prostate and the vesicules, as well as pelvic lymphadenectomy. Theoretically, this is the only curative solution to an aggressive type of bladder carcinoma.

Radical cystectomy, however, has only become widespread worldwide in the last decade, primarily because the methods of urinary diversion and bladder substitution have gone through a great deal of development. There is a great difference in the life quality provided by these methods, with the risk of numerous complications involved, therefore method selection is dependent on several factors.

The questions related to bladder removal and substitution are in tight correlation with each other, nevertheless it must be stressed that these two therapeutic techniques are basically two separate steps.

The malignant process is stopped by successful, ablastic cystectomy, thus fundamentally determining prognosis, while successful bladder substitution gives the patient a chance at good quality of life and proper rehabilitation.

In the followings we report on 25 cases of radical cystectomy and orthotopic ileal neobladder in relation to the oncopathologic questions of cystectomy.

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Patients and Method

At the Department of Urology of the Szent István Hospital in Budapest, 25 radical cystectomies and orthotopic ileal neobladder were carried out due to infiltrative bladder carcinoma between 01. 01. 1996 and 01. 06. 1998. The average age of the patients was 63 years (48–80).

Surgical indication by means of transurethral resection was based on histologically determined pT stage as well as on "N"-, "M"-stages verified by imaging processes (IVU, ultrasound, CT, MRI) (in No, Mo cases). In case of Tis, radical surgery was indicated by the presence of consistent, multiplex recurrence despite a six monthly Intron-treatment (positive tumor cells manifest in at least two samples of the mapping TUR-biopsy), while in the T1 stage, the malignity grade of G3 indicated the need for radical surgery. The stages of T2 and T3 meant the need for cystectomy at any grade value.

Contraindication was implied by internal medical or anaesthesiological unsuitability, renal failure, intestinal diseases, or tumorous infiltration of the urethra. In the event of the latter three, other type of urinary diversion was performed (conduit, ureterosigmoideostomy) and these patients were not included in the present study.

The TNM/pTNM system was applied according to the UICC, the "grading"-system according to the WHO principles.

Table 1 shows a summary of the case of classifications according to the pT stage, giving the results gained during the course of TUR as well as the results obtained after the detailed pathohistological processing of the radical surgical preparations. The state of the regional lymph nodes is also given as N and pN.

Table 2 demonstrates the case classification according to the degree of malignity (grade), corresponding with the TUR and main surgery results. In case of heterogeneous tissue structure the classification was based on the area of highest malignity degree.

Table 3 comprises all other data projected on the pT categories: period of anamnesis, grade, preoperative kidney stagnation, multiplicity, death caused by tumorous propagation.

Table 1
Values of the T- and N-stage prior to and after cystectomy

pT-stage	T-stage		N-stage	
	Based on TUR	After cystectomy	Prior to cystectomy	After cystectomy
pT_{is}	3	2	N_0	N_0
pT_1	3	3	N_0	N_0
pT_2	16	2	N_0	1 case N_1
pT_3	3	14	N_0	1 case N_2
pT_4	–	4	–	2 case N_2
Total No. of cases	25			

Table 2
Grade value prior to and after cystectomy

Grade	Prior to TUR	After cystectomy
G1	2	–
G2	6	5
G3	17	20
Total No. of cases	25	25

Table 3
Relation of factors indicating tumor nature to pT-stages

pT stages	After cystectomy				Kidney stagnation		Multiplex tumor	Exit. due to tumor prop.
	T	G						
		1	2	3	1	2		
pT_{is}	2	–	–	2	1	–	2	–
pT_1	3	–	–	2	1	–	2	–
pT_2	2	–	2	–	–	2	–	–
pT_3	14	–	3	11	1	2	6	5 cases { 2 → 12 months; 1 → 4 months; 1 → 22 months
pT_4	4	–	–	4	–	3	2	2 cases { 1 → 3 months; 1 → 5 months
Total No. of cases	25	24			10		12	7

To indicate the period of anamnesis, three groups were formed in respect to the first symptom and the time elapsed till radical surgery:

1. shorten than 1 month,
2. between 1–6 months,
3. longer than 6 months.

To label kidney stagnation the following numbers were used: 1 = no stagnation, 2 = one-sided, 3 = two-sided stagnation.

The Table also comprises the seven patients who died because of tumor propagation, however, no studies on survival could be performed due to the shortness of the follow-up period.

Table 4 shows the number of TURs prior to cystectomy (1, 2 or more) as well as the time elapsed between the first TUR and the main operation (1, 2 months or more).

Table 4
Relation to T-stages of preoperative anamnesis periods and number of TURs

pT-stages	No. of TURs till cystectomy			Time elapsed between first TUR and cystectomy			Anamnesis		
	1×	2×	3 or more	1 month	2 months	3 or more months	1	2	3
pT_{is}	1	–	1	–	–	2	1	–	1
pT_1	1	–	2	1	–	2	–	–	3
pT_2	2	–	–	2	–	–	–	1	1
pT_3	10	3	1	7	3	4	3	6	5
T_4	3	–	1	2	–	2	–	2	2
Total No. of cases	25			25			25*		

*Explanation: 1 – anamnesis shorter than 1 month
2 – anamnesis shorter than 1–6 months
3 – anamnesis longer than 6 months

Results

The pT categories determined after TUR and radical surgery differed from each other in 16 cases (Table 1). The latter cases showed higher pT values: 1 from 3 Tis-es (T2) and 15 from 16 T2-s (T3 and T4) proved to be of higher category. It can be seen that the TUR-based "T-staging" underestimated the actual real state in 16 cases. The same also goes for the "grading" deviations in Table 2: the results obtained after the main operation proved higher malignity degree in 5 cases (two "went up to" G1 G2, three to G2 G3).

As seen from Table 3, the higher pT values went with higher grades, which phenomenon is known in other areas of oncology, too. Significant differences were not found in respect to the period of anamnesis and the repeated preventive TURs. Early cystectomy – mainly surgery shortly after the first TUR – was performed in 17 cases. As also observable, the patients who died due to tumor progression were already in progressive stage at the time of surgery (T3, T4), with the tumors also showing higher degree of malignity (G3).

Those cases are noteworthy, where despite negative N-staging and margin negative surgery, tumorous progression gave start or continued.

In three cases one-sided, in 7 cases two-sided ureteral dilatation was detectable at the time of cystectomy. Among these only 3 belonged to the T4 category, showing that the tumorous infiltration of the bladder wall at the ureteric orifitium can cause intramural occlusion at a relatively early stage.

The dilatation in one of the Tis and T1 cases was probably caused by postresection cicatrization. It is interesting that in almost half of the cases (12 patients) multiplicity could be demonstrated.

Discussion

The invasion of bladder carcinoma has 4 forms theoretically.

1. towards the lumen,
2. towards the bladder wall,
3. in both directions,
4. in neither directions (T_{is}).

The type 1 growth form is represented by papillomas, Ta urothelial carcinomas. "In situ" carcinomas correspond to type 4, while the tumors characterized by the type 2 and type 3 invasion infiltrate the bladder wall either frontally in block manner, or interstitially. Sometimes canalicular invasion through the venous and/or lymphatic vessels can be demonstrated even in the early T-stage.

The tumors infiltrating the bladder wall require radical cystectomy since they show the most significant signs of malignity. In practice, however, is is rather difficult to establish indication of radical surgery because neither the tumor's nature, nor the progressive state can be assessed with assurance [1, 2].

Though the degree of infiltration is labelled by the T symbol, it only provides us with a "snapshot" without giving information on the rate of the process. It is not entirely reliable either as the result is influenced by subjective factors: the clinician might perform an insufficient resection, the pathologist might be uncertain because of defective embedding, preparation [3]. Apart from all these, progression could continue or even accelerate within the period between the time of TUR and radical surgery. It is a relatively frequent occurrence that the TUR/pT-staging underestimates the true conditions [2, 4]. Our own results are also reflective of this.

The most important questions should be the early recognition of the nature of the tumor. Numerous studies aim at finding correlation between tumor malignity and certain microbiological, molecular-biological, genetic criteria. Such is the p53 tumor suppressor gene – located on chromosome 17p – the mutation of which often accompanies tumors of higher malignity degree [4]. Due to the uncertainty of the results, it is still the classic histological study which can be used in practice for judging the "grade".

The histopathological method is also uncertain due to its subjectivity.

The first, most important step in the tumorous infiltration of the bladder wall is the breaking through, infiltration of the basal membrane, which requires the function of special enzymes. These enzymes are produced by tumor cells of mainly higher malignity grade [1], thus the category of the "grade" may bear importance. It seems therefore that the tearing through of the lamina propria means a quality difference – this is why we think the T1, T3 cases to be indications for radical surgery. Hautmann [6–8] and Gilfrich et al. [5] are also on this opinion.

In May, 1998, at the Congress of the American Urological Association, the Clinic of Urology in Mainz reported on their 30 years' prognostic results. Separate analysis of each decade revealed no essential differences in the results, which also applied to the T1, G3 groups. Here they found that in the case of T1, G3 stage, cystectomy performed shortly after the first TUR resulted in a 5 years' survival of 93%, while radical surgery following several TURs ended in a 5 years' survival of 72% [5].

Pages et al. [9] and Lebret et al. [10] have also shown that 75% of T1G3 tumors progress later and become muscle-infiltrative processes.

Based on these they emphasize the significance of so-called "early cystectomy" – which is in accordance with our opinion: attempt should be made that the diagnostic value of the first TUR not be impaired, that is resection should be accomplished to the adequate depth. Early main surgery performed in 17 of our cases was unsuccessful, partly because several TURs were needed in the *in situ* cases, and partly because the preventive TURs were carried out in other Institutes.

A further dilemma is the state of the regional lymph nodes. According to Vieweg et al. [11], in the pT3 stage lymph node positivity becomes confirmed in a probability of 37% during the course of lymphadenectomy. As seem from Table 1, the N-positive cases were accumulated at stages T3–4, and a similar type of accumulation is manifest in Table 3 in relation to tumorous progression. These results are therefore in accordance with the international data. According to Hautmann [6–8] lymphadenectomy can have a curative effect in 30–40% of cases. Among our 25 patients, lymph node positivity was found during the course of lymphadenectomy in 4 cases (pN1 in one case and pN2 in three cases). The latter three patients died as the consequence of tumor progression.

Concerning both the pT and the pN categories, it was our experience that verification of these stage criteria prior to cystectomy resulted in a relatively high proportion of "under staging" (Table 1). In the future, therefore, the punctuality of diagnosis should be increased, at the same time keeping in mind the above fact in the interest of proper surgical indication. Our few data demonstrate that in quite a number of our patients tumorous progression continued despite radical surgery (7/25). Three of our patients showed progression even besides negative N-stage, which leads to the conclusion that histologically undetectable micrometastases were already present at the time of surgery. Data of the international literature show quite a deviation. Over 50% of Studer's [12] radical cystectomy patients died within 5 years due to progression. The Clinic in Mainz reported on a 5-year tumor-free survival rate of 59% in their 30 years' study [5]. In June, 1998 Hautmann [6–8] gave account of a 76.6% figure as regards 5-year survival.

The period of anamnesis, the number of previous TURs, the time elapsed between TIR and radical surgery – as prognostic factors – did not bear significance in our material. Data are also available where cases receiving conservative treatment (TUR, radiation- or drug-therapy) presented similar, worse, or better results. The big case number of Solsona [13] in 1998 revealed similar results on survival in TUR-treated and cystectomy patients. It is emphasized by this author, however, that an important condition of conservative therapy is the negative finding of the biopsy taken deeply from the tumor base and its environs. "Post-biopsy" may decrease the probability of "under staging" and the ablasticity of TUR can be checked. In Hungary, Kondás et al. reported on surprisingly favourable survival results in relation to his TUR-treated, invasive bladder tumor patients [14, 15].

Besides numerous arguments and counter-arguments, this question is still open.

Conclusions

– The biological nature of bladder tumors is hard to determine, and only with certain probability.

– "Staging" is also uncertain, with the relative frequency of "underestimation".

– There is a probable presence of micrometastases in the advanced stage.

– Radical cystectomy – as the possible curative solution to infiltrative urothelial bladder carcinoma – can be successfully performed with proper indication and surgical technique.

– At present, the comparison of the results of cystectomy and radical TUR is still an open question.

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FACTORS AFFECTING PROGNOSIS OF RENAL CELL CARCINOMAS

D. L. Répássy

Department of Urology, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary

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Author analyzed the survival of 126 patients operated on because of kidney carcinomas. The data on anamnesis, laboratory results and TNM histological classification were compared with the results on "relative survival" and correlation analysis was performed. Based on these, the 12 most important criteria (with the highest correlation coefficient) were emphasized and regression equation was formed based on the TSP-Time Series Processing – Version 4 (Hall). Using this method, a numerical prognostic index can be established for the judgement of prognosis regarding certain patients.

Introduction

The judgement of prognosis regarding any disease belongs to one of the most difficult tasks of medical science. This issue is of importance because it might provide hints for choosing certain therapeutic methods – since on many occasions the effectiveness of a drug or therapy can only be evaluated on the basis of the prognostic results. This is especially valid in the case of renal carcinomas, which at times demonstrate varying biological behaviour and aggressiveness [1–4, 6, 7, 9, 10, 12]. It could be said that kidney tumors are differently malignant, thus their prognosis varies. Therefore it is hard to judge whether the recovery of a kidney carcinoma patient is the result of the applied treatment or the process is a benign one form the beginning. Surgical procedures still play primary role in the treatment of renal carcinomas, nevertheless undiscovered micrometastases might already be present at the time of the tumorous kidney removal, causing possible death years later throughout progression. Accordingly, determination of prognosis can only be possible in the long run. The prognosis of renal carcinomas is influenced by several factors, which have been reported on in the world literature since decades. The latest is a prognostic index system compiled by Golimbu et al. [17], classing the nature of the disease – similarly to the index of other tumorous diseases – by means of scoring. In the followings we have attempted to elaborate a prognostic index system which, based on retrospective survival studies, quantifies the probability of survival. Thus it is suitable for determining the prognosis of disease by numerically defining survival.

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Materials and Method

Throughout the 15 years between 1969 and 1985, nephrectomy due to kidney tumors was performed on 248 patients at the Department of Urology of the Semmelweis Medical University in Budapest, Hungary. The followings were recorded during the retrospective analysis: data regarding anamnesis, symptoms, routine laboratory studies, TNM categories, venous invasion, infiltration of the cavity system, histopathologic features, as well as data on survival. Those cases were not included where documentation was lacking or data on survival were not reliably accessible. Accordingly, 126 patients participated in the prognostic analysis. Survival was expressed in years, from the time of surgery. The so-called relative survival was determined, being equivalent to the ratios of observed survival and expected survival.

$$\text{Relative survival} = \frac{\text{observed survival}}{\text{expected survival}}$$

Expected survival = "healthy" population of the same age and sex, prospective survival calculated for the same age-group.

The computer programme package by Hakulinen [18] was used for the analysis. Significancy calculations regarding the average relative survival data were carried out using the Student's *t*-test. Three categories were used to survey the case histories in respect to the length of anamnesis:

1. shorter than one month,
2. between one and six months,
3. longer than six months.

The eryhtrocyte sedimentation rate was also grouped in three:

1. below 20 mm/h,
2. between 20–50 mm/h,
3. above 50 mm/h.

Regarding all other anamnestic semiologic and laboratory data, an alternative was set up pertaining to the presence or absence of certain symptoms. Haematuria, flank pain, fever, anaemia, weight loss, hypertonia, varicocele, policytaemia were all accessed, as well as other symptoms which could be related to the tumorous disease. Weight loss was defined as being positive if it was more than 10% during the six months prior to surgery, without any reason independent of the tumorous disease.

Pathologic data. These were evaluate in accordance with the TNM classification of the UICC, the basis being histopathologic studies of the surgical preparations. The 4 T-categories were applied according to the UICC, however, a separate category was used for the venous invasion, so they could be analysed separately in respect to prognostic significance. Here, labelling was in like manner as in the method of Paulson and Selli [22, 23], using the symbols PV+ or PV–. Likewise in accordance with the UICC principle, lymph node positivity was only related to the regional lymph nodes, while juxtaregional lymph positivity was regarded as distant metastasis. Since the prognostic signifi-

cance of the infiltration of the cavity system was also included in our study, this was also among the pathologic data, independent of the T categories.

Histologic features. During the course of the retrospective processing, repeated serial sections were prepared from the surgical preparations and blocks, respectively, and the routine hematoxylin-eosin-stained histologic preparations were reclassified according to the following criteria:

1. Nuclear atypia, nuclear grade (according to Skinner et al. [13]):
   G-1: Small nuclei indistinguishable from those seen in normal tubular epithelial cells;
   G-2: Slightly irregular nuclei without abnormal nucleoli;
   G-3: Enlarged, pleomorphic nuclei with prominent nucleoli;
   G-4: Extremely bizarre giant nuclei.

When the tumor contains different areas according to the nuclear classification, it should be categorised into the higher grade.

2. Histologic structure:
   1: Compact, solid architecture;
   2: Tubular, adenomatoid;
   3: Papillary;
   4: Cystic.
3. Tumor cell type (partially according to Thoenes et al. [16]):
   1: Clear cell;
   2: Chromophobe type;
   3: Chromophilic basophilic type;
   4: Chromophilic eosinophilic cell type.

Regarding the classification according to histologic structure and tumor cell type, if different patterns are mixed, the category with the higher "nuclear grade" should be taken into account.

Homogeneous tumors contain three categories according to these three basic classifications. Heteromorphic tumors have a combination of more of the following three categories: different cell types (clear and granular) and/or histologic elements (tubulopapillary) and/or structure of nuclei.

The grade of this mixture, heteromorphism can be classified as follows:

4. Grade of heteromorphism:
   1: homogeneous structure (one of each pattern – i.e. three);
   2. a mixture of 3+1 patterns;
   3: a mixture of 3+2 patterns;
   4. a mixture of 3+3 or more different patterns.

Prognostic estimation: the data pertaining to symptoms, laboratory tests, anamensis, as well as the staging- and grading-related histomorphologic findings were all compiled and correlation analysis was carried out to demonstrate the factors which show the closest connection with the survival data. Those 12 were selected (Table 1) which had the highest correlation coefficient. The results of relative survival of each category of those

Table 1
Twelve prognostic factors with highest correlation coefficient

Factor	Coefficient
Nuclear grade	0.63919
Heteromorphic grade	0.54371
Histological structure	0.45339
Cell cytoplasm type	0.39295
T-category	0.23952
N-category	0.19628
M-category	0.34922
Venous invasion	0.14445
Calyceal system involvement	0.22528
RBD sedimentation rate	0.28695
Weight loss	0.27031
Anaemia	0.21876

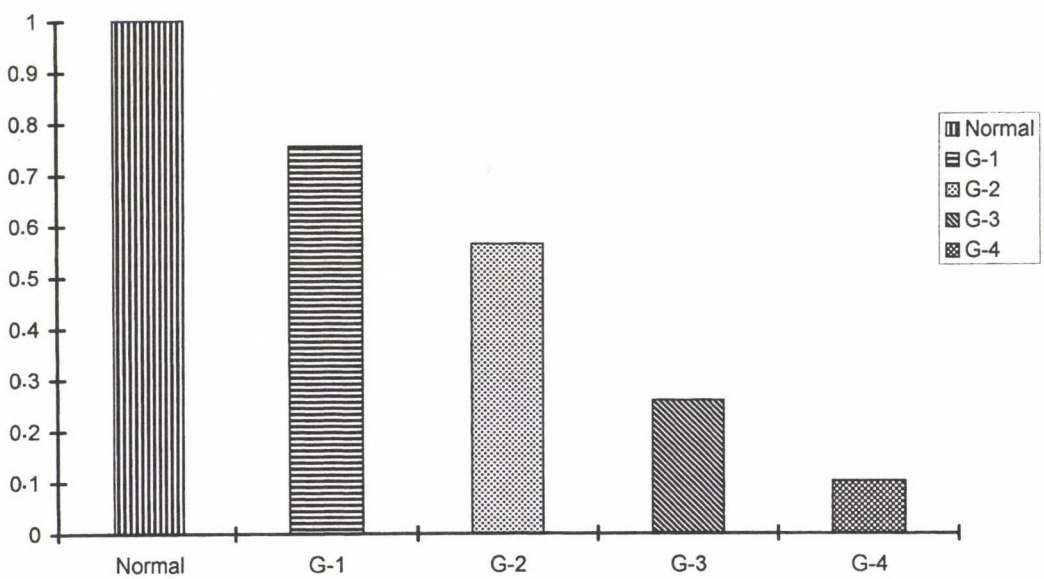

Fig. 1. Relative survival based on nuclear grade

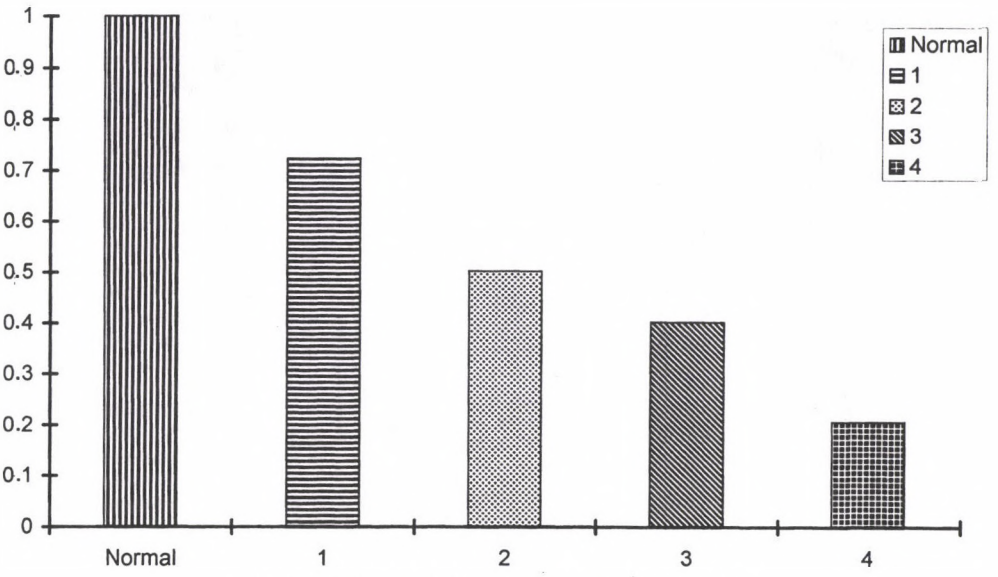

Fig. 2. Relative survival based on heteromorphic grade

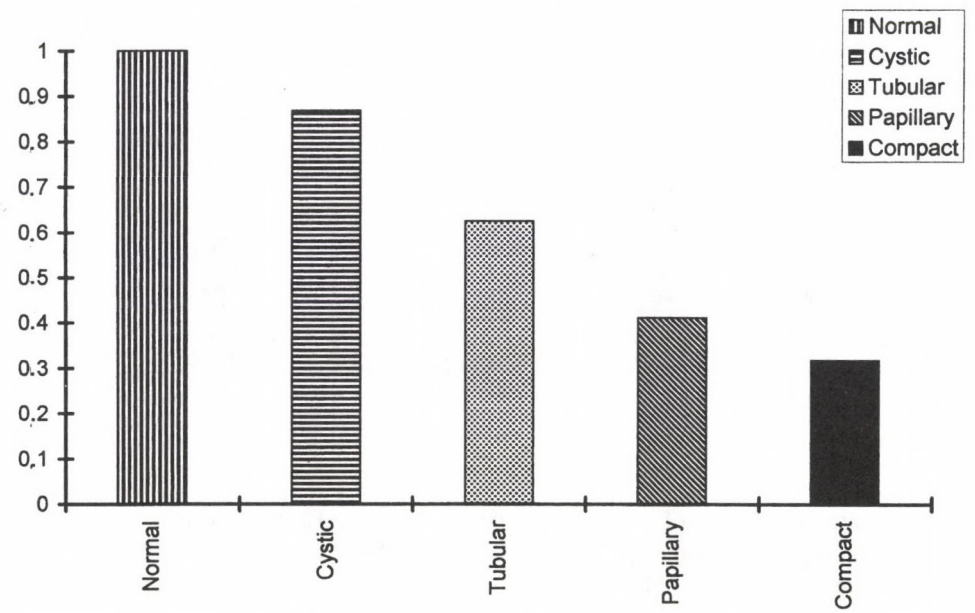

Fig. 3. Relative survival based on histological pattern

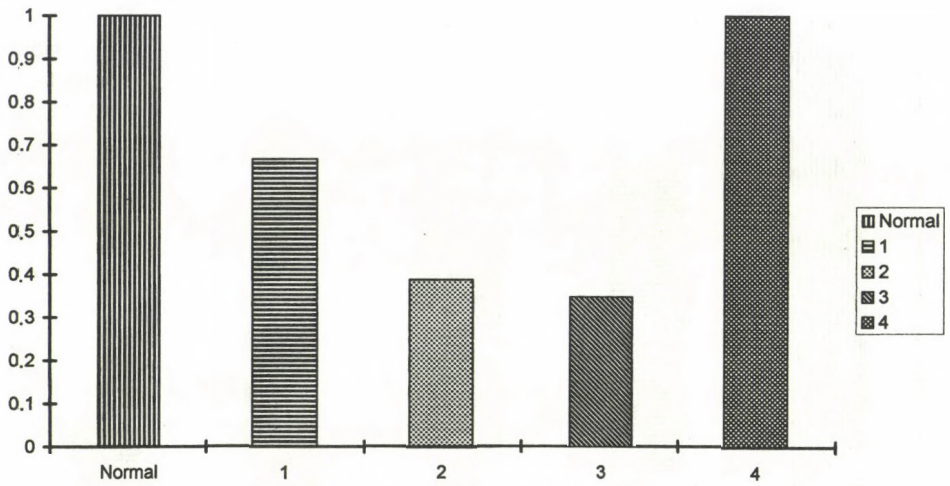

Fig. 4. Relative survival based on cell type

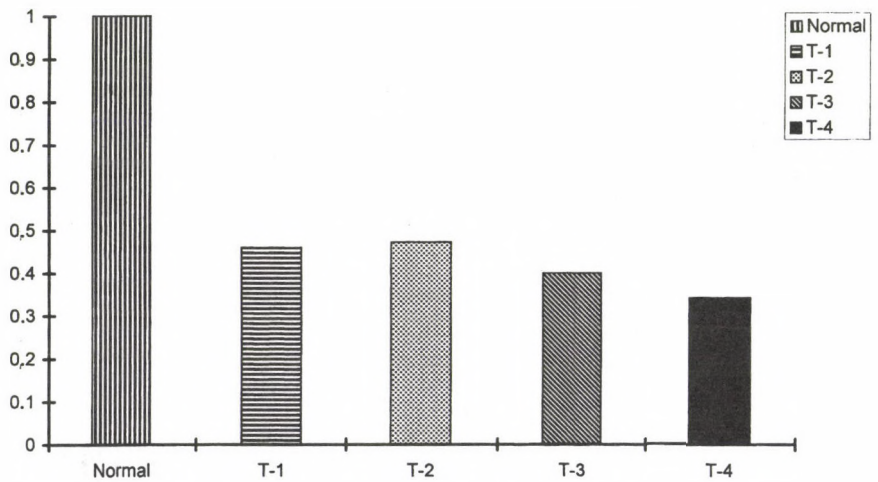

Fig. 5. Relative survival based on T-stage

12 factors are presented in Figs 1 to 12. Specifying these 12 prognostic factors, a prognosis-estimating regression equation was formed with the help of a so-called TSP computer programme [20], as follows: $Y = C + a_1x_1 + a_2x_2 + \ldots + a_nx_n$ – where C is a constant reduced by the multiplication of the individual factors and their coefficients (ax) (Table 2). Therefore, replacing the various prognostic criteria by factual values, a patient's relative survival can be estimated; i.e. the percental value indicating the actual and probable survival ratio can be calculated.

This programme has been elaborated by Hall [19].

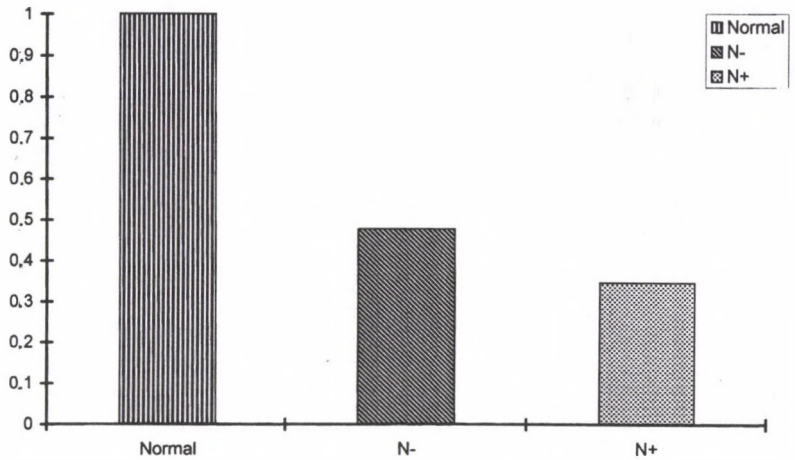

Fig. 6. Relative survival based on N-stage

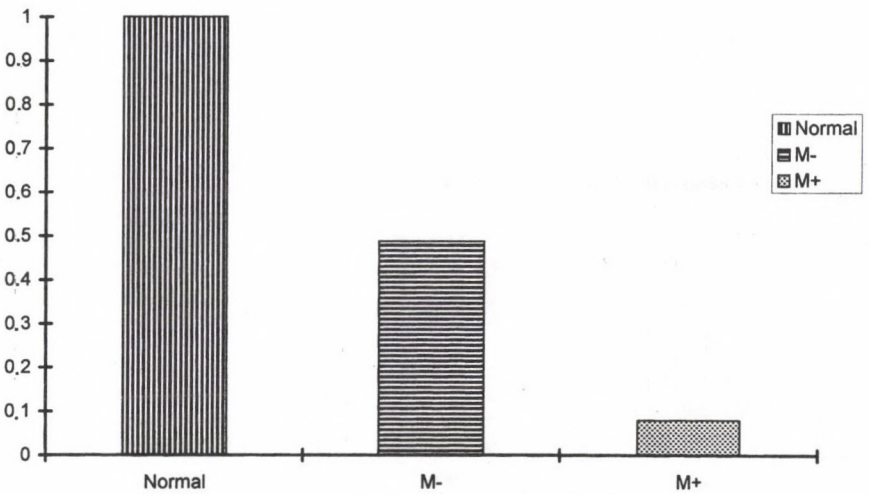

Fig. 7. Relative survival based on M-stage

Discussion

In the recent years more and more papers have dealt with the diagnostics, clinics, therapy, and last but not least, the prognostics of renal carcinomas. Besides numerous theoretical and practical problems, questions related to prognostics are also in the limelight, since the biological behaviour or renal carcinomas varies according to the case in question. Not once is it striking and difficult to explain why in certain cases rapid pro-

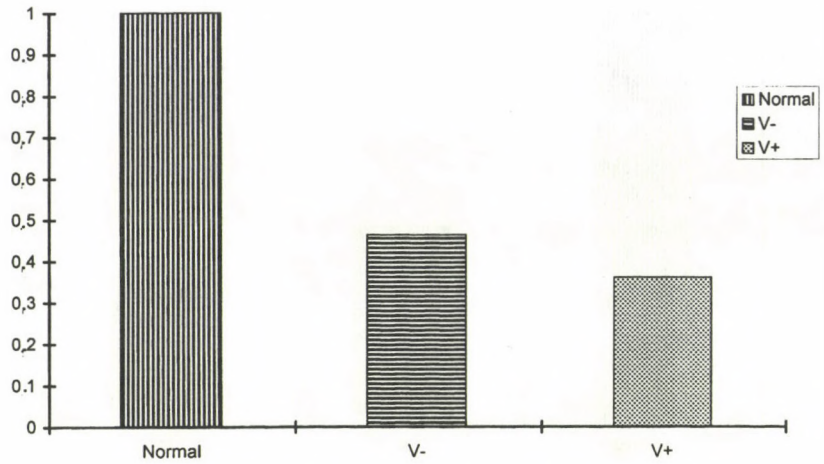

Fig. 8. Relative survival based on venous involvement

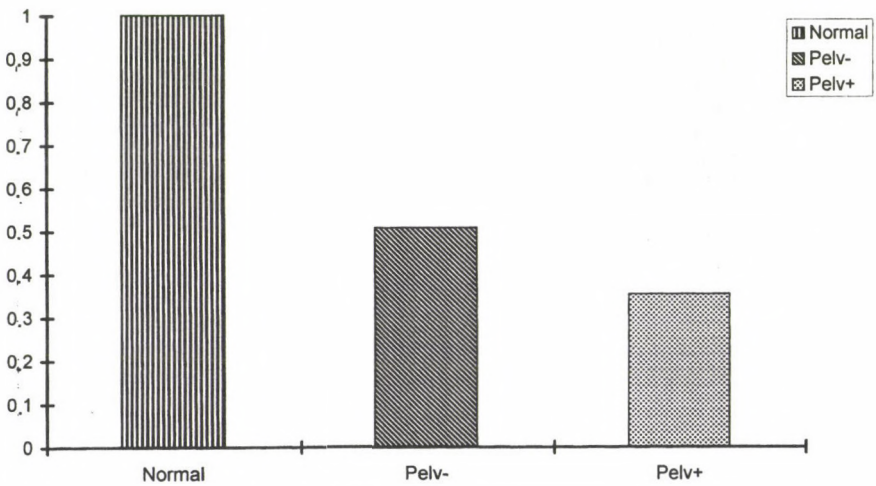

Fig. 9. Relative survival based on pelvic involvement

gression and in a few months time a patient's death occurs following nephrectomy, while in other cases a complete cure is achieved. The expectable prognosis is not only an important feature in the eyes of the clinician, the patient, and relatives, but is also essential in determining the degree of certain therapeutic methods.

Our retrospective study included the separate analysis of certain symptoms, laboratory findings and TNM categories, in respect to significance. It was found that the criteria indicative of prognosis were interrelated to a certain degree: e.g. the vein punctures

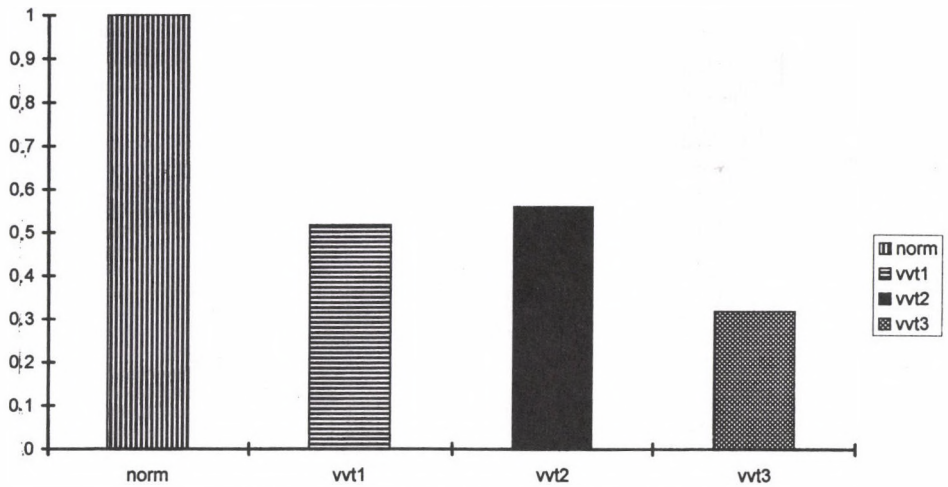

Fig. 10. Relative survival based on sedimentation rate

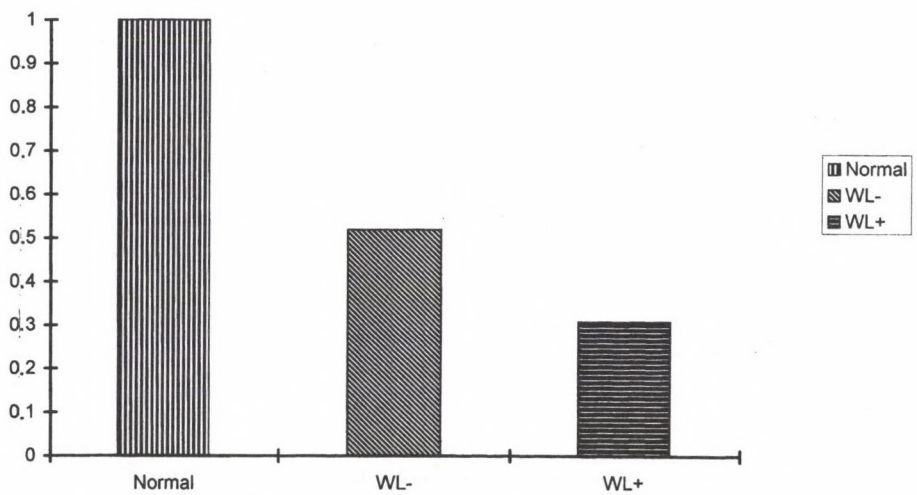

Fig. 11. Relative survival based on weight loss

and lymph node invasion showed mostly parallel, simultaneous positivity, the tissue structure and the granular structure of the cytoplasm, the nuclear grade also correlated with each other, and not only separately with the survival data. Furthermore, correlation was found with the stage as well. Besides NM and V positivity accumulation was detectable in respect to the cases of higher nuclear grade. All these can more or less be applied to every prognostic factor. Therefore, prognosis is influenced by these factors together, and partly in relationship with each other. According to our correlation analysis

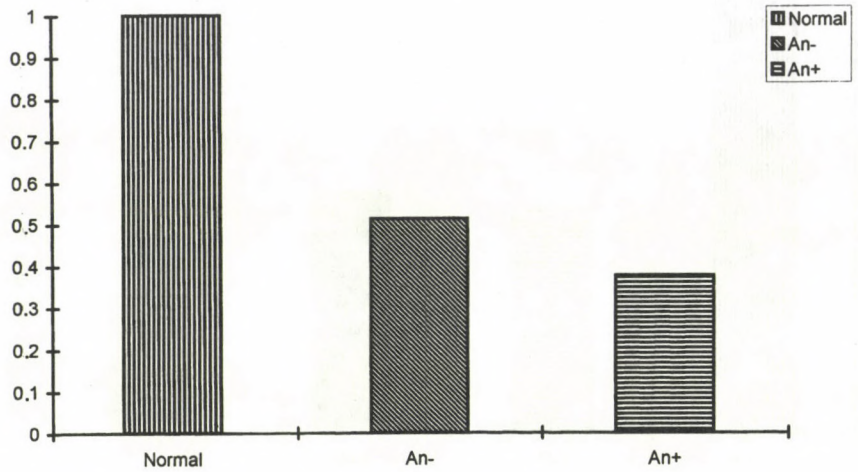

Fig. 12. Relative survival based on anaemia

Table 2
Regression equation for estimation of RCC patients

$ES = C\ (constant) + a_1x_1 + a_2x_2 + \ldots + a_nx_n.$
+ (–0.1053) × nuclear grade
+ (–0.1216) × histological pattern
+ (+0.0425) × cell type
+ (–0.0744) × heteromorphic grade
+ (–0.0217) × pT-category
+ (+0.1006) × pN-category
+ (–0.1933) × M-category
+ (–0.0612) × V-category
+ (+0.0014) × pelvic involvement
+ (+0.0022) × sediment rate
+ (–0.1291) × weight loss
+ (+0.0769) × anaemia

the developed sequence shows that the most important prognostic signs are obtainable on the basis of the histologic structure – within which the most significant are the nuclear structure and the heteromorphy of the tumor structure. It is also unambiguous that organ metastasis observed during the course of surgery is also a rather bad prognostic sign. It seems that the rest of the pathologic data and the clinical signs are not so closely related to the survival data. It is natural, however, that the stage of the kidney tumor,

firstly the presence of organ metastasis, as well as lymph node positivity or vein puncture are all determinants of prognosis. In many cases, micrometastases unverified at the time of examination and surgery are already present, later on causing death of the patient, possibly after several years. In such cases therefore, prognosis cannot be judged by means of the TNM-categories. The biological behaviour of the tumor can be concluded to a certain degree during the course of tissue structure analysis. It stands to reason therefore, that chances for the presence of distant micrometastases are greater in case of renal carcinomas of higher malignity grade. Accordingly, it is our opinion (and our data also show) that not only the pathologic stage-categories and laboratory findings, but the histologic features as well play important role in the judgement of the biological behaviour of kidney tumors [5, 8, 11, 14, 15]. It is therefore our proposal that the previously mentioned 12 factors should collectively be taken into consideration in the judgement of prognosis, though with different coefficients according to their importance. It should be emphasized that in view of these still unapproachable biological problems – within this the essence of malignant tumors –, it is not possible to draw overall conclusions. Factors more reliably indicating the prognosis of renal carcinomas are still unknown. This is one of the reasons why our results show great dispersion. Since our data – although being continuous-like – were categorized, we cannot expect such exact results as, for example in case of a phenomenon characterized by continuous data. Our data are therefore integral in character, with a value-stock of 0–1 alternative in many cases. A further problems is that a few results are of subjective character from the outset, e.g. the histologic studies. The quantitative analysis of such qualitative data is always arbitrary, by which we mean that for example, the histologic type grouped into the 3 category is not 3 times more malignant than the one grouped into the 1 category. Despite these problems the applied technique has several advantages. One of the most significant results is that a number of factors can be handled together. It can be seen from the correlation results that even the value of the greatest coefficient is only around 0.5; meaning after all a weak correlation. It should be taken into consideration, however, that this "weak correlation" characterizes a biological system where the correlation coefficient of 0.4–0.5 cannot be evaluated as inadequate. The question related to the prognosis of renal carcinomas is till unsolved. Nevertheless, studies on the prognostic indicator factors are necessitated since without these, the results of any therapeutic method could be falsely evaluated. It is our opinion that the outlined 12 prognostic factors contain important information and are suitable for drawing prognostic consequences.

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SCHISTOSOMIASIS OF THE URINARY BLADDER

D. L. Répássy[1], S. Csata[1], G. Sterlik[1] and A. Iványi[2]

[1]*Department of Urology,* [2]*Department of Pathology, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary*

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Authors review a case of urinary schistosomiasis, where the process caused left-sided urinary obstruction. Because of the suspicion of a tumor transurethral resection was performed, whereafter the ureter passage became unhindered. Diagnosis became clear upon the histological examination of the resected tissue. Based on the cited literature, reference is made to the mortality rate of the disease in the expanded endemic areas, as well as to the high number of patients at risk. A brief summary is given of the pathology, symptoms, diagnostics of the disease, with mention of differentiation and therapeutic possibilities as well. With regard to importation of the disease, attention is called to the importance of careful anamnesis.

Introduction

Treatment of human schistosomiasis is a major problem in the Middle East, Far-East and African countries. The disease affects over 200 million people, with a further 600 million inhabitants at risk [4, 5, 13, 14, 18, 19, 22]. Depending on the duration and frequency of recurrence of the schistosoma haematobium infection, the disease involves various parts of the urogenital system at different sites and in varying degrees: the lower ureter segment, the urinary bladder, the seminal vesicule [4, 13, 14, 18]. We find it important to review our case because the disease is difficult to diagnose, is quite rare, and has a danger of being imported [6].

Case Report

A 31-year-old male patient was admitted to our Department on 12th May, 1998.

Anamnesis: the patient had repeated epididymitis in 1996, and appeared for urological examination on 24th March, 1998 due to haematuria and haemospermia, also complaining of pain in the left kidney.

Status: no pathological alterations were observable.

Laboratory findings: urine slightly opaque, sedimentation: 5–6 leukocytes, 8–10 erythrocytes.

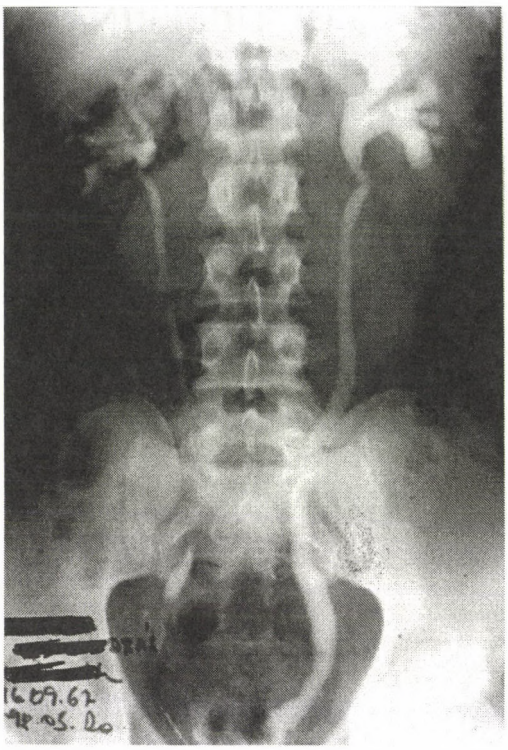

Fig. 1. I.v. urography shows good secretion on both sides. The right side shows intact cavity system and proper filling of the ureter, the left side exhibits a medium degree of pyelum- and ureter-dilatation, reaching till the juxtavesicular segment

Examinations. Abdominal ultrasound: both kidneys were found in normal position, with intact renal cortex parenchyma, and no alterations were detectable in the cavity system and ureter of the right kidney. The left-sided kidney and ureter showed II degree dilatation. The bladder contour was seen to be intact. *Intravenous urography:* blank view revealed no positive shadow of stones. 10' and further pictures were without manifestation of any pathological alterations on the right side. A medium degree of cavity system dilatation was manifest on the left side, which could be followed till the juxtavesicular segment of the ureter. The bladder contour was seen as intact (Fig. 1). *Cytoscopy:* the bladder epithelium was found to be moderately inflammatous and oedematous, the right orifitium was normal and showed good action. The left orifitium site revealed a compact tumorous structure the size of an almond, covered with furred thick mucous membrane. These was only a pinhole suspicion of the orifitium. The alteration gave rise to the supposition of neoformation, therefore transurethral resection (TUR) was indicated.

TUR was performed on 13th May, 1998. The tumor was resected at the site of the left orifitium and further histological studies required biopsy from the hind wall. *Histological diagnosis:* Schistosomiasis (Bilharsiasis) ves. Urin. (Fig. 2).

In knowledge of the diagnosis, the patient was asked whether he had been to any countries where he could possibly have been at risk of schistosoma haematobium infection. It then became clear that during the last few years, he spent several weeks in schistosoma endemic areas, in 1994 he had been to Africa, Mexico, Thailand and Egypt. Therefore, he most probably became infected in one of these countries, however, the recurring epididymitis, haematuria, haemospermia referred to an infectious chronic condition.

The patient was transferred to an infectology department on 25th May, 1998, where he received a days' treatment of 4×40 mg/kg Biltricide, and allowed home on the following day. He was called back for control studies 3 months later, when he was complaint free, with negative urine findings. The i.v. urography showed blank view with no

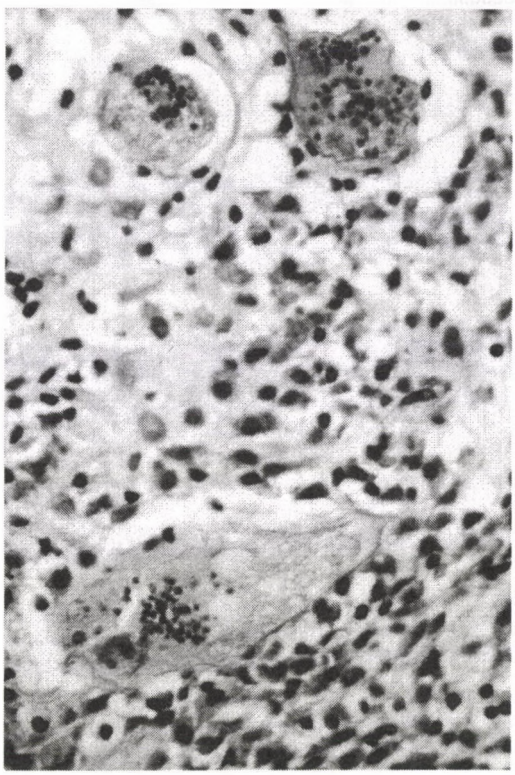

Fig. 2. Schistosoma, the cross- and longitudinal sections of the eggs are observable in the mucous membrane of the bladder, one of the eggs ends in a strikingly pointy appendage

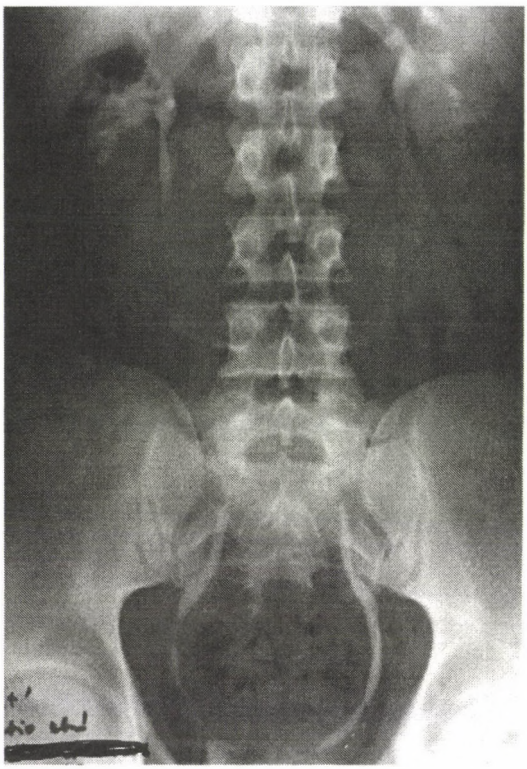

Fig. 3. I.v. urography displays good secretion and filling of the ureter on both sides. There is no more sign of the left-sided medium degree of dilatation

visible pathological alterations. The 10' and later pictures showed proper kidney- and ureter-filling on both sides. There was no more dilatation of the left pyelum and ureter (Fig. 3).

Discussion

The examinations gave rise to the suspicion of ureterocele and bladder carcinoma, respectively, and only the histological studies provided the correct diagnosis.

Pathology. Schistosomiasis is caused by the 3 major species of blood contamination (trematodes) [4, 13, 14, 18]. This parasitosis is the cause of death of 200 thousand people annually. The *Sch. mansoni*, *Sch. japonicum* give rise to intestinal schistosomiasis, expansively present in Africa, but also occurring in the Arabian peninsula, South America (Brazil, Venezuela, etc.) and the Caribbean islands, including Porto Rico. Schistosomiasis of the bladder is usually caused by the schistosoma haematobium.

Small centers of this trematode are found throughout the Near- and Far-East in China, the Philippines and in India [4, 13, 14].

The *Sch. mansoni* can be found in the portal veins of the large intestines, the *Sch. haematobium* can occur in the venous plexus of the true pelvis (around the lower third of the ureter, the vesicula seminalis, the prostate, the tuba uterina, the ovaries, the cervix and the uterus), while the *Sch. japonicum* can be found in the liver, spleen and intestines.

Life cycle of the pathogens. The three species show similarities morphologically. The cycle can even last till the 8th, 12th week. Infection is by means of the skin: the cerkaries bore through the skin, get into the blood circulation and reach the portal veins. Upon settling at the above-mentioned sites, they copulate and empty their eggs so as to maintain their cycle [4, 13, 14]. The eggs get into the blood vessels surrounding the large intestines and the bladder. By means of their digestive enzymes and pointed shape they drill through the walls of the intestine and bladder, get into the urine and stool, then in water they develop into filiform larvae within a few hours. They must find a suitable host (special type of slug) within 24 h or else they will perish. Climate and canals continuously under water during the course of agricultural irrigation provide ideal conditions for the existence and multiplication of the disease spreading slugs. The larvae in the slugs develop further and asexually multiply 2–3 times, in such manner thousands of fork-tailed virulent larvae come into being. These then leave the slug 4–8 weeks later, and swimming around in water are capable of living for 2 days. Within this period they have to get into human contact. In endemic areas, 1–2 minutes of showering is enough to become infected.

The worms feed on red blood cells, which leads to anaemia. The eggs stuck in the tissues give rise to granuloma formation with the infiltration of lymphocytes, plasma cells and eosinophylic cells, and epitheloid as well as giant cells around the eggs. What remains after the process is scar tissue containing calcified eggs [4, 13, 14, 15].

The schistosomiatic formations of the urethra make their appearances in a variety of forms. In the active phase of the infection characteristic features are the tiny, yellowish tubercles, 'pseudotubercles', protruding from the slightly hyperanaemic mucous membrane. By fusion of these tubercles, bilharzial nodules are formed. Three variants of the polyp form are known: granulomatous, calcified – fibrous and villous forms. The raspberry- or strwawberry-like pseudotumors with diameters of 0.5–3 cm are mostly situated on the base of the bladder, around the orifitium. Frequent accompanying phenomena are the cystic and glandular ureteritis, though their pathogenesis is unclear. Further accompanying features are the blockage of the mucosal glandular elements, the degeneration of the Brunn-nests, as well as urothelial metaplasia. The glandular ureteritis is detectable in the form of velvety, blood-filled, widened mucous membrane, while cystic ureteritis is manifest in the form of transparent vesicles. In cases of acute, repeated infection calcified plaques can be seen where the deposited sclerotic eggs are covered by intact urothelium. The numerous deposited eggs, however, do no harm to the blood supply of the lamina propria, which could lead to the atrophy or ulceration of the urothelium. In the inactive phase, the sclerotic eggs are visible through the transparently thin epithelium, resembling underwater sand grains ("sand patches"). Cicatrisation may

develop on the effect of recurring infection and upon treatment. There is a lesser chance of leukoplakia or malignity developing in the upper urethra as compared to the bladder [4, 14, 16, 18, 19].

The healing granulomas are followed by fibrotic tissue formation, the extent of which is dependent on the severity of the infection, the number of reinfections as well as the reaction of the organism. As a consequence of changes showing diffuse longitudinal expansion, the urethral wall becomes rigid, leading to the development of segments of various diameters. The rigidity of the ureteric orifitium may lead to reflux [2, 4, 14]. It is firstly the lower segment of the ureter that becomes involved, as was observable in our case [1, 4, 11, 14]. The rigid ureter wall causes functional disturbances, but possibly without obstruction. During the course of localized, concentrical scar tissue formation one or more short- or long-stretched constrictions, partial or complete obstruction may develop along the path of the ureter. The consequence of obstruction is the elongation, windy course of the ureter, with the development of dilatation and atonia. The scarred adhesions and the periureteritis cause the rupture and dislocation of the ureter. All the afore-mentioned, the damages to the ureter wall, as well as the calcified eggs and plaques, promote the formation of stones in the ureter. In the majority of the cases the changes occur in combination with each other, usually on both sides, although in different degrees. The consequential damage to kidney function and the frequent upper passage infections may lead to renal insufficiency [1–3, 14].

The disease occurs three times more frequently in males. In endemic areas the first infection occurs prior to school age [4, 15].

Although the majority of those infected are complaint-free – as was our patient – symptoms may be manifest in 50–60%, with possible severe organ damages in 5–10% of the cases [4, 14].

Cerkaria dermatitis: after the cerkaria bores through the skin, clinical symptoms appear in the form of circumscribed, itchy erythaemic or petechial skin alteration, which become macules, papules, lasting for a maximum of 5 days.

The acute schistosoma syndrome may occur in any schistosomiasis infection: it is rare in schistosoma haematobium infection – in our case this process was missing. The severity of the disease can be from a mild-course right till the rare event of being a threat to life. Besides fever, discomfort, urticaria, diarrhea, muscle pain, dry coughing, leukocytosis and considerable eosinophylia, the liver and spleen could also be temporarily swollen. Following 2–8 weeks, the patient becomes symptom-free [8, 14, 17].

Micturition, dysuria, proteinuria and at the end of urination, haematuria appear as early symptoms of urethral disease caused by the schistosoma haematobium. The appearance of these complaints led our patient to our Department. In rare cases the circulating eggs may lead to transverse myelitis, epilepsy [14].

Diagnosis: Reliable diagnosis is ensured by the demonstration of the characteristic eggs in the mucus, stool, urine, biopsy material. In our case too, the eggs were detectable in the material taken for histological studies [4, 14]. The schistosoma haematobium eggs may sometimes also be manifest in the stool. The eggs should be looked for between 9–24 h, or in urine of 24 h.

For serological studies the 'rapid ELIZA' Western blot-method is used (with a sensitivity of 100%). It is a good method for the verification of the infection and the identification of the parasite.

In advanced cases the cystoscopic examination may show hypertrophic mucous membrane ("sand patches"), ulcers, flattened epithelium-metaplasia. Sometimes the X-ray projections of the lower abdomen show calcification of the bladder wall and the ureters. Urography and retrograde pyelography are very useful in respect to the detection of urethral constrictions and dilatations. Ultrasound examination can be chosen as an imaging technique, it does not, however, make possible the detection of calcification. The prognostic symptom of "turtle back" calcification is made visible by computer tomography [9, 12, 14].

Differential diagnostics. In endemic areas and in case of importation, schistosomiasis of the bladder should be distinguished from other causes of urethral complaints, thus from urogenital tumors, urethral bacterial infections, nephrolithiasis forms [4, 14, 19, 21]. It is essential that case history be taken with proper care, covering all the facts.

Treatment. Medical treatment should only be applied when living eggs are found. The safeness and efficiency of the current medicaments make possible the per os treatment of all infections and developed diseases. Prasiquantal (Biltriciol, 40 mg/body weight kg, twice within 24 h) is suitable for the treatment of every species. After six months the ratio of recovery is 87% in the case of schistosoma haematobium [4, 14].

Surgical treatment. The polyps causing obstructional uropathy must be removed surgically; the constriction overcome by means of Boary-type plastic surgery, ureter-substitution with small intestines, transrenal drainage, dilatation. Cases of anuria, uraemia necessitate haemodialysis and transplantation [2, 4, 7, 10, 19, 20, 21, 23].

In our case the granulomatous tumor of the bladder wall causing constriction of the left ureteric orifitium was removed by means of transurethral resection. The application of TUR and medical treatment resulted complete recovery, the ureter passage became restored and the patient complaint-free. There was no need for open surgery (neoimplantation, ureter-substitution).

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RETROPERITONEAL MALIGNANT FIBROUS HISTIOCYTOMA

D. L. Répássy[1], S. Csata[1], G. Sterlik[1] and P. Hazslinszky[2]

[1]*Department of Urology,* [2]*Department of Pathology, Szent István Hospital, H-1096 Budapest, Nagyvárad tér 1, Hungary*

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Authors review the case history and follow-up a rare malignant fibrous histiocytoma patient, based on the relevant literary data. The tumor filled the retroperitoneum on the right side, in front of the right kidney. Intravenous urography and computer tomography revealed a 10 × 15 cm sized mass, suspect of being a kidney tumor. Upon surgery, the tumor was found to be a retroperitoneal malignant fibrous histiocytoma. In connection to the case, a brief review is given of the storiform type of malignant fibrous histiocytoma, regarding its etiological, clinical and pathological aspects, the difficulties in diagnosis, as well as the therapeutic possibilities. Authors regard their case worthy of publication because of the retroperitoneal location and significant size of the tumor, and because of the unproven diagnosis prior to surgery. Even after 4 years the patient is symptom- and complaint-free, and CT has revealed no metastases.

Introduction

Malignant fibrous histiocytoma (MFH) is a concept first introduced by Ozzello et al. in 1963, then later applied by O'Brien, Stout and Lattes for describing further types of MFH. It is the tumor of the elderly, amounting to 0.5% of total malignant tumors [6, 9, 18–20, 25].

The tumor is of rare, connective tissue origin with the possibility of occurrence in the retroperitoneal space [1], in which case it could be diagnosed as a primary kidney tumor.

In the followings, a review is given of a case where a retroperitoneal tumor (MFH) located in front of and below the right kidney was removed, leaving the intact kidney preserved. Authors find the case worthy of publishing partly because the tumor reached an uncommonly significant size, partly because diagnosis is difficult even with the current up-to-date examining methods, and because even histopathological differentiation requires thorough grounding.

Case Review

A 74-year-old female patient was transferred from another Department's Internal Medicine Unit on 22nd April, 1994, due to a kidney tumor causing diffuse abdominal pain, distension, puffiness and lack of appetite.

A fist-sized mass was palpated to the right of the umbilicus, deviating upon breathing together with the kidney. From the laboratory findings the only noteworthy was the increase in the red blood cell count (65 mm/h).

Ultrasound revealed a 100 × 150 mm solid mass of complete echo-structure, contiguous with the right kidney.

I.v. urography showed the right kidney-bed to be filled with a huge tumorous mass, longitudinally reaching from the right processus transversusa plane of the L-I vertebra spondyle till the upper end-lamella edge of the L-V vertebra spondyle. In the paralumbar position, the mass spread to the lateral abdominal wall, dislocating the ureter. It compressed as well as dislocated the renal median calyx group, and some contrast-material secretion was observable in the upper calyx groups, which were also deformed. Normal filling of an intact cavity system and ureter were notable on the left side (Fig. 1).

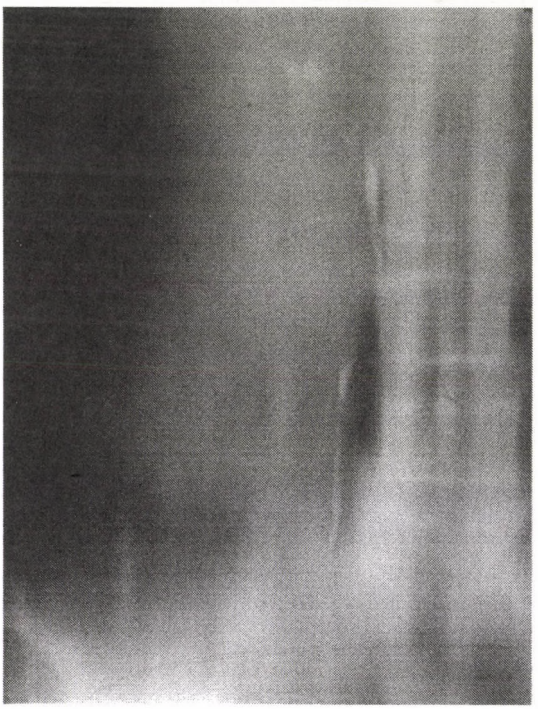

Fig. 1. I.v. urography: the right kidney-bed is filled with a huge tumorous mass

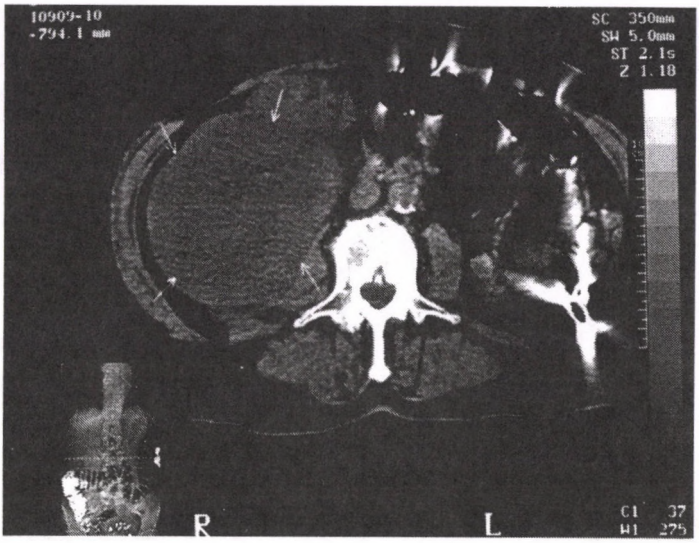

Fig. 2. Abdominal CT: the upper pole of the right kidney is intact, from which there originates a huge 10×15 cm tumorous mass, filling the kidney-bed

Abdominal CT revealed intact upper pole of the right kidney, from which a sizable 10×15 cm tumorous mass was found to originate, filling in the kidney-bed. The tumor reached upwards towards the edge of the liver, the large arteries seemed to have free surroundings.

Radiological opinion: Tu. Renis 1.d. (Fig. 2).

Based on the findings, a perpendicular lumbar cut was performed on the 27th April, 1994 to expose the right kidney-bed, from where a tumor the size of an infant's head was removed without any difficulty. The diminishing suspension ligament of the removed tumor was found adhering to the Gerota fascia of the kidney. The intact right kidney was preserved.

Histological findings: macroscopically an 890 g mass 16×13×10 cm size was found with a ragged fibrous capsule, surrounded by fatty tissue. Cut section did not show characteristic renal tissue. The edges of the tissue sections were of grayish-white colour and mucous-like at places. Centrally the substance looked to be necrotic, with a greenish-brown colour.

Microscopically, tumor tissue surrounded by fibrous capsule could be seen. The majority of the tumor cells were found in the arrangement of elongated, spindle-shaped bundles, showing storiform structure at places. The cells manifested a large degree of polymorphy and atypia, with several dividing cells among them. Histiocytes with wide, light cytoplasm were detectable at places in foci among the spindle-shaped tumor cells. Multinuclear giant cells were also observable at places. *Dg.: Malignant fibrous histiocytoma, storiform type* (Fig. 3).

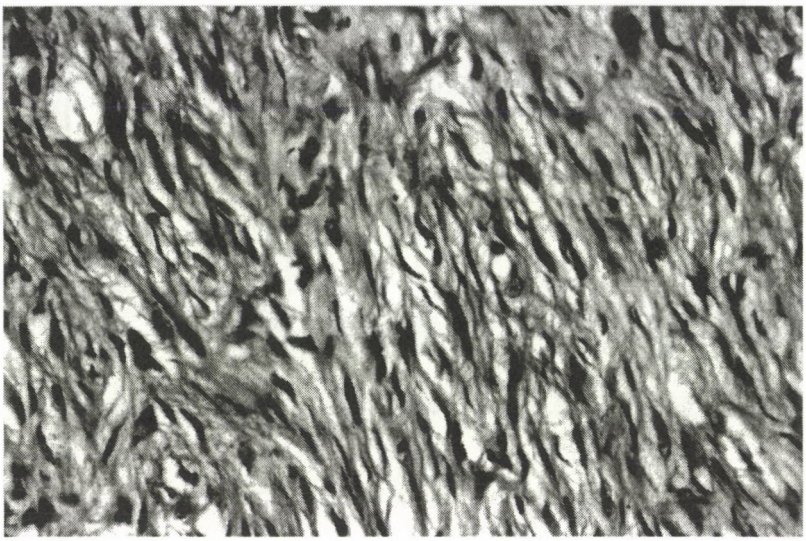

Fig. 3. Showing expressed nuclear polymorphy, spindle-shaped cells are observable together with multinuclear tumor cells. H.E. (×330)

The patient left our Department on the 10th postoperative day. Three weeks later radiation therapy was started on the oncologist's suggestion, which had to be stopped, however, due to nausea and vomiting.

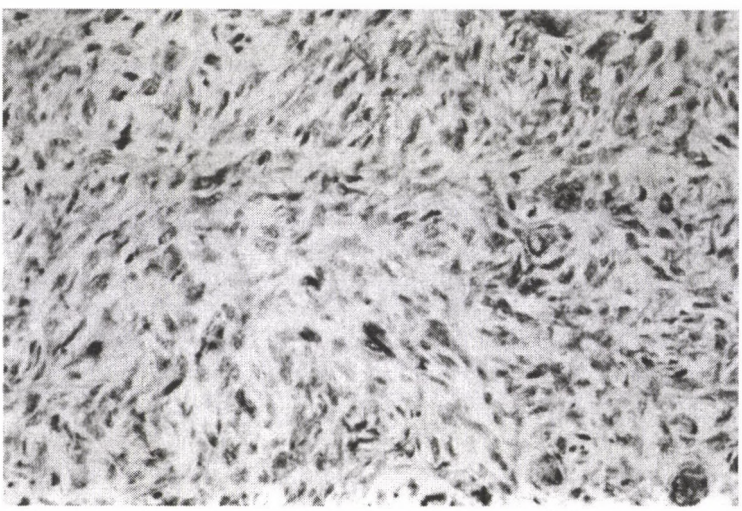

Fig. 4. Immunohistochemical reaction using Vimetine. The plasms of the tumor cells show intensive positivity

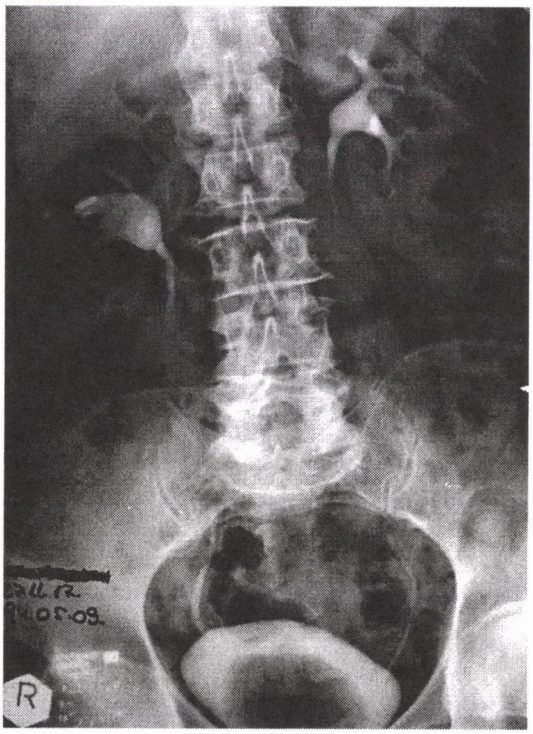

Fig. 5. Control intravenous myography after 4 years: both sides exhibit good secretion and an intact renal cavity system, with no observations of local recurrence

The patient was due for control half yearly, on which occasions no pathological alterations were found. A CT control was performed after 4 years, during which normal secretion and an intact renal cavity system were found on both sides. Local recurrence could not be observed (Fig. 5). The laboratory findings did not show any pathological alterations.

Discussion

MFHS are tumors of mixed structure, containing fibroblast- and histiocyte-like cells in varying degree. The tumor tissues may also comprise a certain amount of tumorous giant cells, inflammatory cells as well as xanthoma cells [13, 17, 21, 24, 25]. The tumor structure could be interspersed with mixoid substance and elastic fibres [29, 30].

A multitude of variants may occur depending on the presence or absence of the above-mentioned elements and their degree of mixing. Certain authors [4, 6, 22] have labelled subgroups – for example, more than 30 variants have been described according to cell type, however, in general only 3 main forms are distinguished:

1. Storiform type,
2. Pleiomorph type,
3. Fascicular type.

The first group is characterized by a vortex-like localization, and sometimes shows monomorph structure. The pleiomorph type contains bizarre cells of varying size and shape. It can be mistakenly identified as rhabdomyosarcoma or liposarcoma. The third type has a fisciculed structure [9–11].

Little is known about the histogenesis of this rare tumor. Many authors think it do be of pluripotent mesenchymal origin [13, 20], according to others it takes its origins from histiocytes [8, 9, 12–15, 22, 27–29]. The most frequent occurrence of MFH is found to be above the age of 70, it rarely occurs under the age of 40 [9]. The patient in this case review was 74 years old at the time of tumor diagnosis.

Only few data are at disposal in respect to the etiology of MFH. Irradiation is thought to play role, following which MFH may develop after several years. Sun radiation, chemical substances like fenacetin also seem to be etiological factors. It may develop after Hodgkin's disease or melanoma multiplex, and in 10% after other tumors. In animal experiments it can develop by macrophage-transformed SV 40 virus and in the bone in case of bone-infarction [7, 9]. According to the near similar data of several authors, it occurs in 64% of males and 36% of females [7, 8, 20].

In respect to site, MFH occurs in 49% on the lower limbs, in 16% on the forearm and in 19% on the upper arm. Its occurrence in the retroperitoneum and abdominal cavity, respectively, amounts to 16%, its appearance is 30% on either one or both thighs, while it occurs in 5% on the hands and legs [2, 9, 21].

In most cases the tumor is manifest as a painless nodule on the limbs, and it may remain painless for over several years. Its development in the retroperitoneum or the abdominal cavity causes symptoms of expansion, like uncomfortable distension, varicocele, hernia, but it may also be accompanied by accelerated sedimentation rate, weight loss and fever [2, 4, 9].

The development of MFH on the neck goes with the appearance of hyperglycaemia, hyperinsulinaemia, since the tumor produces an insulin-like substance. Lung metastases have been reported prior to the diagnosis of bone tumors [5, 6, 22, 30]. The tumor described in the present case review developed in the retroperitoneum and the symptoms correlated with those known from the literature. The patient had an increase sedimentation rate [1, 5, 15], and the size of the tumor allows the assumption that it developed years earlier.

As is the case with other tumors, MFHs also form metastases firstly in the regional lymph nodes. The metastases are similar to the original tumor, in rare cases, however, they will be of storiform type, usually containing inflammatory elements as well [5, 6, 28].

In respect to differential diagnosis, it is extremely difficult to differentiate between the various forms of MFHs and other malignant tumors, owing to the polymorphism of the cells. Differentiation between polymorph MFH and liposarcoma, rhabdomyosarcoma may also be a difficult task. Furthermore, differntial diagnosis might not be easy

in certain cases of anaplastic, pleiomorph carcinomas either [19, 24]. Our aids in the differentiation are the various stainings, histochemical studies (Fig. 4), as well as the electron microscope [3, 16, 17, 26, 27].

In rare cases, the MFH encases the lymph nodes in a diffuse manner, when it should be differentiated from Hodgkin's disease [9, 12, 17–19].

In many cases, MFHs appear together with other tumors, e.g. with gastrointestinal, renal, or malignant skin tumors. Sometimes, malignant tumors may even occur 2–11 years after the development of MFHs. Their appearance has also been reported after 6 years following irradiation [9, 21, 30].

Bertoni et al. observed recurrence in 37.5% of cases, from which one appeared 28 days following treatment [2].

The 5 years survival rate is 36% according to Pezzi et al. 36% [20], while Enziger found recurrence to be 25% and metastasis to be 34% [9]. With a recovery rate of 50% was in his cases. Distant metastases are found to be 90% in the lungs, 8% in the bones and 1% in the liver; the lymph nodes are interlaced by MFHs in 35% of the cases [2, 3].

The development of metastases is in proportion with the deepness, size and grade of the tumor. In general, the more superficial the tumor, the better the prognosis. For example, if the MFH is of subcutaneous location without any linkage to the fascia, there is no metastasis [28]. In this respect, an analogy exists between the atypical fibroxanthoma and the storiform type of the MFH. If the MFH has interweaved the subcutis and fascia, metastasis too, is present in 27% of the cases. When the skeletal muscle is also involved, the degree of metastasis is 43% [21, 22, 30]. The prognosis is also proportional to the size of the tumor [21]. If the tumor is smaller than 5 cm, the 5 years survival rate is 82%, decreasing to 68% if the tumor size is 5–10 cm, and being only 51% if the tumor is above 10 cm in size. Naturally, the recovery rate is also proportional to the grade of the MFH. Pezzi et al. [20] observed an 80% survival rate where the tumor was of grade II, while from grade III onwards the survival was only found to be 60%. The tumors of distal location have better prognosis. Invasion of the arteries, tumor necrosis, as well as local recurrence are all signs of unfavorable outcome [9, 23, 25].

As a summary, it could be said that the prognosis of MFH is in tight relationship with the histological malignity grade, the tumor size, depth and site of location, as well as the cell type [9, 15, 18, 25, 26].

According to the authors of the presented case, the prognosis is better and there are fewer or no metastases in MFH cases containing mixoid or inflammatory cells, as compared to tumors comprising other cell types [9, 20].

Radical surgery is recommended for the treatment of MFHs – including the storiform type. Radiotherapy and cytostatics are also applied treatments, either alone or in palliative mode. However, a single large dose of nitrogen mustard has also been suggested as treatment [5, 6, 25].

The patient in the present review has been symptom- and complaint-free for 4 years since the removal of the significant sized, storiform type MFH, and following her irradiation treatment.

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