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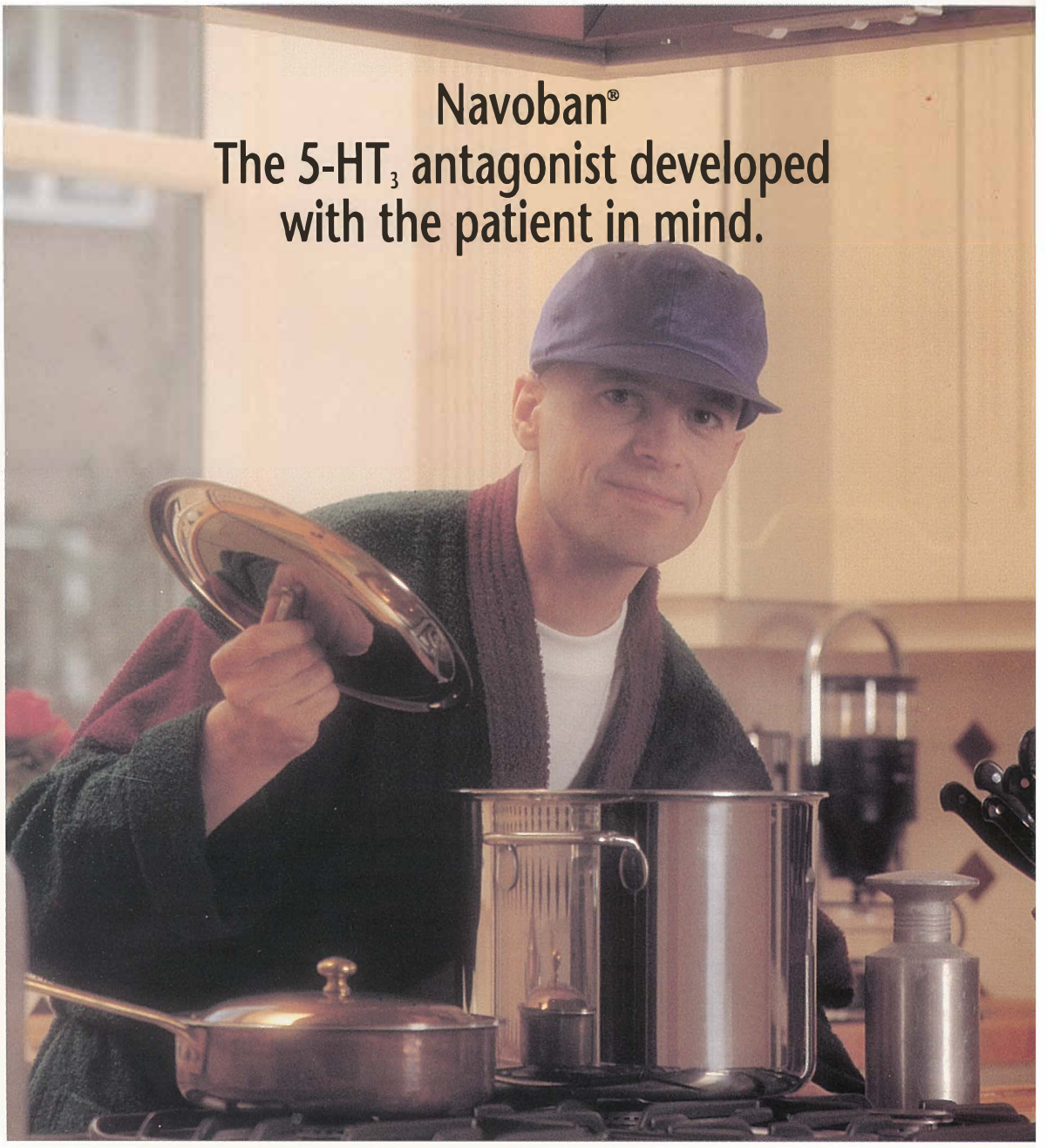

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Persistent primitive trigeminal artery associated with intracranial aneurysms

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Persistent embryological carotid-basilar anastomoses are rarely encountered in cerebral angiograms. Intracranial bleeding caused by an arteriovenous malformation or a ruptured aneurysm is the most frequent coincidental finding asociated with persistent carotid-basilar anastomoses. A case of a persistent primitive trigeminal artery associated with aneurysms of both posterior communicating arteries is presented in this study. Other embryonal anastomotic remnants, e. g. primitive otic, hypoglossal, proatlantal intersegmental and stapedial arteries, are briefly described.

Key words: carotid arteries-abnormalities; basilar artery-abnormalities; cerebral arteriovenous malformations; cerebral angiography

Introduction

The pathoanatomic and especially angiographic evidence of persistent carotid-basilar anastomoses (CBA) appear to be rather rare. These anastomotic channels are the intersegmental arteries connecting longitudinal neural arteries (primitive basilar artery) with primitive internal carotid artery (ICA) in a 4-mm stage embryo. They follow the course of the fifth, eighth and twelth cranial nerves and are therefore called primitive trigeminal (PTA), primitive otic/acoustic (POA) and primitive hypoglossal arteries (PHA). After the vertebral-basilar arterial system and posterior communicating arteries (PCoA) have been formed at a 7 to 17-mm stage embryo, the CBA-s are getting gradually atrophic: first the otic followed by hypoglossal and then by trigeminal artery as last.[1, 2, 3, 4] In the case of persistent function of these channels in an adult person, it appears to be a consequence of non-obliteration of these primitive anastomoses.

The CBA-s are often associate with the intracranial haemorrhage.[2, 5, 6] This observation was mentioned in one of our previously published articles concerning four cases of PTA-s but cerebral angiography failed to demonstrate the cause of bleeding.[2] This is our fifth case of PTA and second with subarachnoidal haemorrhage (SAH) in the last 23 years. Four-vessel cerebral angiography revealed two berry aneurysms of both PCoA-s.

Case report

T. B., a 33-year old woman complained of a sudden onset of unconsciousness. After reco-

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very she experienced weakness, headache and nausea with vomiting. A blood stained cerebrospinal fluid was found on admission, and CT demonstrated SAH. Cerebral angiography, performed with a catheter by femoral route demonstrated an immediate filling of the posterior circulation from the right ICA. Its precavernous segment was connected with the distal segment of basilar artery (BA) via a large anastomotic vessel (Figure 1a). The inflow point of the

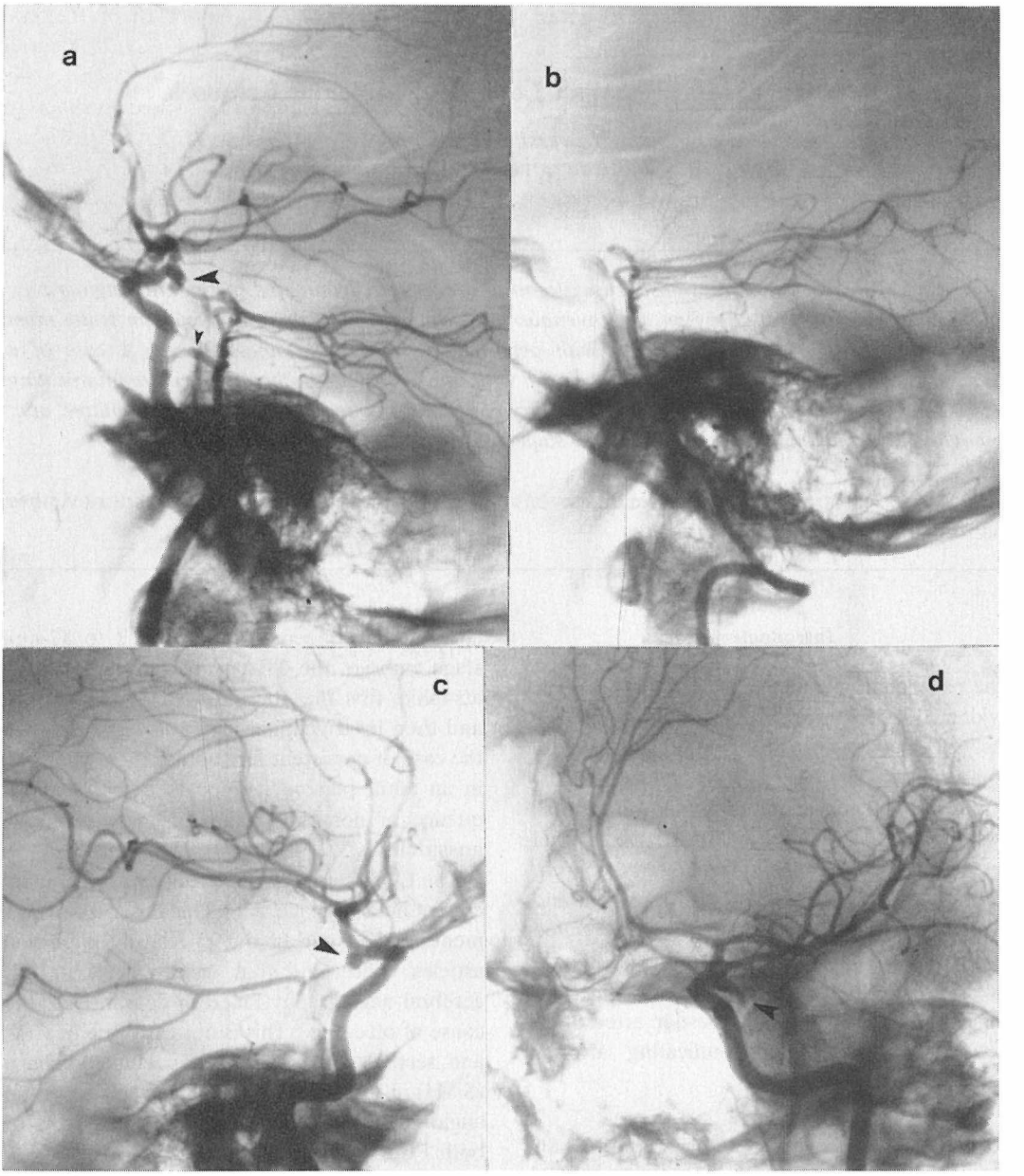

Figure 1. Lateral right ICA angiogram (a) shows a PTA (small arrowhead) connecting precavernous segment of the ICA with the BA, Aneurysm of the PCoA is demonstrated (arrowhead). Lateral vertebral angiogram (b) show hypoplasia of the proximal portion of the BA. Lateral and oblique left ICA angiograms (c, d) demonstrate another PCoA aneurysm (arrowhead).

anastomotic channel was situated between the origins of the anterior inferior cerebellar and superior cerebellar arteries, whereas the proximal segment of BA was hypoplastic (Figures 1a, b). Four-vessel cerebral angiography revealed two tiny berry aneurysms of both PCoA-s (Figures 1a, c, d). The patient was operated on, the ruptured right-sided und unruptured left-sided aneurysms were clipped.

Discussion

Among persistent CBA-s the PTA is the most frequently encountered. It originates from the praecavernous segment of the ICA and is connected with the distal segment of the BA. Firstly, it passes posteriorly through the cavernous sinus lying medially to the ophthalmic branch of the trigeminal nerve. Passing the dorsum sellae it joins the BA between the origins of the inferior anterior cerebellar and superior cerebellar arteries. The course of the PTA may be either straight or tortuous and its caliber may vary (Figures 2a,b, 3a). In our case the PTA was superiorly arched and was of the same caliber as BA (Figure 1a). In some cases BA was hypoplastic proximally to the inflow of the PTA, and this was also observed in our patient's angiograms (Figure 1b). Bilateral PTA-s are rarely encountered. Supracavernous portion of the ICA, distally to the origin of the PTA may be either of a reduced caliber or obliterated.[2, 7] We demonstrated it in one of our previously published cases (Figure 3a, b).[2]

There are two pure forms of PTA as well as some variants.[8, 9] In Salzman type I anastomosis the entire basilar-posterior cerebral artery system is filled via the PTA. In Salzman type II anastomosis the basilar and superior cerebellar arteries are filled via the PTA while the posterior cerebral arteries are filled via the PCoA-s. Combination of both anastomotic types is also observed.[1, 2, 8] In our case, Salzman I type persistent anastomosis was demonstrated. In fact the PTA variants represent an anomalous

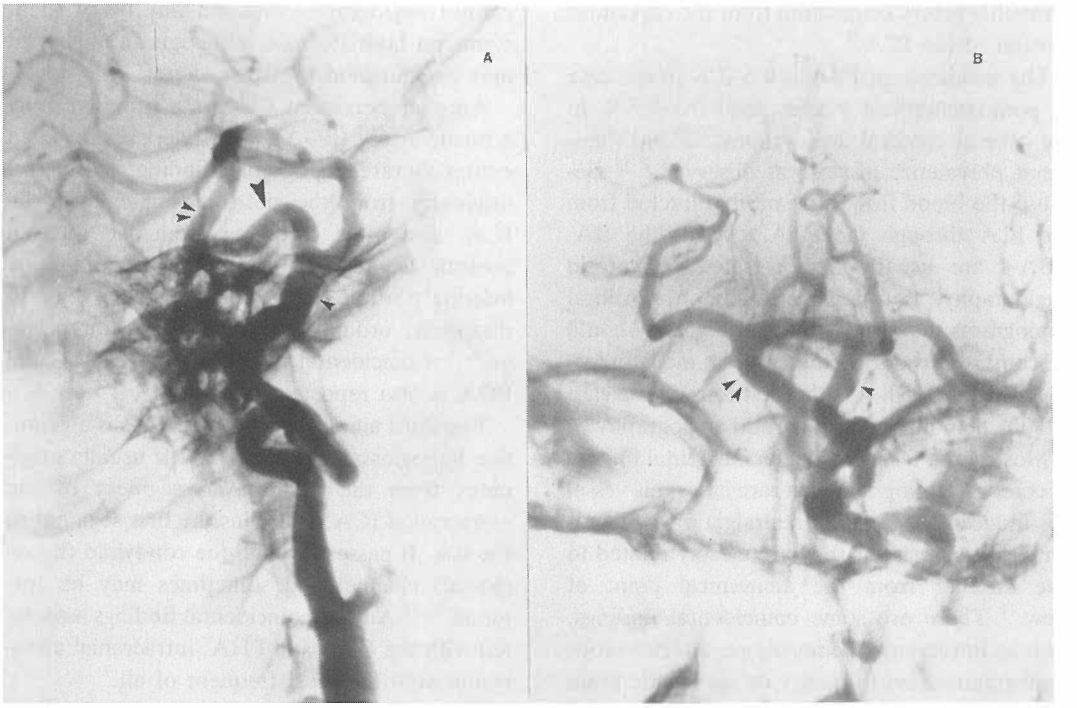

Figure 2. Lateral (a) and AP (b) left common carotid angiograms show a wide PTA (arrowhead) connecting precavernous portion of the ICA (small arrowhead) with the BA (duble small arrowhead). Reprinted from[2].

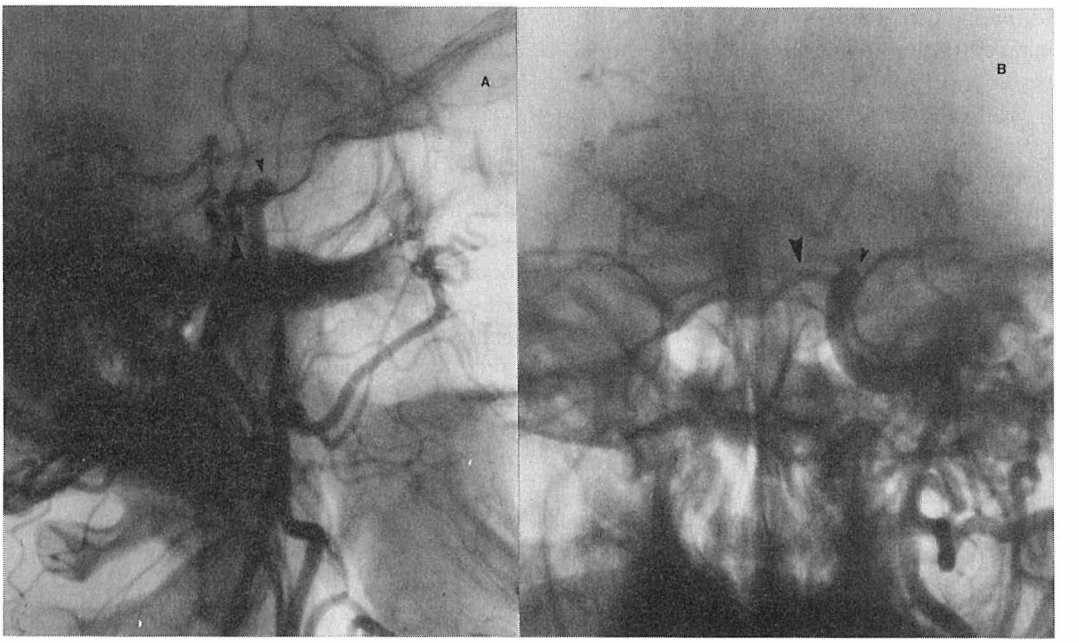

Figure 3. Lateral (a) and AP (b) left common carotid artery angiograms show tortuous PTA (arrowhead) and occlusion of the cavernous portion of the ICA (small arrowhead). Reprinted from[2].

inferior anterior cerebellar artery or superior cerebellar artery originating from the cavernous portion of the ICA.[9]

The incidence of PTA is 0.5–2 % in the case of pathoanatomical studies, and 0.1–0.5 % in the case of cerebral angiography.[2, 10] No significant prevalence of sex was observed.[1, 11] Because the blood flow is primarily directed from the ICA through the PTA towards the BA, CBA-s are usually demonstrated by carotid angiography. For demonstration on vertebral angiograms the ipsilateral carotid artery should be compressed during the contrast media injection. Sutton 1950. was the first to record a case of PTA demonstrated by carotid angiography.[2]

Most of the PTA-s make an incidental finding of cerebral angiography. In rare cases this vessel has induced a trigeminal neuralgia or oculomotor nerve paresis for they are closely related to one another from the anatomical point of view.[11] There are some coincidental findings, such as intracranial hemorrhage, arteriovenous malformations and primary or metastatic brain tumors associated with the PTA. Intracranial aneurysms are by far the most frequent of all the findings observed.[1, 2, 8] In our case the carotid angiography revealed tiny berry aneurysms on both PCoA-s, although an aneurysm may be found on the PTA alone.[9]

Another persistent CBA is a primitive otic/acoustic artery (POA), which appears to be an extremely rare angiographic finding. This vessel originates from the petrosal segment of the ICA, and after emerging from the internal acoustic meatus, it joins either the middle or inferior portion of the BA. It is the first to disappear, ordinarily at a 4-week embryo stage.[4, 7] Coincidental finding of the PTA and POA is olso reported.[9]

The third among persistent CBA-s is a primitive hypoglossal artery (PHA). It usually originates from the atlantoaxial segment of the extracranial ICA, and joins the first segment of the BA. It passes through the condyloid (hypoglossal) channel and sometimes may be tortuous.[11, 12] Among coincidental findings associated with the POA and PHA, intracranial aneurysms were the most frequent of all.[7]

Persistent proatlantal intersegmental artery is also an embryonal remnant which is not a

CBA but a carotid-vertebral anastomosis. This artery commonly arises from the cervical portion of the ICA, and less frequently from the external carotid artery. The site of origin extends from the third to the fifth cervical vertebrae of the ICA. The inflow point includes the terminal segment of the vertebral artery. The course of the proatlantal artery is through the foramen magnum.[3, 13–15]

While describing rudimentary embryonal vessels of the craniofacial region, one should mention the persistent stapedial artery which is an internal to external artery anastomosis. This arterial branch is encountered rarely for it normally disappears at an early stage of embryonal growth. It originates from the petrosal segment of the ICA, extends through the middle ear and ends as a middle meningeal artery.[7] First angiographic evidence of persistent stapedial artery with middle meningeal artery continuation was done in 1972.[8]

Radiologists should be familiar with the morphological aspects and anatomical relationships of persistent vascular anastomoses. Recognition of these vessels in cerebral angiograms might be of great diagnostic importance. The etiology of trigeminal neuralgia, for example, may be ascribed to the PTA. Awareness of these vascular channels may improve surgery planning in otorhinolaryngology and neurology and might influence both planning and performing of radiological occlusive procedures.

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Interventional ultrasound in renal transplantation

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The authors present their six year (1988–1993) experience in the use of interventional ultrasound in patients with transplanted kidneys. During that time 165 kidney transplantations (55 /33 %/ from living donors and 110 /67 %/) from cadavers were performed in KBC Rijeka. Interventional US was indicated in 49 cases: 18 (37 %) biopsies, 10 (20 %) aspirations, 17 (35 %) drainages and 4 (8 %) percutaneous nephrostomes. Indications included ultrasonically evident rejections, collections in or around grafts (lymphocele, urinoma, hematoma, abscesses, hydronephrosis and pancreatic pseudocyst). The value of interventional US for early diagnosis and therapy of the mentioned pathological conditions endangering the patient's life or leading to different stages of graft dysfunction in the initial and late posttransplantation period is emphasized. Early complications of intervetions were not reported until in four patients epididymitis, febrility and 2 arterio-venous fistulas, without false negative of false positive results were noted. Recurrences (2 lymphoceles, 1 urinoma and 1 abscess) in 5 patients (8 %) were treated by additional intervention: drainages in lymphoceles and abscess, reoperation in urinoma.

Key words: kidney transplantation; ultrasound; interventional; radiology

Introduction

Early and late complications of kidney transplantation such as acute and chronic renal failure, acute tubular necrosis, lymphoceles, urinomas, abscesses, hydronephrosis and anuria may disturb graft function, and call for timely diagnosis and therapy. The introduction of ultrasound in the routine follow up during the transplantation period, together with early diagnosis and prompt US-guided intervention, have decreased the occurrence of general or local complications and convalescence time.[1–5]

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UDC: 616.61-089.843-073

Material and methods

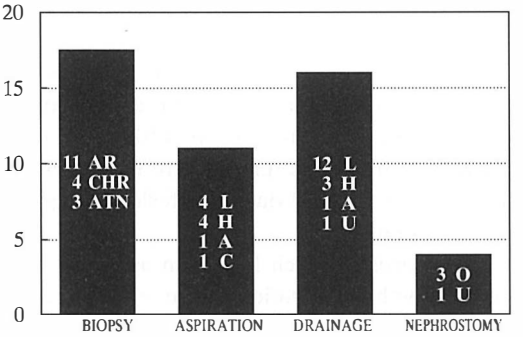
Interventions were performed in sterile surgical conditions and under US-control by means of "ALOKA SSD-220-LS" device with a 5 MHz interventional probe. All interventions were done in local anesthesia except one drainage of a lymphocele when general anesthesia was used owing to the patient's condition. A "Tru-Cut" needle ("biopsy gun") or 22 or 25 gauge biopsy needle were used for biopsies. Aspirations were

performed using 14 and 16 gauge needles or prepared sets for drainages and nephrostomies.

Results

During a six year period (1988–1993) in KBC Rijeka were done 165 kidney transplantations (55 (33 %) from living donors and 110 (67 %) from cadevers). In the Ultrasound Unit, 49 interventions in patients with transplanted kidney were performed. Biopsies were done in 18 (37 %), aspirations in 10 (20 %), drainages in 17 (35 %), and percutaneous nephrostomies in 4 (8 %) cases (Table 1).

Table 1. Interventions under ultrasound control.



AR = acute rejection, CHR = chronic rejection, ATN = acute tubular necrosis, L = lymphocele, H = hematoma, A = abscessus, C = cyst, U = urinoma, O = obstruction

Indications for biopsies were based on clinical stage and laboratory data with ultrasound images of graft crises which failed to respond to therapy. Biopsy showed acute rejection in 11 patients (61 %) and chronic in 4 (22 %), while 3 patients (17 %) presented with acute tubular necrosis (Figure 1).

Aspirations were performed in 4 (40 %) lymphoceles, 4 (40 %) hematomas, 1 (10 %) abscess and 1 (10 %) pancreatic pseudocyst. The parenchymal abscess was first aspirated 3 times with instillation of Gentamycin "in loco" and finally drained (Figure 2). Pancreatic pseudocyst was aspirated 9 times (with 2.5 l of liquid removed on first aspiration; finally, successful sclerosation with tetracycline was performed.

Twelve (70 %) lymphoceles, 3 (20 %) hematomas, 1 (5 %) abscess and 1 (5 %) urinoma were drained. Sclerosation with povidoneiodine in 10 (91 %) and tetracycline in 1 (9 %) were

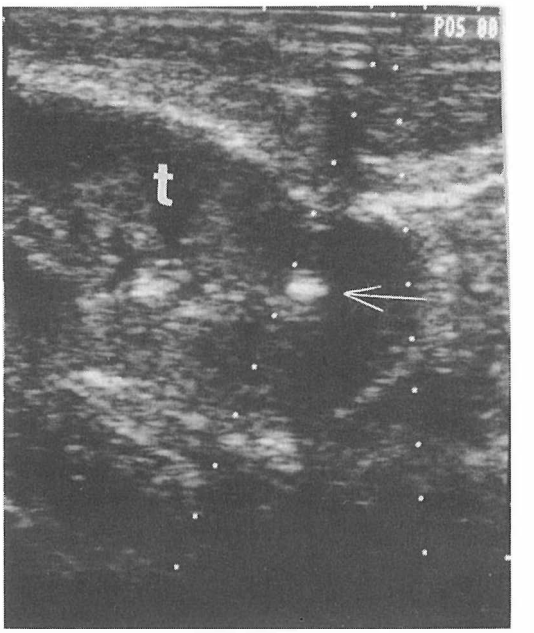


Figure 1. Longitudinal scan of the trasnplanted kidney (t) during aspiration biopsy of the upper pole (arrow: top of the needle).

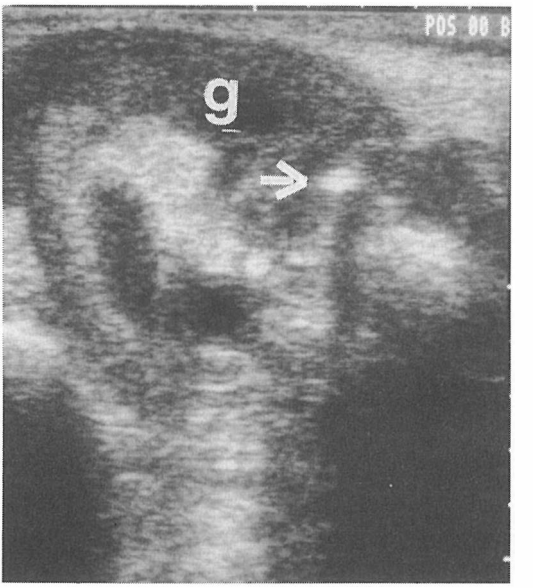


Figure 2. Semioblique scan of the graft (g) with drained isoechoic mesorenal abscsess (arrow: top of the drain).

performed beside lymphocele drainage (Figure 3). Percutaneous nephrostomies were done in 4 (8%) cases. Obstructions in ureterocystoneostomy were found on anterograde pyelography through nephrostoma (Figure 4 and Table 2).

All 12 patients (100%) with cytologically confirmed acute rejection or acute tubular nereduced dimension and heterogeneous echoes

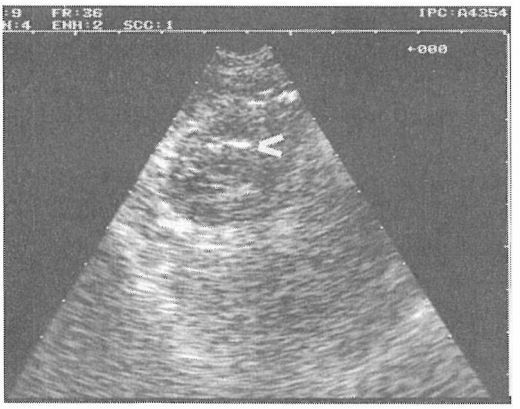


Figure 3. Semioblique scan of the lymphocele (l) during sclerosation with hyperechoic air microbubbles (arrow: the top of the drain).

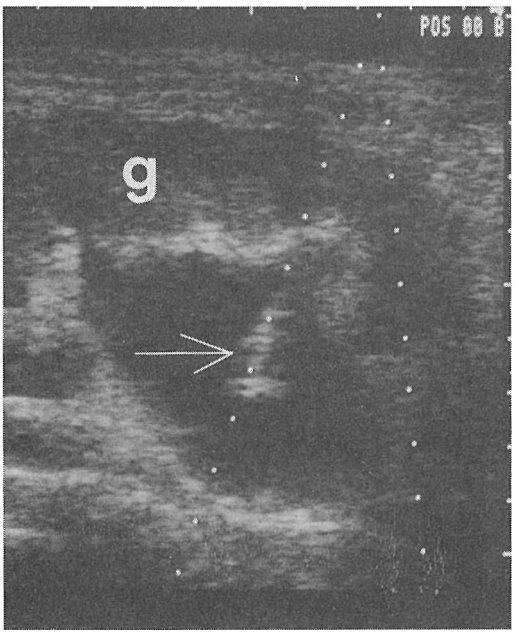
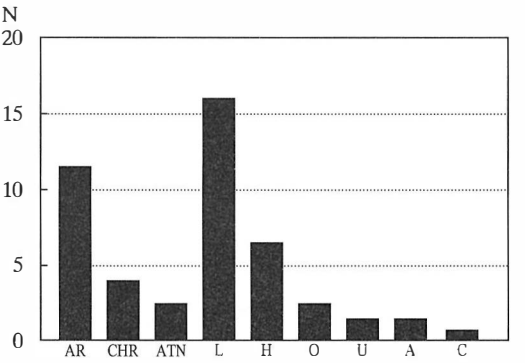


Figure 4. Longitudinal scan of the graft (g) with dilated pyelocaliceal system during percutaneous nephrostom placement (arrow).

Table 2. Indications of interventional ultrasonography



AR = acute rejection, CHR = chronic rejection, ATN = acute tubular necrosis, L = lymphocele, H = hematoma, A = abscess, C = cyst, U = urinoma, O = obstruction

are signs of chronic rejection.[1–4] Meanwhile, cyclosporine damage yields a similar ultrasonic crosis had normal graft function after medicamentous therapy until in two (50%) of four patients with chronic renal failure transplantectomy was performed due to deteriorated general condition.

Lymphoceles, which had been aspirated and drained with sclerosation, were eliminated as hematomas. Urine leakage from ureterocystoneostomy was suspended after percutaneous nephrostoma instillation in 2 patients. Reoperation was reguired in one case. Fourth patient had natural dilatation of pyelocaliceal system discovered lately.

Late postinterventional complications were noted in 4 patients (9%): these included epididymitis, fever and 2 a-v fistulas.

Discussion

The introduction of ultrasound in the follow up of posttransplantation period has enhanced the possibilities of earlier detection of graft disfunction or peritransplant collections.[1–5]

Allograft enlargement, edema of the medulla, and increased parenchyma-pyelon ratio are parameters which, together with clinical state and laboratory data, help to confirm the diagnosis of acute rejection. Parenchyma reduction, reduced dimension and heterogeneous echoes

are signs of chronic rejection.[1–4] Meanwhile, cyclosporine damage yields a similar ultrasonic image, which requires the use of other diagnostic methods.[3,4,6] Although, Duplex Color Doppler sonography is helpful to some extent, in order to distinguish between those states, definitive answer is obtained by biopsy.[1,2,4,7,8–10, 12] Its conduction under US guidance reduces the rate of complications (temporary hematuria, injuries of the hilus; a-v fistulas). The use of a "biopsy gun" or fine aspiration needle showed similar results.

Hypeochoic formation around the graft, which can disturb its function, demands evacuation. Ultrasonic image of lymphocele, urinoma or fresh hematoma are similar, even their localization may refer on origin (dorsal part-hematoma, parachilar-urinoma) and demand diagnostic puncture.[1–5,7,10–12] Aspiration was sufficient in small hematomas and lymphoceles while in bigger, due to recurrences, drainage had to be used.

Collection of heterogenous echoes in one graft referred to abscess which was confirmed by cytology. Instillation of Gentamycin "in loco" on 3 occasions insufficently reduced lesion, and therefore percutaneous drainage and topic application of antibiotics was indicated which eliminated abscess after two weeks.

Hydronephrosis of pyelocaliceal system and dilated ureter referred to an obstruction on the ureterovesical connection. Percutaneous nephrostoma enabled urine drainage and anterograde pyelography showed the place of obstruction.

Recent literature[6–12] and our experience[1–5] point out necessity of ultrasound follow up of transplanted kidneys and its value for timely interventional diagnostic and therapeutic approach in the damage of graft function.

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Transcatheter embolization of congenital arteriovenous malformations of the limbs

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The authors present 32 palliative transcatheter embolizations in 16 patients with congenital arteriovenous malformation (AVM) of the limbs. The clinical study was aimed at establishing the role of previously ligated supplying artery(ies) in the feasibility of superselective catheterization needed for embolization. This series also dealt with the question whether Gelfoam embolization could be of predictive value for tissue glue embolization. Although Gelfoam embolization gave favourable result in all cases, its effect was only temporary. Moreover, because of its basically different characteristics, Gelfoam did not prove to be useful for simulating haemodynamic changes caused by tissue glue embolization. The tissue adhesive, however, proved to be a very reliable embolizing material, causing definitive vascular occlusion. Although it was not easy to handle, by gaining more and more experience it could be applied safely in skilled hands. Using relatively inexpensive coaxial catheter systems together with a quide wire with excellent torque control, superselective catheterization could be accomplished in all cases including those where the supplying artery(ies) had been surgically ligated.

Key words: arteriovenous malformations; embolization, therapeutic-methods; transcatheter embolization, congenital arteriovenous malformations, superselective catheterization, tissue adhesive embolotherapy, coaxial catheter systems

Introduction

Despite significant diagnostic and therapeutic progress, the treatment of congenital arteriovenous malformations (AVMs) remains one of the most challenging areas of vascular surgery. In most cases different therapeutic interventions (e.g. excision of the lesion or surgical ligation of the feeding vessel/s) were of no curative value.[1-4] A common disadvantage of different therapeutic interventions is the early occurrence of recurrent lesions as these do not prevent the formation of collaterals. By purely surgical methods only small, well circumscribed, fully exstirpable lesions can be cured.[2,5] If the lesion is large and/or is localized in certain critical areas (e.g. in the pelvis), or occurs in the infiltrating form of predominantly arteriovenous defects,[6,7] the surgical approach is bound to fail. In certain cases mutilating operations, in cases of extremities – amputations would be required.[3,8]

The development of transcatheter emboli-

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zation opened new therapeutic perspectives; for the majority of patients with extensive AVMs the only recommendable form of therapy is the *transcatheter embolization.*[1,2,9] If the lesion is resectable, the speed and safety of surgery can be greatly improved using preoperative vascular occlusion. Thus the surgical procedure causes less hemorrhage.[2]

This study was aimed at establishing whether Gelfoam could be used for imitating haemodynamic changes expected after tissue glue embolization. It was also conducted to determine the role of the previously ligated feeding artery(ies) in the feasibility of superselective catheterization which is basically needed for embolization.

Materials and methods

Table 1 shows characteristics of the patient groups. We performed 32 embolizations in 16 patients. The age of 12 children ranged between 3–13 years (average 9.1 years), the four adults were 20, 28, 39 and 50 years old. The group consisted of 6 men and 10 women.

The embolized lesions were classified according to Hamburg Classification (1988).[7] All the patients had predominantly arteriovenous shunting defects with deep a-v fistulae. In five patients the lesions were of infiltrative character.

All of the children and one of the adults (case No. 7) were embolized under general anaesthesia while the remaining adults were treated in local anaesthesia.

In one therapeutic session we catheterized and selectively embolized 1 to 3 arteries. Nine patients had undergone previous treatment which resulted in ligation of one to three supplying arteries to the lesion. Each patient had 1 to 4 embolization sessions. The interval between sessions varied from 2 to 24 months.

The following materials were used for embolization, partly in combination with one another: *Surgical sponge* (Gelfoam) was used in 7 patients (13 sessions); *N-butyl-2-cyanoacrylate* (NBCA, Histoacryl^{R}, Braun Melsungen, Federal Republic of Germany) mixed with the lymphographic contrast medium Lipiodol Ultrafluid (Byk Gulden) was applied in 1 : 1 or 1 : 2 ratio in 13 cases (18 sessions); *Absolute ethanol* was used as an additive to surgical sponge in 3 cases.

In certain sites, e.g. with the lesions located on the hand or leg/foot, and in all cases with the use of tissue glue, superselective catheterization was necessary. In most cases we used 5F angiographic catheters (Radiofocus,^{TM} Terumo, Japan), and 3F TIC^{TM} therapeutic infusion catheters as coaxial catheter systems, and/or Cragg convertible guide wires (both Meditech, U.S.A.) together with a 0.025 inch superglide guide wire (Radiofocus,^{TM} Terumo, Japan) were applied.

General aneasthesia was used not only to anaesthesize the patient, but also to facilitate the superselective catheterization by preventing vascular spasms. For the same reason, low-osmolar contrast media were used (Hexabrix 320^{R}, Byk Gulden Konstanz, Iopamiro 300^{R}, Bracco, Omnipaque 300^{R}, Nycomed).

We estimated the volume for the vascular bed to be embolized and thus the amount of embolizing material required through contrast injections. Depending on the vascular volume, we injected 0.5–2.0 mL of surgical sponge and contrast medium mixture into the arteries. For embolization with Histoacryl-Lipiodol mixtures we used 0.1–0.5 mL amounts per artery.

Results

All the lesions favourably responded to embolization. The patients' complaints (pain, restriction of movements) diminished, the palpable thrill became less accentuated, and even disappeared in patients No. 3, 4, 7, 14 and 16 (Figures 1 a, b, c). Patient No. 6 had a chronic limb ulcer which improved after embolization; a part of its area healed and the remaining area became shallower.

The favourable clinical outcome was independent of the embolizing agent used for the intervention. Two to four months after 9 embolizations with surgical sponge performed in 5

Table 1. Data on patients treated by embolotherapy.

Patient age/sex	Site	Type acc. to Hamburg classification 1988	Previous treatment (vessel ligation)	Symptoms, clinical problems	No. of embolized arteries/ stage	No of emboliza-tions	Emboli-zing material	Clinical improvement	Time between stages (months)	Complications		Duration of clinical follow up since initiation of therapy (mo)
										major	minor	
1/11/F	thigh pelvis	PAVSD	+	pain, swelling	1 3	2	G NBCA	good, marked reduction in symptoms	14	none	none	85
2/11/F	thigh knee	PAVSD	+	pain, enlarged veins, swelling	3 3	2	G NBCA	marked	10	none	none	81
3/13/M	hand wrist	INFILTRATING	+	pulsatile mass, dilated veins, swelling, bruit	1 2 2 1	4	G-ethanol G G + NBCA NBCA	good, bruit, ceased residual AVMs remain	9 7 18	none	none	89
4/6/F	foot heel	INFILTRATING	+	pulsatile mass, bruit, enlarged veins, swelling, moderate extremity hypertrophy	1 1 3 1	4	G G + ethanol NBCA NBCA	pulsatile mass and bruit disappeared difference between the lenght of both legs decreased	7 6 24	pulmonary embolism	skin necrosis (d = 10 mm) skin necrosis (d = 15 mm)	81
5/11/F	thigh knee	PAVSD	+	pain, swelling	2	1	G	slight improvement	–	none	none	78
6/28/M	thigh	PAVSD	+	bluish discoloration, swelling, pain, chronic ulcer	1 2 1 2	4	G G G G + ethanol	marked reduction in symptoms, ulcer healed	2 2 5	none	none	76
7/39/F	hand	INFILTRATING	+	pain, swelling, atrophy of the distal phalanx of the trumb, bruit	2	1	NBCA	after temporary paraesthesia and amputation, marked improvement, bruit ceased	–	necrosis of the distal phalanx of the thumb	none	71
8/12/M	thigh	PAVSD	+	intermittent pain, decreased exercise tolerance	3	1	NBCA	marked improvement	–	none	none	75
9/12/F	forearm	INFILTRATING	+	discoloration, forearm hypertrophy, pain	2 2	2	NBCA NBCA	the degree of hypertrophy decreased, pain ceased	7	none	none	54
10/3/F	foot heel	PAVSD	–	pulsatile mass, enlarged veins, swelling	1 1	2	NBCA	after surgery (skin transplantation) free of symptoms	–	necrosis of 5 by 3cm on the plantar surface	none	36
11/9/F	foot	PAVSD	–	swelling, discoloration, intermittent pain	2 1	2	NBCA NBCA	marked reduction in symptoms	3	none	none	49
12/20/F	thigh	PAVSD	–	swelling, discoloration, hypertrophy, pain	1	1	G	slight improvement	–	none	none	35
13/50/F	leg	PAVSD	+	pain, dilated veins, discoloration, swelling	1	1	NBCA	slight improvement	–	none	none	32
14/8/M	ankle	PAVSD	–	dilated veins, hypertrophy swelling, bruit	1	1	NBCA	marked improvement, shunt totally disappeared	–	none	none	23
15/3/M	wrist	PAVSD		pain, swelling	2	1	NBCA	marked improvement	–	none	none	19
16/11/M	forearm	INFILTRATING		dilated veins, bruit hypertrophy	2 2	2	NBCA NBCA	marked, shunt totally disappeared	5	none	none	13

M = male
F = female
G = Gelfoam
NBCA = n-butyl-2-cyanoacrylate (Histoacryl^{R})
PAVSD = predominantly a-v shunting defects

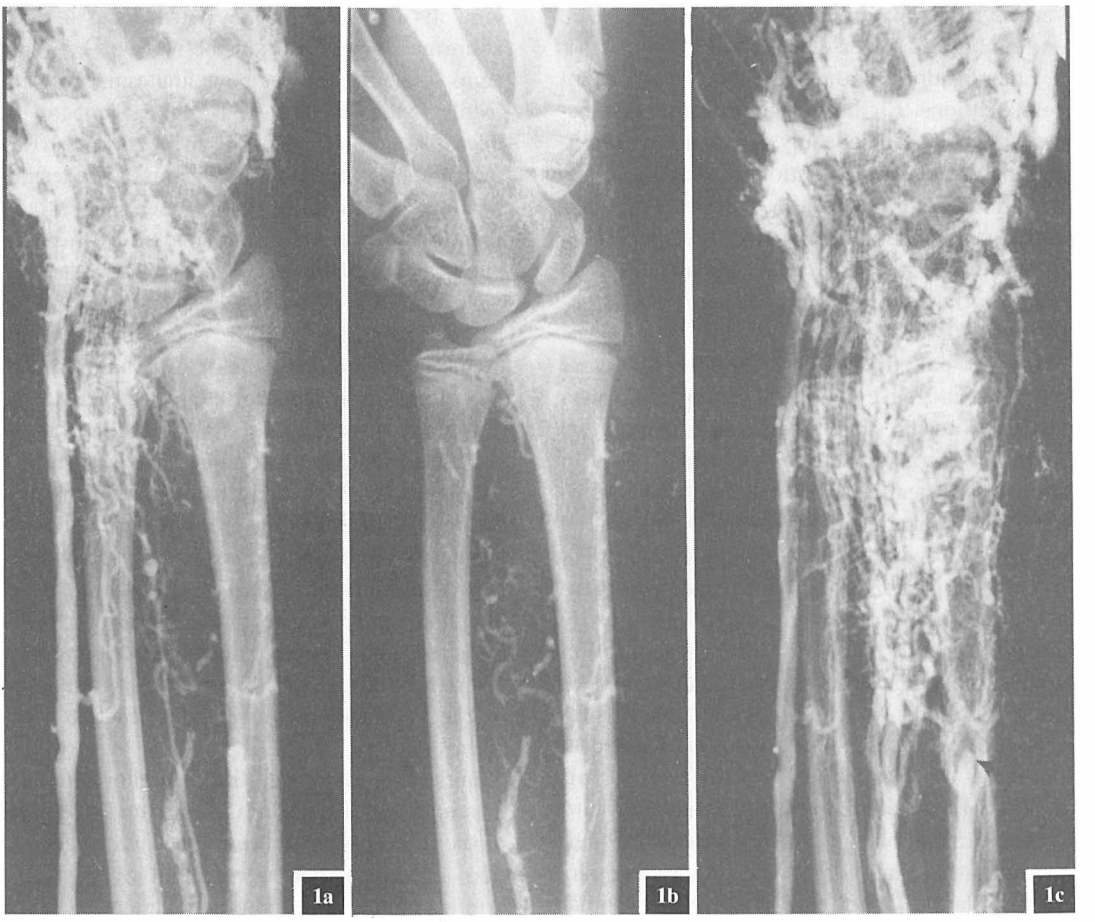

Figure 1a. Arteriography of the right forearm and hand reveals a large infiltrative a-v lesion supplied by all three arteries of the affected region. Both radial and interosseal artery have been ligated in the distal third of the forearm (arrows). From these stumps and the enlarged ulnar artery many branches provide vascular supply to the lesion. Note intensive early venous filling.

Figure 1b. After embolizing both the interosseal and radial arteries along with their end-branches, the embolizing material (tissue glue mixed with oily contrast medium fills "cast-like" the abnormal vasculature, the "nidus" of the lesion.

Figure 1c. Follow-up arteriography performed immediately after embolization shows that the lesion has been deprived of vascular supply in the region of the embolized arteries. The part of the lesion fed by the branches of ulnar artery remained unchanged. The ulnar artery alone ensures efficient vascular supply to the hand.

patients, the control angiography showed a nearly intact vascular pattern, proving recanalization. In four patients the following, and in one patient the last embolization were performed with Histoacryl^{R}. In nine cases (patients No. 7–11 and 13–16) we used cyanoacrylate even for the first embolization session.

Nine patients had undergone surgical ligation of the feeding artery(ies) (patients No. 1–8 and 13), while in certain cases the ligation had been combined with intraoperative embolization. The previous ligation (e.g. of the radial artery in patients No. 3 (Figures 1 a, b, c and 7) of the posterior tibial artery in patient No 4, of the right hypogastric artery in patient No 1 only made the embolization procedure more difficult, but did not prevent its performance. The collaterals originating from the stump, while in the case of ligated hypogastric artery, the branches of the contralateral hypogastric artery ser-

ved as supplying branches to be catheterized and embolized superselectively.

Embolizations with Gelfoam were free of complications. Eighteen embolizations with tissue adhesive entailed only few serious complications. It is worth mentioning that the overwhelming majority of these undesirable phenomena were encountered at the very beginning of this series and they could be attributed to inappropriate skill and experience in the application of tissue glue.

In the patient No. 4 a small pulmonary embolus had developed, which regressed in a few days. In the same patient we observed two small cutaneous ulcers of 10 and 15 mm in diameter, after Gelfoam-ethanol and Histoacryl^R embolizations. The necroses responded to conservative treatment. In patient No. 7 a more widespread cutaneous necrosis with gangrene of the terminal phalanx of an already atrophic thumb occurred after embolization with tissue glue. The necrotic phalanx had to be amputated. In patient No. 10 the lesion supplied by the peroneal artery was located in the lower third of the leg. We injected 0.1 mL of 1 : 1 mixture of Lipiodol and Hystoacryl into it, but the embolizing material passed through the malformation and got into a 3 cm long part of the plantar artery and the posterior tibial artery, causing a 5×3 cm necrosis over the Achilles tendon spreading over the sole. The necrotic area had to be covered with a halfthick cutaneous transplant.

In our material, 18 treatments with tissue adhesive, intended to cause permanent vessel occlusion, resulted in unambiguous improvement. After repeated multi-arterial treatment of several extensive lesions, the complaints reappeared much later (in 24, 18 and 7 months) and in less severe forms (patients No. 3, 4 and 9).

Discussion

In the embryonic life the arterial and venous systems develop from the primitive capillary plexus. Intertruncular malformations result from a lack of regression of the primary reticulum. It can lead to the persistence of wide abnormal communications between arteries and veins.[4] The shunt may be a single macroscopic fistula (which is rare) or a range of macro- or microfistulae. It may be direct or occurring through a remnant of the reticulum. The lesions belonging to the latter group, independently of their localization, are characterized by the compliant, low-resistance central vessels, the "nidus", and by the multiple arterial supply as another common feature.[10] Successful treatment entails removing the nidus from the lesion and blocking the feeding arteries as close to the lesion as possible. The main access vessels should normally be left patent to allow further treatment.[1,2,5,11–13] Only transcatheter embolization can meet all these requirements because the ligation and even the resection of the numerous feeding arteries are not sufficient. Actually, the entire arteriovenous tissue should be removed. The interruption of the supplying arteries modifies the pressure gradient and leads to the involvement of new arteries that were latent.[14]

In the majority of infiltrating and/or extended arteriovenous lesions localized in the distal parts of the limbs operative techniques like skeletization and/or segmental resection of the main arteries only lead to temporary reduction of the shunt.[15] Surgical resection of the a-v-fistulae on the joints (knee, wrist, ankle) is impossible.[14] At present, transcatheter embolization is the only possible solution.[1,2,12]

The haemodinamically active AVMs can cause cardiac failure, degenerative alteration of vessel walls, aneurysm formation or hypertrophy of the involved limb. The usual leading complaints are painful varicosities, bleeding and ulceration.[10] Due to the peripheral shunt and the circulatory hypoxy of the tissues (especially the osteoblasts in the bone growth zones) the local haemodynamic disturbances, can cause a nonspecific reaction of mesenchymal proliferation and hypoxic hyperostosis.[15]

The strategy of treatment – irrespective of surgical and/or embolizing technique – is based on the following principles:[15]

a. Early treatment in childhood. This yields

particularly good results in children with vascular bone syndrome of the extremities, as well as in haemodynamically active forms threatening with vascular or cardiac decompensation.

b. The purpose is to reduce the haemodynamic disturbances which do not necessarily mean a 100 % success.[16] The procedure is considered to be successful when the patients have no complaints of pain and dysfunction and a stable condition is achieved.

c. Individual treatment.

d. Functional radicality. Since AVMs rarely allow the performance of an anatomically radical intervention, the treatment should be functionally radical with maximally preserved functions.[1,2]

The basic principle of transcatheter embolotherapy should be the *moderation* of the treatment.[17,18]

There shouldbe a few-day or rather a few-week intervals between individual embolization sessions.[1]

In our opinion, this interval can be extended to a longer period, even to months. Especially after successful embolizations with fluid substances resulting in definitve vascular occlusion it may take even months to properly estimate the results of embolization or for the newly formed collaterals to develop as well as new symptoms to occur. In our patients (No. 3, 4 and 9) with extensive infiltrating lesions the reappearance of complaints with a decreased intensity occurred much later. Moreover, after the latest embolization (performed 55, 44 and 47 months ago as the fourth, fourth and the second session, respectively) these patients have not required further embolization until now.

Successful embolization can be accomplished only by using fluid substances capable of bringing about "capillary embolization".[2,12,19,20]

Ethanol is a well known sclerosing agent that induces thrombosis by denaturing blood proteins, precipitating the protoplasm of endothelial cells and segmentally fracturing the vessel wall.[21]

In the treatment of vascular malformations ethanol has demonstrated its curative potential as opposed to palliation seen with other embolic agents.[22,23]

But extreme caution and superselective catheterization are basic requirements when using alcohol. Since its monitoring is rather difficult or impossible, exceptional care must be taken with its use to minimize the possibility of non-target embolizaton of intact tissues to prevent necrosis and neuropathy.[21,22]

Some authors emphasized the suitability of polyvinil-alcohol foam (Ivalon)[12] or of a cork protein derivate (Ethibloc^{R}, Ethicon).[20]

Since the above mentioned substances were not commercially available in our country, we chose n-butyl-2-cyanoacrylate (Histoacryl^{R}) as embolic material. Tissue glue as a fluid substance is one of the most potent agents for AVM obliteration, since the material reaches the capillary bed and obliterates it.[19]

Unfortunately, handling of tissue glue is rather complicated and requires considerable experience. In our opinion its application in skilled hands is safe, and it proved to be a reliable embolizing agent for AVM treatment.

This simple surgical ligation of the feeding arteries having no therapeutic value is not only superfluous, but is actually harmful and contraindicated because it can prevent successful embolization.[2,3,5,9,24]

Using relatively inexpensive coaxial catheter systems (TIC^{TM}, therapeutic infusion catheters and Cragg convertible guide wires, Meditech) together with specially developed guide wires with excellent torque control (Radiofocus^{TM}, Terumo, Japan), superselective catheterization could be accomplished in all cases including those where the supplying artery(ies) had been surgically ligated. So, we did not need otherwise excellent but very expensive coaxial catheters (e.g. Tracker catheter, Target Therapeutics, U.S.A.). Moreover, we did not encounter any catheter-related complications like adherence of the catheter tip to the intima of the vessel to be embolized.

We were not even forced to exchange the inner catheter for another one, due to early solidification of the tissue glue inside the catheter.

It is especially difficult to weigh risks against benefits of a scheduled catheter embolization, if a regional *ischemic syndrome* arises due to the so-called "steal-effect" whithin a hyperdynamic AVM. An ischemia may also frequently occur if a previous therapy (surgery or interventional radiology) has removed the arterial influxes without eliminating or reducing the corresponding a-v fistulae.[25] The peripherial embolization of the influx to the a-v fistulae (e.g. through surgical ligation or the so-called central type embolization with materials not penetrating the actual fistular bed) may cause the reorganization of fistular influx, which, together with the simultaneous elimination of the afferent arteries, promotes the development of an ischemic syndrome.[25] As a result, the choice of materials for transcatheter embolization of AVMs is of great significance.

To solve this problem by reducing the risk associated with the embolization with the tissue glue, we made attempts to imitate haemodynamic changes expected after glue embolization. Using Gelfoam particles mixed with contrast media, we embolized the lesion as close to the nidus as possible. The results were favourable but only temporary, because the recanalization of the treated region occurred within days or weeks. In addition, due to different characteristics of Gelfoam particles, compared to fluid substances, the application of the former did not prove to be suitable for predicting the hemodynamic alterations after using tissue adhesive. Bringing about vessel occlusion at a small arterial or even precapillary level is insufficient for any conclusions regarding its effect on a capillary-type embolization.

Furthermore, the obliteration of a given capillary bed may lead to more serious sequallae. Neither the rate of injection, nor the amount of the embolizing material needed for glue embolization of the same vascular bed could be calculated on the basis of gelatin sponge occlusion.

The strategy of treatment has been modified during our interventions. Considering that the embolization performed with Gelfoam particles resulted in good, but only temporary vessel occlusion, and taking into account the fact that due to different embolizing characteristics Gelfoam did not prove to be reliable in predicting the haemodynamic changes caused by vessel occlusion with tissue glue, we primarily applied Histoacryl^{R} in the *second phase* of our studies. Similarly, except in three sessions, we avoided using absolute ethanol for embolization, since it cannot be monitored during injection.

The treatment strategy was strictly individual and was modified from patient to patient. We adhered to the principle that in patients undergone surgical vessel ligation(s), the collateral arteries originating from the vessel stump and supplying the AVM were embolized in the first session; i.e. in a distal part of the limbs the embolization was started by occluding the arteries (e.g. interosseal artery, peroneal artery) which did not supply hand or foot. Because of the multiplicity of the feeders, one or two branches of the intact (non-ligated) artery(ies) were also embolized in the same stage. The other vessel occlusions were performed in further session(s).

In accordance with the literature, our results demonstrate that the transcatheter embolization is a palliative albeit rather effective form of treatment in cases of inoperable or surgically inaccessible congenital AVMs. Though in most of these cases, cure cannot be a realistic aim, many patients can be made symptom-free by multiple sessions of percutaneous interventions with an acceptably low complication rate.

It can be anticipated that even in the near future new technical developments will provide interventional radiologists with new palliative therapeutic methods.

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CT and US in endocrine orbitopathy

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Authors present a case of a patient with endocrine orbitopathy with regard to the reports in literature. The disease was limited mostly to the medial rectus muscle. Ultrasonography and computed tomography have exactly reflected the dynamics of the clinical pattern. Using CT and US, the authors also measured normal values (3.09 mm) of the medial rectus muscle in 100 patients with "non-ophthalmological" diseases. They recommend the orbital US-examination for the diagnosis and follow up of endocrine orbitopathy.

Key words: exophtalmus, tomography, x-ray computed ultrasonography

Introduction

Endocrine orbitopathy (EO) develops in more than 70 % of Graves disease.[5] It occurs mostly in hyperthyreosis, but is not rare in euthyreosis and even in hypothyreosis.[1–4, 8] Recently it has been regarded to be an organ specific disease.[4, 9] Its characteristic feature is infiltrative swelling of the orbital tissues which can involve all of the orbital components. The most frequent symptom is exophthalmos.[4] The progressive process can result in blindness. The disease can cause diagnostic as well as therapeutic difficulties. The role of computed tomography (CT) and ultrasonography (US) has become increasingly important in its diagnosis and follow-up.[4, 9, 12–14]

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We are going to demonstrate the significance of these methods. The size of the medial rectus muscle (mrm) is of predictive importance.[5] The data in the literature are differring[5, 10, 13] We established its normal value by serial measurements (CT + US). Finally, we have defined the role of modern radiologic methods in EO.

Case report

T. A., a 58-year-old male was admitted to the Department of Ophthalmology on September 4, 1989. He complained of an intense headache in the right side of the forehead, pain in the right eye and diplopia in any position of gaze. No dizziness, nausea or vomiting accompanied the complaints. The temperature was normal. Nothing noteworthy had happened in his previous history. The visual acuity was 1.0 on both eyes. Fundus, visual field and intraocular pressure were normal. No protrusion could be measured. The findings of otorhinolaryngological

examination were negative, and the patient was referred to the Neurological Department for further examination, where an ophthalmologic consultation was held. The laboratory examinations performed (Se-elfo, CPK, LDH, AST, Latex, KIK, T3, T4, T3U) were all negative. *Ocular myositis* was suspected on the basis of clinical symptoms and CT + US findings (Figures 1, 2, 3, 4, 5).

Using intravenous steroid therapy, vitamins, analgetics and later subconjunctive Oradexon^{R} the pain in the head and eye abated, the mobility of the right bulb became less restricted. Beside the minimal regression of the symptoms

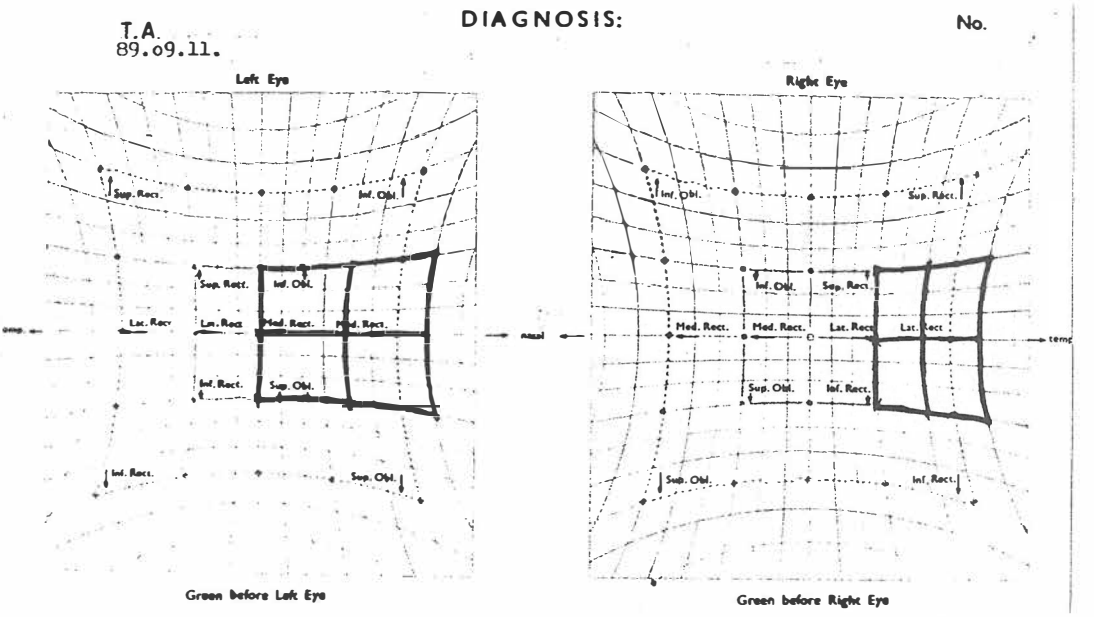


Figure 1. Examination of diplopia with Hess-screen shows the involvement of mrm on the right side.

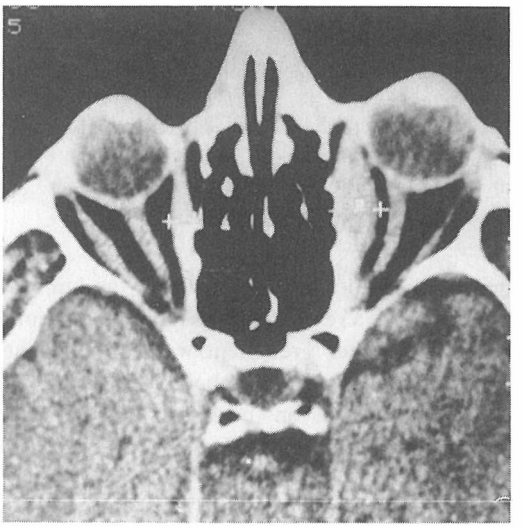
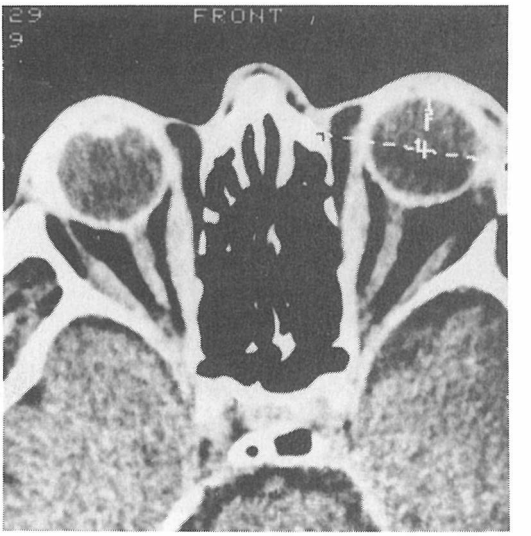


Figure 2. CT-examination of the orbit: the thickness of mrm on the right is 9 mm, and on the left 5 mm.



The right mrm is wider even at the insertion. The right optic nerve is temporally dislocated.

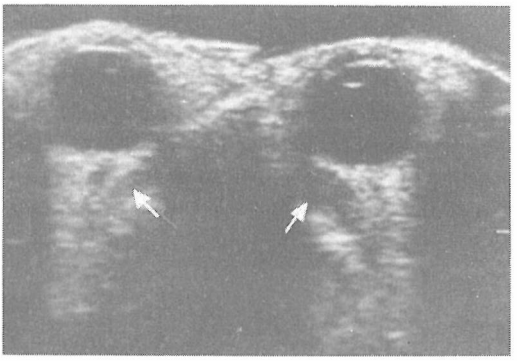


Figure 3. US-examination of the orbit: mrm-s (arrows) show the size already established by CT.

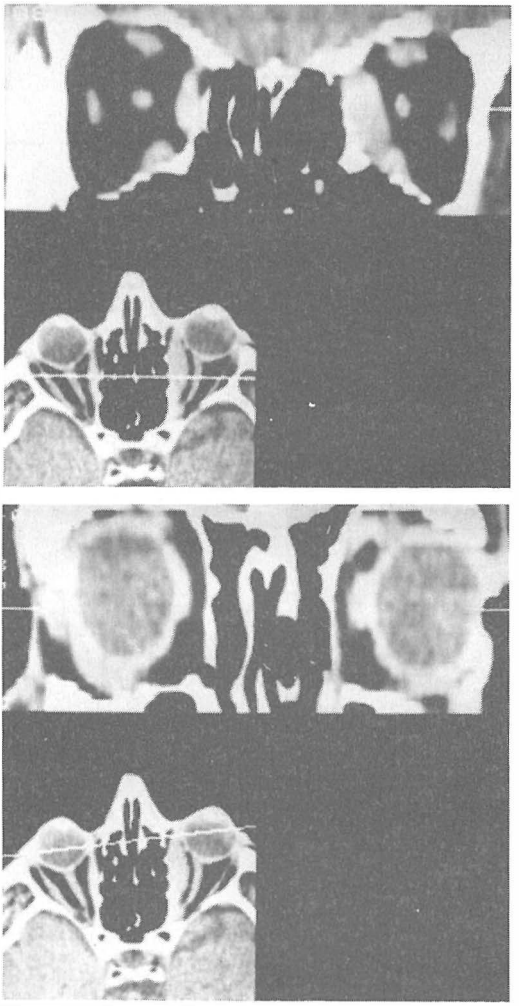


Figure 4. Coronal (indirect) CT
a) at the thickest part of the muscle
b) at the insertion of mrm-s.

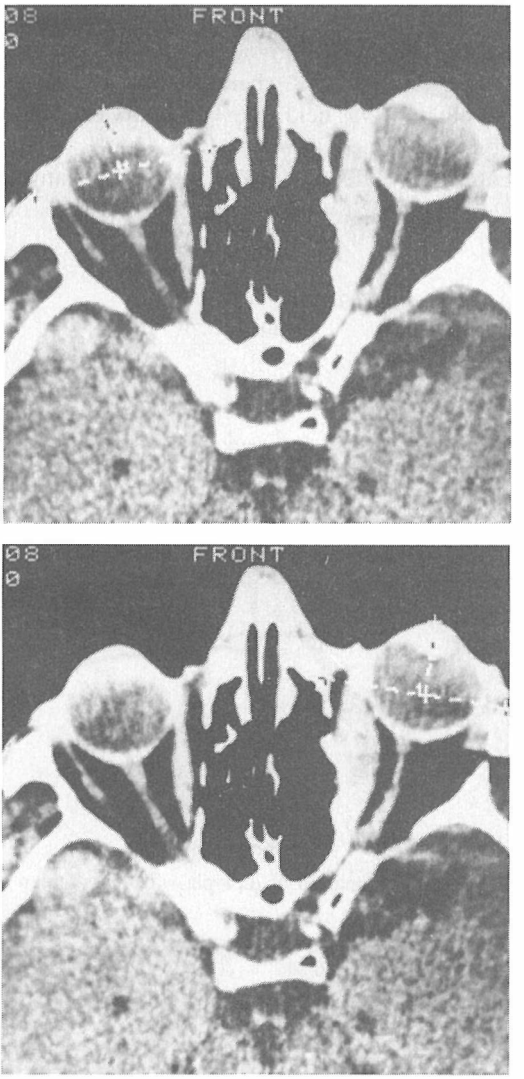


Figure 5. Measuring of the protrusion on axial CT
a) 12 mm protrusion on the left
b) 14 mm protrusion on the right.

on the right side, pains occurred in the left eye as well where a restriction was found in extreme position of gaze. Treatment was continued at our Department on September 19, 1989. Slightly swollen eye-lids on the right side, the bulb in protrusional position. Hertel 17/14 mm. The conjunctiva on both sides was a bit more vascular than the average. The eye-movements were partially restricted both on the right and the left side. The process was followed up by CT

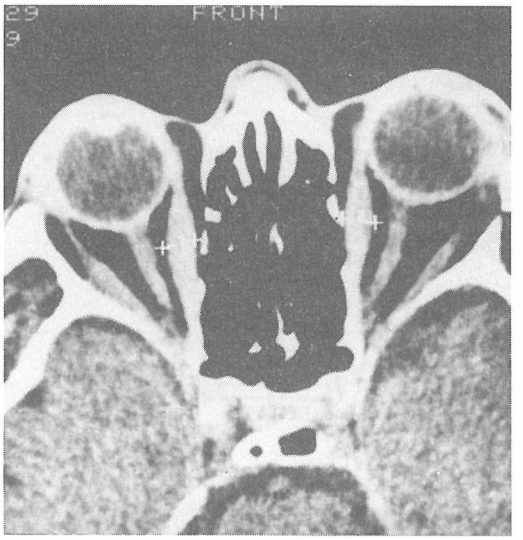


Figure 6. Follow-up CT: the thickest part of the mrm-s on both sides is 6 mm.

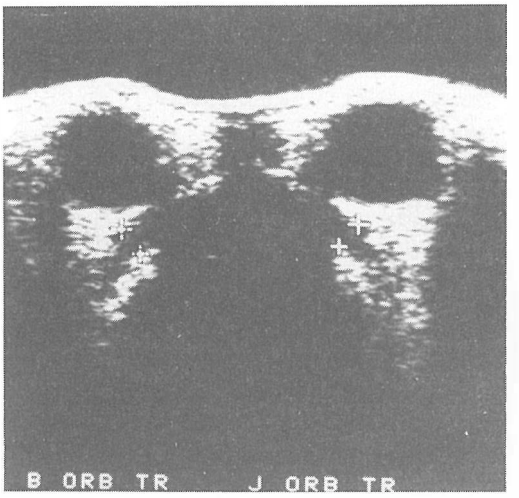


Figure 7. Follow-up US: the same result as in Fig. 6.

and US methods (Figures 6, 7, 8). The steroid therapy was continued. The patent's condition gradually improved: the diplopia and headache ceased, and the protrusion subsided (Figures 9, 10). The patient was discharged symptomless on November 27, 1989. On January 2, 1990 he was admitted again because of recurrent diplopia.

We continued examinations in the direction of *EO*. The measurements of hormone-levels, loading-tests and the laboratory examinations of auto-immunization were negative. Thyroid scintigraphy and US were carried out (Figures 11, 12). Steroid therapy was continued. The protrusion subsided together with the pain in the eye, but the diplopia did not change. The patient was discharged with diplopia-correction on February 14, 1990 (Figures 13, 14a, b). He is followed up regularly.

Discussion

CT-examination in EO

The most common symptom is medial and inferior rectus muscle enlargement, but all of the muscles may be involved. Clinically, the disease is often considered unilateral, but CT may expose a bilateral process. Asymmetry between the two sides is frequent. Optical neuropathy develops in the case of compression caused by muscle enlargement in the apex. Muscle enlargement is limited to the belly.[2]

According to Jacobson et al. the thickening of the muscle is not directly proportional to the severity of the clinical aspect,[6] while other authors have different opinion.[5, 9] Curtin thinks

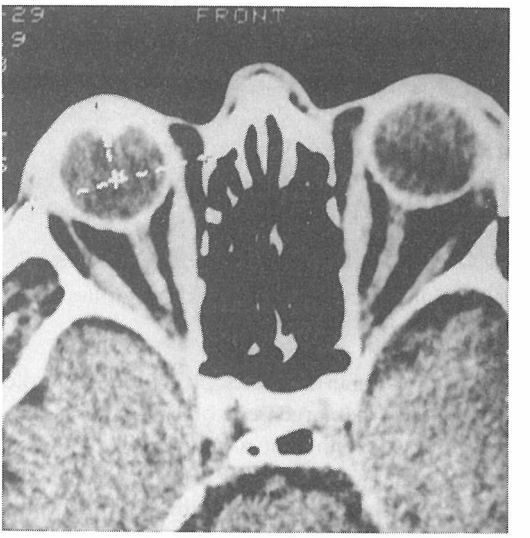


Figure 8. The change of protrusion on CT:
a) 14 mm on the left side
b) 12 mm on the right side.

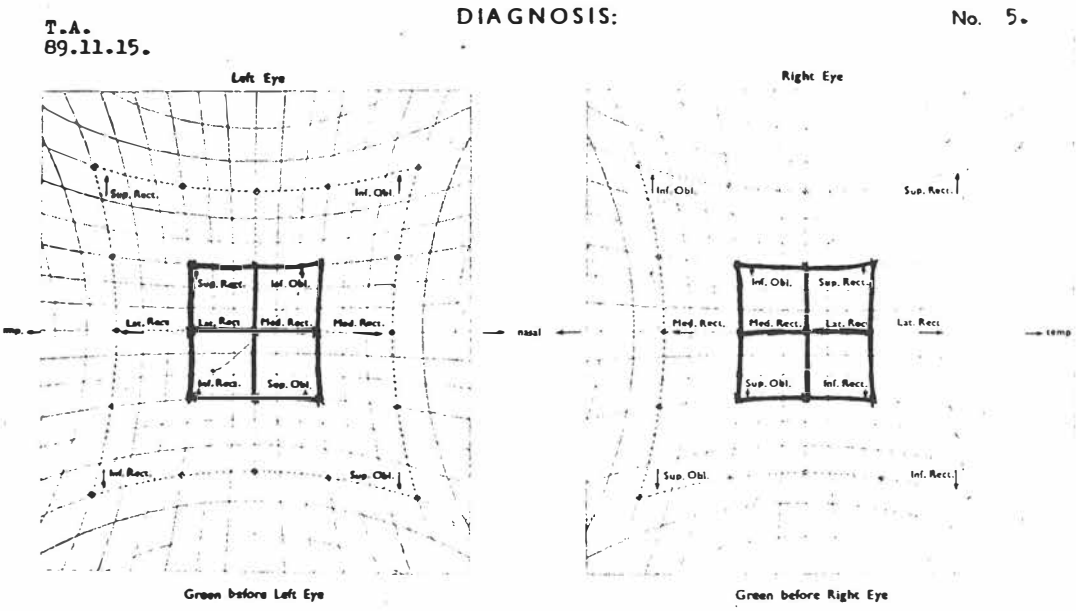


Figure 9. Examination of diplopia with Hess-screen: no abnormal deviation was shown.

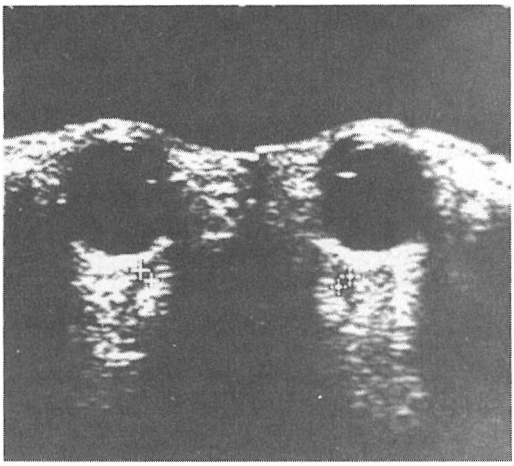


Figure 10. Follow-up US: the thickness of the mrm-s returned to normal – 3 mm.

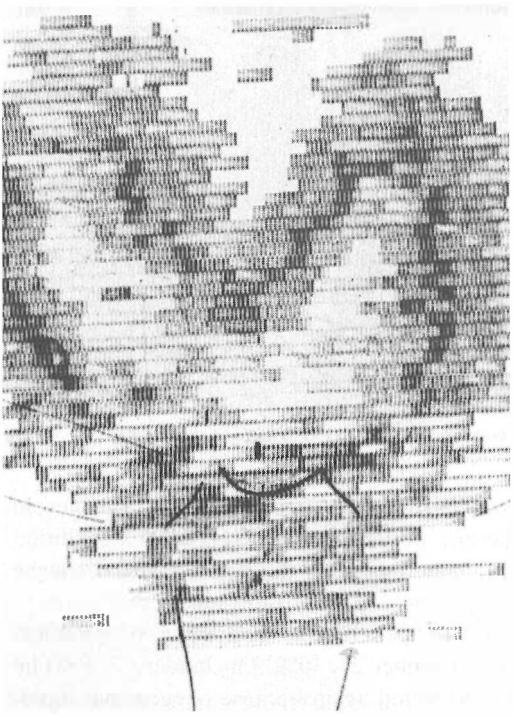


Figure 11. Thyroid scintigraphy: the thyroid gland is enlarged, its activity is slightly irregular, increased at the isthmus.

that two symmetric orbits play a leading role in the muscle-enlargement of EO, whereas other authors claim that asymmetry is typical.[3, 11, 13] A change in the size of the muscle can also be observed on CT scan.[4, 8, 12] CT also plays an important role in radiotherapy planning.[12] The size of the extra-ocular muscles (EOM) can be normal or even englarged, as in

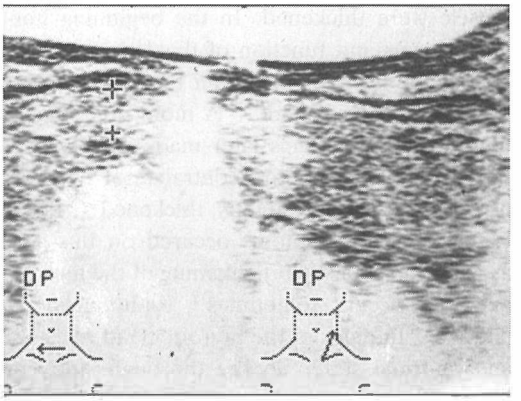


Figure 12. US of the thyroid: the abnormally enlarged isthmus (8 mm). There is a small cyst on the right side in the upper third of the left lobe.

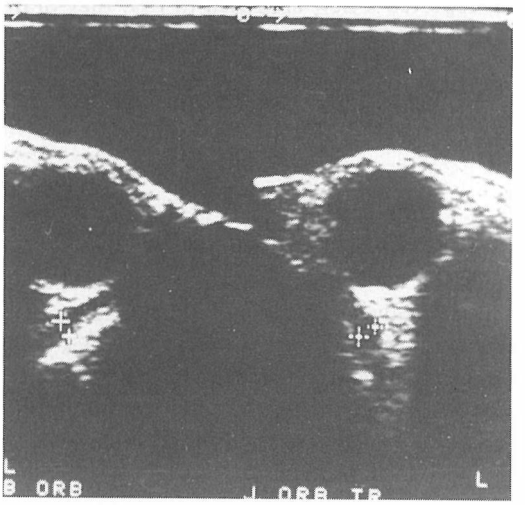


Figure 13. Control US: mrm-s became 1 mm thicker (4 mm).

EO the mass of retrobulbar adipose tissues can occasionally grow, and consequently the bulb will protrude.[2] CT-examination plays the most important role in defining the extension of EO, especially in the orbital apex.

US-examination in EO

The orbit can be measured using both A and B scan. It is generally thought that A-scan yields more information than B, especially in defining the internal structure of the muscles.[7, 13, 14]

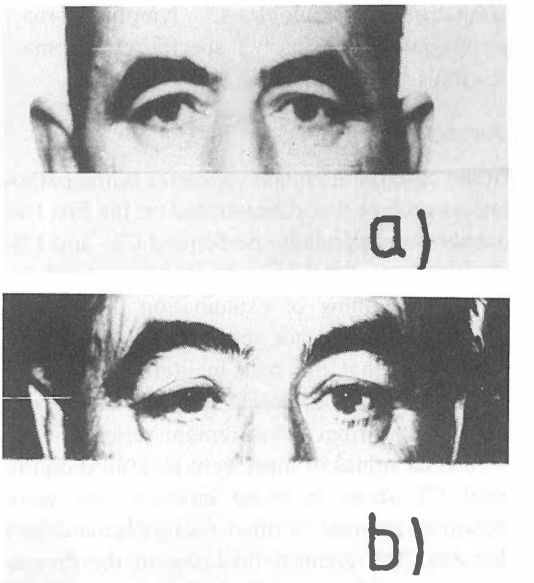


Figure 14. Photo of the patient's face
a) two years prior to admittance
b) on discharge: the right bulb is in convergent position.

Given-Wilson et al. examined patients with EO using a 7.5 MHz small-parts probe in B-scan and real-time method.[5] The medial rectus muscle of 20 patients with EO and 21 patients with neurological disease was examined using real-time method and CT. The normal limit values measured by US were 1.75 and 4.07 mm, mean 2.9 mm.

Shammas et al. examined exophthalmic patients with A-scan.[13] They reported a pathological difference between the two sides, when tissuesensitivity difference was greater than 0.75 mm or, decreased by 20 dB, when it was greater than 0.50 mm. According to their opinion (in agreement with Ossoinig) in Graves-disease each EOM must be measured because by measuring only the medial and external rectus muscle some EO can be overlooked.[10, 13] According to Willinsky, the upper normal limit value of mrm is 3.6 mm, and higher values can be measured in most patients with EO.[15]

Other clinical pictures accompanied by EOM enlargement:

Pseudotumor-myositis,[2, 7, 8] intracranial A-V fistula,[2, 7, 13] metastatic carcinoma,[2, 13] neurofi-

bromatosis,[13] amyloidosis,[2] lymphangioma,[2] acromegaly,[2] sinusitis,[1, 11] specific granuloma,[1] vasculitis,[1] hematoma.[1]

Our experience

In our case the undulant character of the pathological process was demostrated on the first two occasions by parallelly performed CT- and US-examinations, and later by US-examinations. At the beginning of examination the normal value of mrm had not yet been known, later it turned out that the data in literature are not uniform.[5,10,13] Considering these facts, we continued our former measurement series.

Normal values of mrm were measured on the axial CT scans in those patients who were examined because of other (non-ophthalologic) diseases. The greatest thickness of the muscle was measured perpendicularly to the internal orbital wall. (The smallest distance which can be measured by Somatom DRH-Siemens CT is 1 mm.)

We have prospectively evaluated the data of 100 patients (48 men, 52 women). The age of men ranged from 7 to 74 years, and of women from 5 to 79 years. The measured mean value was 3.09 mm, standard deviation ± 0.471 mm. The lowest value was 2 mm, and the highest 4 mm; the most frequent value was 3 mm. The protrusion was also measured (according to Given-Wilson).

US-examination proved that-using Picker LSC 7000 equipment, 5 MHz linear transducer, mrm can always be demonstrated and measured. Our method was essentially the same as that of Given-Wilson, except for the use of Kitecko gel pad. US was performed preceeding or following CT-examinations in 10 patients. At the time of the first measurements there was a 1-1 mm difference compared with thickness value obtained by CT-technique, later the same values were established in accordance with the data of Given-Wilson et al.[5] Our first comparative examination was carried out in this case.

In the beginning of our case history we had diagnostic problems. The patient was admitted with unilateral inflammatory symptoms. The belly and the insertion of the involved ocular muscle were thickened. In the beginning hormone levels and function of thyroid gland seemed to be normal. Based on these symptoms, myositis was suspected.[7, 8] A more precise evaluation of CT-findings later made it clear that the size of mrm in the contralateral eye was not normal: it was slightly thickened (5 mm). Later, clinical symptoms occured on this side as well. In EO a slight thickening of the muscle-insertion occurs sometimes.[2] Radionuclide – and US – findings of the thyroid gland revealed an abnormal state. So the thorough study of CT-symptoms, and the dynamics of clinical appearance, have finally led to the diagnosis of EO.

Here, it must be mentioned that Mourits et al. reported a new approach to EO: they draw distinction between the inflammatory and inflammation-free forms of EO.[9]

Conclusion

Our conclusion is the same as that of Given-Wilson's: the measuring of mrm with real-time US is relatively cheap and simple, it can be repeated, without restriction, it is quick and non-invasive and yields similar results as CT. The thickness of mrm in EO correlates with the risk of development of optical neuropathy. So, US measurement of mrm is a valuable technique for the prospective evaluation of EO patients, as well as for the post-therapeutic follow up. Our opinion is that in a case of suspected EO it is worth to perform a US-examination as the first imaging method. In uncertain cases, or when radiotherapy is required, US must be supported by CT-examination!

Abbreviations: mrm = medial rectus muscle
EO = endocrine orbitopathy
EOM = extra-ocular muscle
CT = computed tomography
US = ultrasonography

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Radiol Oncol 1994; 28: 114-8.

Accuracy of preoperative CT scanning in staging of gastric carcinoma

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Fourty-five patients with gastric carcinoma underwent preoperative computed tomography (CT) scanning. These cases were retrospectively staged using TNM classification in four stages. The results were correlated to surgical/pathologic findings. CT stage and laparotomy stage were in accord in 21 (47%) cases. Twenty-four patients were incorrectly staged by CT: 17 (38%) were understaged and 7 (15%) were overstaged. In 8 patients CT failed to demonstrate lymphadenopathy despite the presence of malignant lymph nodes at surgery. In 3 patients CT demonstrated enlarged lymph nodes, but no malignant involvment was found at surgery. In our series the sensitivity of CT for pancreatic invasion (44%) and omental involvement (18%) was poor. Relatively high sensitivity (86%) and specificity (97%) were achieved by CT in detecting liver metastases. In summary, our experience reported here indicates that CT staging of gastric carcinoma can not replace surgical and pathologic staging. But the main role of preoperative CT scanning is in the assessment of operability in patients with carcinoma of the stomach. It can be used to avoid surgery in patients with minimal symptoms and advanced disease.

Key words: stomach neoplasms, tomography, x-ray computed, staging

Introduction

Today fiberoptic endoscopy including biopsy is routinely used in the diagnosis of gastric carcinoma. The main problem, however, is the evaluation of extragastric spread of the malignant disease (staging), which indicates operability. Traditionally, tumor extent is staged during laparotomy, and according to the findings obtained, either radical or palliative surgery is undertaken. Computed tomography (CT) as a noninvasive preoperative staging method in patients with gastric carcinoma is advocated by some authors, while others report on discouraging results.[1-8]

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UDC: 616.33-006.6-073.756.8

Materials and methods

Fourty-five patients, aged 48 to 80 years, with endoscopic, x-ray and histologic evidence of gastric carcinoma were included. There were 28 male and 17 female patients. All patients had preoperative CT examinations of the abdo-

men. The examinations were performed with a Somatom DRH (Siemens) scanner. Contiguous 8 mm CT sections were obtained from the lower esophagus through the transverse duodenum, with the patient in supine position. Section thickness and intervals were reduced when this was considered necessary. All patients recived either 600 ml of Gastrografin (28 patients) or water (17 patients) orally 1 hour prior to examination.[9, 10] The last cup was given imediately prior to examination. Fourteen patients recived contrast medium intravenously, administered as a bolus of 100 ml of 300 ml/I/ml ioxitalamat (Telebrix).

Separate CT staging parameters were analysed as follows: infiltration of the stomach serosa, pancreatic and omental invasion, liver and lymph node metastases. The criterion used for the evaluation of direct invasion of contiguous organs and perigastric fat on CT scans was the lack of fat plane between the gastric wall mass and an adjacent organ and the appearance of soft tissue density in perigastric fat. Lymph node sizes up to 8 mm were considered normal.[11]

According to the results of CT staging and surgical pathologic findings), patients were distributed in to four stages, using modified "TNM" classification (Tables 1 and 2).[9, 10, 12 13]

Results

The correlation of CT staging and surgical/pathologic findings (TNM staging) is listed in Table 3. The same TNM stage was confirmed in 21 patients (47%); 17 patients (38%) were underassessed. In 10 patients distributed by surgical/histological findings in stage IV, on CT, 6 patients were found to be in stage III and 4 patients in stage II. CT overstaged 7 patients, particularly in four cases: 2 of them were distributed in stage III and 2 in stage IV, all of them were evaluated as stage II on laparotomy (Table 3).

Table 1. TNM classification of gastric carcinoma.

STAGE	DESCRIPTION
	PRIMARY TUMOR (T)
T1	Tumor is limited to mucosa or submucosa
T2	Tumor involves mucosa, submucosa, muscle, or serosa, but does not penetrate serosa
T3	Tumor penetrates through serosa but without invading contiguous structures
T4	Tumor invades adjacent contiguous tissues, diaphragm, or abdominal wall
	NODAL INVOLVEMENT (N)
N0	No metastases to regional nodes
N1	Involvement of perigastric nodes within 3 cm of primary tumor along lesser or greater curvature
N2	Involvement of regional nodes > 3 cm from primary tumor or along branches of celiac axis
N3	Involvement of other abdominal nodes: paraaortic, hepatoduodenal, retropancreatic, mesenteric
	DISTANT METASTASES (M)
M0	No evidence of distant metastases
M1	Distant metastases present

Source – modified from references 12 and 13

Table 2. TNM staging system.

Stage	TNM stage
I	T1, N0, M0
II	T2 or T3, N0, M0
III	T1-T3, N1-N2, M0 T4, N0-N2, M0
IV	T1-T3, N3, M0, T4, any N, M0, any T, any N, M1

Source – modified from references 12 and 13

Sixteen cases of nodal involvement on the basis of lymph node enlargement were detected by CT. Due to a high rate of false-positive and false-negative result the statistical values, i. e. sensitivity (67%) and specificity (86%), were relatively low.

CT showed pancreatic invasion in seven of 16 patients with pancreatic invasion present on surgery or pathologic examination, resulting in

Table 3. Results of CT staging compared with surgical/pathologic findings.

CT	SURGICAL STAGING I	II	III	IV	Total
I	4*	2″	0	0	6
II	1′	6*	5″	4″	16
III	0	2′	3*	6″	11
IV	0	2′	2′	8*	12
Total	5	12	10	18	45

* CT data correctly staged disease in 21 patients (47%)
″ CT data incorrectly understaged disease in 17 patients (38%)
′ CT data incorrectly overstaged disease in 7 patients (15%)

a sensitivity of only 44% and a specificity of 93%.

Omental invasion was correctly predicted by CT in 2 patients, whereas in 9 patients CT failed to demonstrate direct omental invasion found on surgery resulting in a sensitivity of 18%.

Out of 6 patients who had ascites diagnosed by CT scanning, two had peritoneal carcinosis during laparotomy. In one patient CT demonstrated infiltration of the aorta by the primary tumor, but it was not confirmed on subsequent surgical procedure. Table 5 shows the sensitivity, specificity, positive and negative predictive values, and accuracy of CT staging parameters used in gastric carcinoma staging.

Discussion

Our results are not suggesting that computed tomography should be a primary diagnostic examination in gastric carcinoma staging.

CT stage and laparotomy stage were in accord in 21 patients (47%). In 24 patients CT did not accurately assess the true extent of disease: in 17 patients (38%) it was underestimated and in 7 patients (15%) overestimated. In this series the accuracy of CT staging compared to surgical/pathologic findings was the best in TNM stage IV. Since gastric cancer is usually diagnosed as advanced[14] and, unfortunatelly, unresectable disease in approximately 50% of patients,[15] laparotomy is often unnecessary, and preoperative CT scanning in these patients could be the most valuable (Figure 1). Most of these superfluovs exploratory laparotomies jeopardizing the quality of patients' life could be avoided.

CT also enables a surgeon to plan operative strategy since extensive gastric resection require great experience and knowledge.[16]

In our study, CT did poorly in depicting adenopathy, with sensivity of 67% (Figures 2 and 3). Some investigators have had better results with reported sensitivity of 97%,[1] but also others had worse (Cook et al.) – 49%.[4] A high rate of false-negative results is attribut-

Table 4. Assessment of gastric carcinoma extent by CT scan (n = 45).

SIGN OF DISEASE	True positive	True negative	False negative	False positive	Undefined
Serosal infiltration	15	20	8	2	0
Lymph node enlargement	16	18	8	3	0
Liver metastases	6	18	1	1	0
Pancreatic infiltration	7	25	9	2	2
Omental invasion	2	31	9	0	3

Table 5. CT staging versus surgical/pathologic staging (n = 45).

SIGNS OF DISEASE	STATISTICAL VALUES (%) Sensitivity	Specificity	Positive predictive values	Negative predictive values	Accuracy
Serosal infiltration	65	91	88	71	78
Lymph node enlargement	67	86	84	69	76
Liver metastases	86	97	86	97	96
Pancreatic infiltration	44	93	78	74	74
Omental invasion	18	100	100	78	79

able to the incapability of CT to detect micro metastases in normal-sized nodes. Some authors report on particular difficulties in the detection of lymph node metastases in some noble groups: nodes adjacent to the primary tumor mass, those in gastrohepatic ligament and the greater curvature lymph node chain.[17] Possible causes of false-positive CT findings, as reported by Sussman et al.,[12] are reactive hyperplasia or benign lymph node enlargement due to an adjacent inflammation or infection. In 6 patients of our series, CT examination proved liver metastases with only one false-positive and one false-negative result (sensitivity of the method 86%, specificity 97%). Sussman et al.[12] reported worse results, but it is important that in their investigations they did not use i. v. constrast medium, which would, presumably, reduce the false-negative rate markedly. We would also like to emphasize the fact that in all patients in our study the size of liver metastases was over 2 cm. CT scan is of relatively low sensitivity in the diagnosis of direct invasion of neighboring organs by gastric cancer: pancreas 44%, omentum 18% (Figure 4).

In summary, our experience reported here indicates that CT based staging of gastric carcinoma can not be a substitute for surgical and pathologic staging. CT plays the main role in the preoperative diagnosis of advanced disease (TNM stage IV), i. e. in inoperable cases, when CT findings can be used to avoid unnecessary surgery in patients with minimal symptoms.

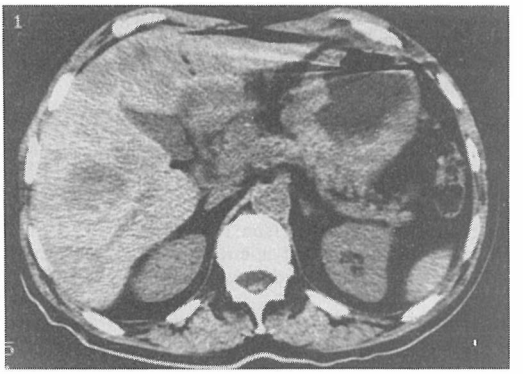

Figure 1. Circumferential thickening of the gastric wall with invasion into the pancreas. Adenopathy and liver metastases. CT stage IV disease confirmed on surgery.

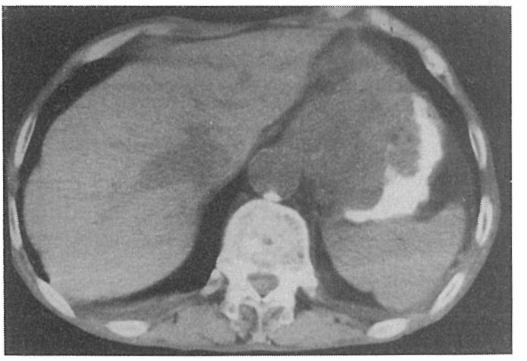

Figure 2. Advanced gastric cancer. Exophytic intraluminal mass. Adenopathy.

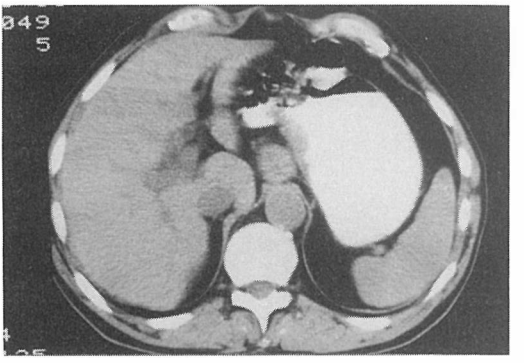

Figure 3. Localized gastric wall thickening involving the medial wall measuring 14 mm. Adenopathy.

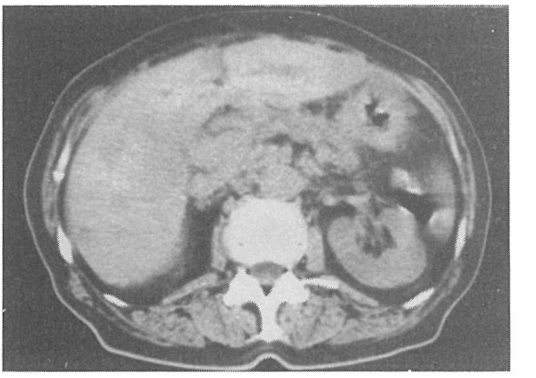

Figure 4. Metastases in liver parenchyma. Enlarged lymph nodes along the upper mesenterial artery. Thickened stomach wall.

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The role of ultrasound in conservative treatment of blunt hepatic injuries

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In the presented 10 year period altogether 932 patients after blunt abdominal injury were examined and 65 traumatic lesions of the liver were sonographically diagnosed; of these, 58 were directly visualized whereas in 7 patients only free abdominal fluid was presented. We have sonographically diagnosed 7 (21.1 % of directly visualized lesions) shallow hepatic lacerations, 14 (24.1 %) subcapsular hematomas, 26 (44.8 %) paripheral parenchymal hematomas and 11 (19 %) deep hepatic ruptures. Using ultrasound examination immediately after the injury as well as sonographic follow-up, we have conservatively cured all shallow hepatic lacerations, 86 % of subcapsular hematomas, 80 % of peripheral parenchymal liver hematomas, while all deep hepatic ruptures were laparotomized. Ultrasound yielded high sensitivity (87.9 %), specificity (100 %) and accuracy (98.9 %) in visualization of blunt hepatic injuries.

Key words: liver-ultrasonography; wounds, nonpenetrating; abdominal injuries; liver, blunt injury, ultrasonography

Introduction

Because of its size, location and fixation, the liver is frequently subjected to trauma. Next to the brain and spleen, it is the organ most commonly hit by blunt violence.[1] Although the spleen is very often involved with a blunt abdominal trauma,[2] liver injuries have a greater clinical significance due to the vital importance of this organ and very limited operative possibilities.

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The blunt injuries lead to ruptures or lacerations varying in size and sometimes in number. They are most commonly the result of traffic accidents or falls. Internal stress or countercoup effects during a blunt hepatic injury may set up subcapsular or central lacerations or only a subcapsular hematoma in case of mild impacts.[1]

The liver is easily accessible to ultrasound examination due to its anatomic position. In blunt liver injury the basic indicator is a hematoma.[3] In the early stage it is a heterogeneous intraparenchymal zone. During the organisation of a hematoma, internal echoes increase with retraction and diminish in size of a blood collection. By using ultrasound, we can detect a very

small amount of blood around the liver and in Douglas pouch.[4]

The sonographic appearance of blunt hepatic injury has already been reported.[3, 5–7] This study is aimed to examine the connection between the prognosis and particular sonographic pattern of hepatic injuries as well as the possibilities for conservative treatment of such injuries by means of ultrasound.

Patients and methods

A total of 932 patients with blunt abdominal injury were examined between January 1982, and January 1992, at the Ultrasound Diagnostic Unit of the Clinical Hospital Center Rijeka, Croatia.

For the sonographic examination of the liver we used right subcostal and intercostal approach. Other positions of the probe such as suprapubic, paraumbilical, left and right subcostal as well as intercostal approach, were used for the visualization of peritoneal recesses.

Abdominal pansonography was performed by means of the following equipment: Fisher Emisonic, Bruel & Kjaer 1486, Aloka SSD 260 LS and Hitachi EUB 515 with sector, linear and convex transducers of 3.5 and 5 MHz.

Results

From the total 932 ultrasonographically examined patients with blunt abdominal injury, 277 had positive finding of a traumatic intraabdominal lesion, while liver injury was visualized in 58 patients, i.e. in 20.9 % of all positive ultrasound findings. Table 1 presents the frequency of particular sonographic categories of hepatic injury.

Shallow hepatic lacerations (Table 1) were presented as perihepatic blood collections with diameter of 2–5 cm and did not show a tendency to progress on ultrasound follow-up. After a physical examination, ultrasound was the only diagnostic and follow-up method during conservative treatment. With satisfactory clinical course these patients were discharged from hospital after 10–15 days.

Subcapsular hepatic hematomas (Table 1) were mostly located near the visceral surface (Figure 1). The greater diameter of hematomas were less than 9 cm. After the initial volume compensation, all the patients were hemodynamically stabile. Hematoperitoneum did not exist and we began with conservative treatment. During the first 24 hours, in 2 patients (14 % of this group) control ultrasound examination showed hematoma to have increased over 10 cm. Between the 3rd and 5th day after the injury hypotension and threatening hemorrhagic shock developed in both patients, while control sonography performed at that time showed free liquid (blood) in Morrison's subphrenic and Douglas pouches as well as disappearance of the previously visible hematoma. The ultrasound finding indicated secondary liver rupture. Explorative laparotomy was done (Table 2) and patients were cured with liver sutures.

The most common sonographically detected blunt hepatic injuries were intraparenchymal hematomas (Table 1, Figure 2). At the time of

Table 1. Sonography of blunt hepatic injuries.

Type of injury	Sonographic appearance	Number	%
Shallow hepatic laceration	Hypoechoic collection near the hepatic contour, without sonographic evidence of hepatic lesion	7	12.1
Subcapsular hematoma	Hypoechoic blood collection which elevates Glisson's capsule without interruption of its continuity	14	24.1
Peripheral parenchymal hematoma	In fresh stage isoechoic or even hyperechoic, after 24 hours heterogeneous (mostly hypoechoic) focal lesion in the hepatic parenchyma distant from the hilus	26	44.8
Deep hepatic rupture	Hypoechoic rupture line in the parenchyma with capsular interruption and free intraperitoneal fluid	11	19.0
Total		58	100.0

Table 2. Treatment of a blunt hepatic injury with respect to the sonographic appearance.

Type of injury	Urgent laparotomy	Sec. liver rupture	Conservative treatment
Shallow laceration	0	0	7 (100 %)
Subcapsular hematoma	0	2 (14 %)	12 (86 %)
Peripheral parenchymal hematoma	2 (7.7 %) due to concomitant injury	3 (11.5 %)	21 (80 %)
Deep rupture	11 (100 %)	0	0
Total	13 (22.4 %)	5 (8.6 %)	40 (69 %)

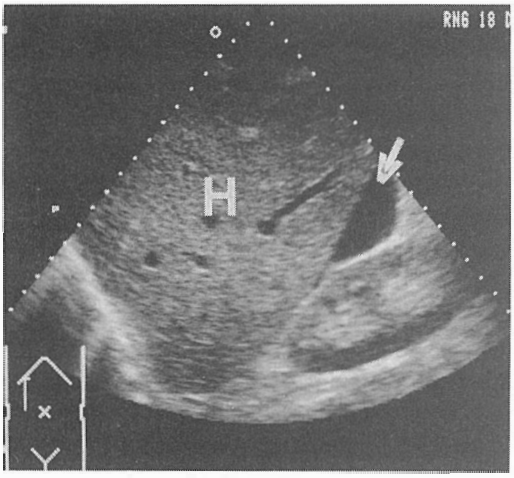

Figure 1. Intercostal sector scan of subcapsular hepatic hematoma (arrow). H = liver.

hematoma imaging none of these patients presented with free intraperitoneal fluid. Intraparenchymal hematoma in 21 patients (80.7 % of this group) measured less than 5 cm in the greatest diameter. In 4 patients (15.4 %) the diameter was 5–10 cm and in one (3.8 %) greater than 10 cm. The patients with hematoma smaller than 5 cm were hemodynamically stabile (except 2 concomitant splenic ruptures which required surgical treatment) and conservatively cured by regular ultrasound follow-up of hematoma regression. Two patients with 5–10 cm large hematoma were successfully cured without surgery, using ultrasound follow-up. In other two patients the intrahepatic hematoma progressed, and ultrasonography detected endoabdominal effusion three and six days after the injury. These two patients as well as the patient with hematoma greater than 10 cm were laparotomized and successfully managed by surgery (Table 2).

Deep hepatic rupture (Figure 3) was sonographically diagnosed in 11 (19 %) patients (Table 1). All the patients of this group were hemodynamically unstable and required immediate volume compensation. As many as 8 patients (72.7 % of this group) had sustained multiple trauma (mostly a concomitant craniocerebral injury, thoracal injury or lesions of the extremities). In all patients of this group ultrasound examination detected abundant intraperitoneal fluid (hematoperitoneum), interruption of the Glisson's capsule and hepatic parenchymal injury. In 4 patients (36 % of this group) ultrasound examination presented segments of total destruction of the normal sonographic architecture of liver parenchyma with hypoechoic foci representing fresh hemorrhage, and

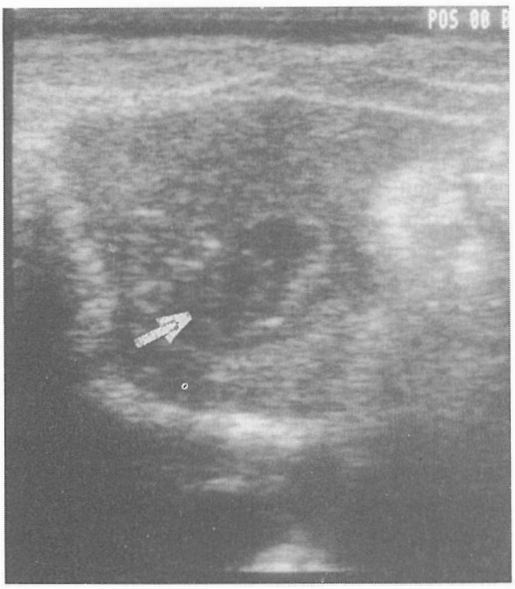

Figure 2. Subcostal linear scan of intraparenchymal hepatic hematoma in regression (arrow).

in two of them (18% of this group) even a massive central hematoma. After laparotomy, 5 patients (45.5% of this group) were treated by liver sutures, debridement or segmentectomy, and rarely by lobectomy and/or perihepatic "packing", while 6 polytraumatized patients (54.5%) have succumbed.

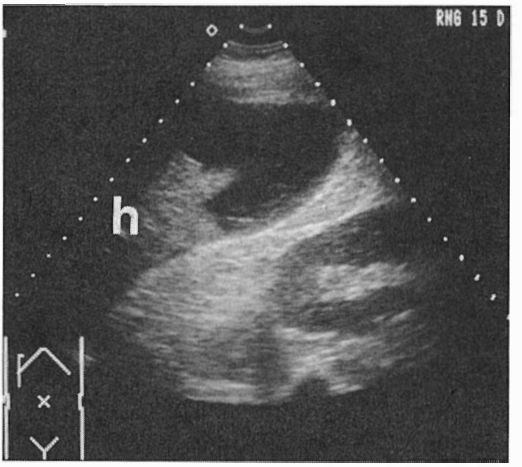

Figure 3. Subcostal sector scan of deep hepatic rupture.

From the total of 277 patients by whom ultrasound examination detected a traumatic lesion of one or more abdominal organs, in 58 (20.9%) liver injury was directly visualized by ultrasound. In other 7 patients (2.5%) only free intraperitoneal fluid was sonographically presented and explorative laparotomy detected a liver injury. Thus, directly and indirectly, we presented altogether 65 blunt hepatic injuries, which means 23.4% of all sonographically detected blunt abdominal injuries.

Among all false negative results of abdominal pansonography in blunt abdominal trauma, only one (0.2%) related to liver injury.

If we consider direct and indirect sonographic finding of blunt hepatic injury as a real positive result, the sensitivity of the method is 98.5%, specificity 100% and accuracy 99.8%. In view of exclusively direct sonographic visualization of blunt hepatic injury, sensitivity is 87.9%, specificity 100% and accuracy 98.9%.

Discussion and conclusions

We have diagnosed liver lesions in 23.4% of all sonographically detected blunt abdominal injuries, which is in agreement with the data from literature.[2] The relation between the direct and indirect ultrasound findings of liver injury was abouth 8:1. Therefore, we have to insist on proper liver scanning when free abdominal fluid is sonographically evident. Vollmer et al. consider that liver injuries can be detected only indirectly,[8] which is opposite to our results. Ultrasound is required to determine the posttraumatic liver status in most of blunt abdominal injuries.

Shallow hepatic lacerations with restricted perihepatic hematoma are not frequent hepatic lesions (Table 1). In all such cases treatment has to be conservative, and the prognosis is favourable. Subcapsular hematomas represented one fourth of all liver injuries (Table 1). Most of them can be treated without surgery, especially when the hematoma is smaller than 10 cm in diameter. Ultrasound follow-up is necessary for early diagnosis of secondary liver rupture, which is a rare complication (Table 2). Almost a half of all blunt hepatic injuries were presented as intraparenchymal hematoma. Generally, shortly after the trauma, sonographic diagnosis of intrahepatic hematomas may be difficult or even impossible, since fresh hematomas have the same echogenicity as normal liver parenchyma. This impression changes after hours or if there has been no diffuse bleeding but an accumulation of fluid.[2] In this group of our patients hematomas were situated on the liver periphery. Most of them were less than 5 cm in diameter; these were cured conservatively (Table 2) provided that regression is followed-up sonographically. In about a half of hematomas greater than 5 cm, conservative treatment would be possible on condition of stable hemodynamics. Deep hepatic rupture was found in 19% of all hepatic injuries (Table 1). These lesions were severe, and had doubtful prognosis. Severe lacerations or ruptures of the liver have a high mortality rate. Death early after the trauma occurs due to severe hepatic

hemorrhage which does not stop for several reasons: the walls of the valveless hepatic veins are thin, the liver is extremely vascular and the diaphragm massages the liver.[1]

Following our results, we can conclude that shallow hepatic lacerations, subcapsular hematomas and peripheral parenchymal hematomas of the liver less than 5 cm represent low risk injuries. However, secondary liver rupture is an exception which requires conservative treatment with regular ultrasound control. Intrahepatic hematomas greater than 5 cm in diameter represent moderate risk injuries. They require an intensive clinical and ultrasound follow-up, while secondary liver rupture is a real threat in the first two weeks after the injury. Finally, massive hepatic hematomas (especially central), scaltered of a hepatic segment or lobe and rupture of the great hepatic veins are severe injuries with high mortality risk.

Hoshi et al. reported a significant increase in GPT level in patients who sustained blunt liver injury.[9] Tanaka et al. found out that the use of ultrasound, significantly decreased the number of laparotomies[5] owing to its precise determination of intraperitoneal bleeding extent.

A major emphasis should be laid on the exact preoperative diagnosis since unnecessary laparotomies can entail a mortality of 0.25 %[10] and a morbidity of up to 4.9 %.[11] We consider ultrasound to be a convenient diagnostic technique for this purpose. High rate of direct sonographic visualization of blunt hepatic injuries, simplicity and promptness render ultrasound a method of first approach to the patient with suspected blunt hepatic injury; this has also been confirmed by the results of other authors.[6, 7]

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Determinants of long-term survival in stage I non-small cell lung carcinoma (NSCLC)

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It is well recognised that surgical resection currently provides superior survival in patients with stage I non-small cell lung carcinoma (NSCLC). The determinants [cell type, type of operation, age, sex and tumour (T) characteristics] of long term survival were analyzed in 297 (40 %) out of 735 patients with Stage I NSCLC. There were 222 (75 %) males and 75 (25 %) females with a ratio 3 : 1. Age range was 40y-81y with a mean 63.2 years. Hospital mortality was 3.3 % (10 patients). The dominant cell type was squamous cell carcinoma [200 (67 %) patients, adenocarcinoma in 71 (24 %) and large cell carcinoma in 26 (9 %)] and lobectomy (including wedge resection and bilobectomies) was the treatment of choice in 218 (73.5 %) patients [pneumonectomy was performed in 79 (26.5 %)]. Age, sex, type of operation and cell type were not determinants of long term survival in this series of patients. The overall 5-year actuarial survival was 52 % and significantly influenced by tumour characteristics i. e. T1 or T2 tumour (T1 = 63 % vs T2 = 49 %, p = 0.003).

Key words: carcinoma, non-small cell lung carcinoma, NSCLC; surgery; stage I; TNM classification, neoplasm staging; survival analysis

Introduction

Potentially curative surgical resection is still the best treatment modality for non-small cell lung cancer, comparing favourably with radiotherapy and chemotherapy which provide poor prognosis at all stages. Superior survival (as high as 70 %)[1] in patients with lung carcinoma has been achieved following surgical resection in Stage I disease.[2-4]

The aim of the current study was to assess the effect of type of operation, age, sex, cell type and tumour (T) characteristics (T1-T2 tumours) on long-term actuarial survival in patients with stage I non-small cell lung carcinoma where staging was carried out according to the revised TNM classification (1986).[5]

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Material and methods

Seven hundred and thirty five patients treated surgically for non-small cell lung carcinoma at

the Regional Cardiothoracic Centre between 1980–1989 were reviewed and all patients in postoperative stage I regardless of their operation, age, sex and pathologic cell type were included in the study. Survival data were obtained from the case and/or family practitioners records and were later confirmed by the Regional Cancer Registry Office, Cookridge Hospital, Leeds, UK.

Hospital mortality was defined as death occurring within the unit at any time in the postoperative period and as such was included in actuarial life table analysis. For the purpose of review all bilobectomies and wedge resections were considered as lobectomies because of the small number of patients in these groups. Local and mediastinal lymph nodes were removed and labelled to facilitate a correct postoperative staging.

Staging was carried out according to the revised TNM classification (1986)[5] and was based on histopathologic examination of the resected specimen and sampled lymph nodes. None of the patients received any form of adjuvant radiotherapy or chemotherapy following lung resection. All patients were followed at 6 weeks and at 3 monthly intervals following surgery for the first 1 year, and 6 monthly thereafter. Patients who died due to non-tumour related cause were included in long-term survival analysis.

BMDP Statistical Software (BMDP Statistical Software Inc. Los Angeles, LA 90025) was used for all statistical and actuarial survival analysis (Cutler and Ederer, 1958) and Generalised Wilcoxon test was performed for calculating differential analysis between the groups. Chi-square testing was used for analysing differences in prevalence between groups. The statistical difference between two groups was assumed to be significant at $p < 0.05$.

Results

During the 10-year period (1980–89), 735 patients were operated on for non-small cell lung carcinoma. Pathological staging revealed, 297 (40.5%) patients out of the total were in stage I disease. There were 222 (75%) males and 75 (25%) females with a ratio 3 : 1 whereas according to tumour (T) characteristics it was 1.5 : 1 in the group of patients with T1 tumour and 3 : 1 in the others (T2). Age range at the time of diagnosis was 40y to 81y with a mean of 63.2 years. There were 223 (75%) patients under the age of 70 and 74 (25%) patients 70 years of age or older. Demographic data is shown in Table 1.

Table 1. Demographic and operative characteristics of patients undergoing surgery for NSCLC – comparison of Group 1 and Group 2.

Age	
69 or younger	223 (75)*
70 or older	74 (25)
Sex	
Male	222 (75)
Female	75 (25)
Ratio M : F	3 : 1
Operation	
Pneumonectomy	79 (26.5)
Lobectomy**	218 (73.5)
Cell type	
Squamous Cell	200 (67)
Adenocarcinoma	71 (24)
Large Cell Carcinoma	26 (9)

* Numbers in paranthesis are percentages.
** Including 19 wedge resections, 11 bilobectomies.

Standard pneumonectomy was performed in 79 (36%) and lobectomy in 188 (54%) patients. Wedge resection (19 patients) or bilobectomy (11 patients) was also carried out in 30 (10%) patients. However, owing to small number of cases, these patients were included in the lobectomy group. Pneumonectomy was the treatment of choice in 77 (34%) patients with T2 tumour however, two (2.5%) patients with T1 tumour underwent completion pneumonectomy due to unresolved postoperative atelectasis. Ten (3.3%) patients died in the postoperative period due to various complications during the hospital stay.

Following the histopathological examination of the resected specimen, squamous cell carcinoma was the dominant cell type and was diagnosed in 200 (67%) patients whereas adenocarcinoma was diagnosed in 71 (24%) and large cell carcinoma in 26 (9%) patients. TNM classification of the tumour was carried out

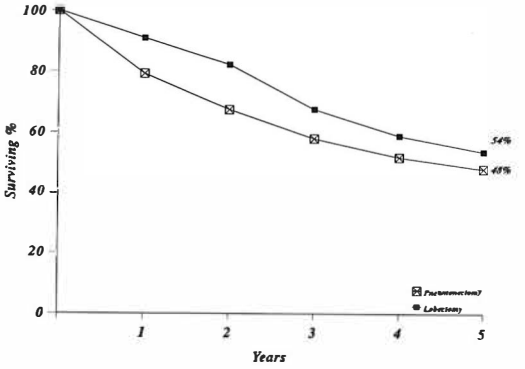

Figure 1. 5-year actuarial survival according to type of surgery.

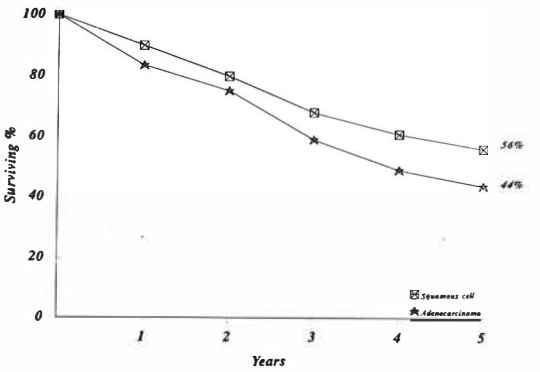

Figure 2. 5-year actuarial survival according to cell type.

according to final histopathology report of the resected specimen and lymph nodes which revealed that 73 (24.5 %) patients were diagnosed having T1 and 224 (75.5 %) patients T2 lung tumour.

Following discharge, the cause of death was non-tumour related in 11 (3.7 %) patients and these deaths were included in actuarial life table analysis. Overall 5-year acturial survival was 52 %. Superior survival was achieved following lobectomy compared to pneumonectomy but the difference was not statistically significant, p = 0.14, Figure 1. Survival based on cell type was also superior in favour of the patients with squamous cell carcinoma (56 %) however once more this did not differ significantly from patients with adenocarcinoma (44 %), Figure 2. Survival in patients with large cell carcinoma was 47 % however no comparison was carried out due to small number of patients in this group therefore it was not included in Figure 2. In addition, age was associated with improved survival in patients less than 70 years of age compared to patients 70 years of age or older (56 % vs 42 %), however the difference was not significant, p = 0.11. Although the favourable survival (63 %) was achieved in female cohort compared to male gender (48 %), the difference was not quite significant, p = 0.06. In contrast to these previous findings, significantly better survival was observed in the group of patients with T1 tumour comparing to patients with T2 tumour (63 % vs 49 %), p = 0.003, Figure 3.

Discussion

The effectiveness of pulmonary resection in achieving long term survival in the treatment of stage I non-small cell lung cancer has been reported by several authors.[1–4] In contrast, radiotherapy alone or in combination with chemotherapy has not been shown to be as effective as surgical therapy under similar circumstances. Sobue et al[6] reported 14.3 % 5-year survival in patient with clinical stage I lung cancer treated non-surgically. Similarly, Sandler et al.[7] reported 17 % three years survival in patients with stage I lung tumour treated with megavoltage radiotherapy. In addition, Haffty et al.[8] showed 21 %, 5-year survival in patients with

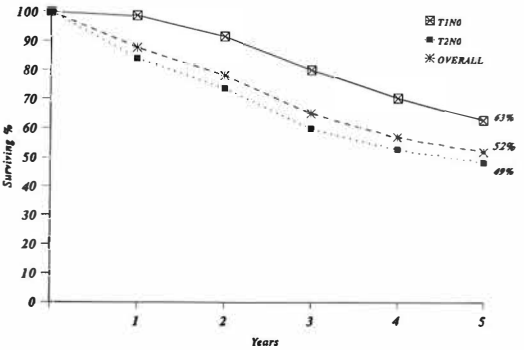

Figure 3. 5-year actuarial survival according to tumour characteristics.

clinical stage I non-small cell lung carcinoma felt to be surgically resectable but treated with radical radiation therapy either for medical reasons or due to failure to obtain patient's consent for surgery. Emami et al.[9] and Capewell and Sudlow[10] reported 29% and 17%, 5-year survival with radical radiotherapy, respectively. These results reveal radiotherapy to be inferior to the surgical therapy in patients with Stage I NSCLC reported previously.

The high male : female ratio observed in this group could be explained by the increased incidence of squamous cell carcinoma thought to be associated with smoking habits. However, the ratio observed in patients with T1 tumour was 1.5 : 1 could be explained by the fact most T1 tumours are diagnosed coincidentally on routine chest roentgenogram.

In this study overall 5-year actuarial survival (including 11 non-tumour related deaths) was 52% as similarly observed by the others.[3, 11] Type of surgery performed was not determinant of the 5-year actuarial survival although survival was generally superior in patients treated by lobectomy as similarly observed by Little et al.[4] In contrast to the findings of Williams[2] et al., we failed to demonstrate a statistically significant difference in survival probability between patients of less than 70 years of age and those older than 70 years although the trend was for poorer survival in the latter group of patients (56% vs 42%, $p = 0.11$). Similarly superior survival was observed in female group, however the difference was not statistically significant (48% vs 63%, $p = 0.067$) as observed similarly by the others.[2, 13]

Vincent et al.[14] and Naruke et al[3] have reported, with the exception of small cell carcinoma, absence of significant difference in survival between the different cell types. Although patients with adenocarcinoma generally do worse than those with squamous cell carcinoma, considered by stage they have similar prognosis.[2, 11, 12] This observation was also confirmed in the present study. Deneffe et al.[15] reported a better 5-year survival for squamous cell carcinoma as compared with adenocarcinoma for any given stage, but unlike with disease stage, the prognostic significance of histopathologic cell type per se, was not clearly defined.

In contrast to the previous findings, the tumour characteristics (T-Factor as defined by the new TNM classification) was the singular most important factor affecting 5-year acturial survival in both patient groups T1N0 = 63%, T2N0 = 49%, $p = 0.0033$. Significant differences in 5-year survival rates according to T1 and T2 has also been reported by Naruke et al.[3] (76.4% vs 56.9%), Read et al.[11] (73.2% vs 49.5%) and also Pairolero et al.[1] (70% vs 58.2%).

In conclusion, this review has confirmed that the long term survival in the stage I non-small lung cell carcinoma is not a function of age, sex, type of operation, or the cell type but is more likely of the T-characteristics of the tumour. On the basis of the observed significant survival difference and the findings of the other authors we would strongly recommend sub-classification of stage I NSCLC.

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Results of nonoperative treatment for esophageal cancer

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From 1983 to 1987, 152 patients with esophageal cancer were treated at the Institute of Oncology, Ljubljana, Slovenia. Ninety-eight of these had radiation therapy alone, 36 radio- and chemotherapy, whereas 18 patients were treated symptomatically only. One, two and five-year survival of 69 irradiated patients with TD > 45 Gy was 32 %, 13 %, and 5 % respectively. There was a significant difference in survival according to the tumor dose delivered (i. e. > 45 Gy or < 45 Gy), length of tumor stenosis, and performance status. Chemotherapy, tumor site, duration of dysphagia, and sex had no influence on the survival. There was no difference in survival between patients treated symptomatically and those irradiated with TD < 45 Gy. The effect of radiotherapy and chemotherapy on dysphagia was poor: in only 1/5 of the patients the improvement lasted more than two months whereas in 2/5 of the patients dysphagia worsened already after two months. It seems reasonable to restrict radiotherapy only to patients with radical intent, these being chiefly the patients in good general condition and with short tumor stenosis.

Key words: esophageal neoplasms-therapy; radiotherapy, antineoplastic agents; survial analysis

Introduction

The prognosis for patients with esophageal cancer is poor. Irrespective of therapeutic modality, only few patients survive five years after diagnosis. It is important to choose such a therapy, that would influence the survival and diminish dysphagia at minimal hospitalization time. Standard therapies for esophageal cancer are surgery and radiotherapy; recently, the use of chemotherapy has been reported as well. The aim of this article is to present the results of nonoperative treatment of 152 patients with esophageal cancer at the Institute of Oncology, Ljubljana, Slovenia, in the period 1983–1987.

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Methods and patients

Of the 152 patients, 136 were male and 16 female, i. e. the sex ratio 8.5 : 1. The age of patients ranged from 35 to 86 years; the highest incidence was in the age group 50-65 years.

Tumor was microscopically confirmed in 141 patients. There were 126 epidermoid carcinomas, 7 adenocarcinomas, 6 undifferentiated and 2 small-cell carcinomas.

Site of primary tumor was as follows: 10 cervical, 30 upper, 76 middle and 36 lower thoracic region.

According to clinical TNM classificiation of

esophageal carcinoma valid in this time period there were 13 (9%) Stage I, 50 (33%) Stage II, 55 (36%) Stage III, and 34 (22%) Stage IV tumors. Twelve patients had fistuals, 11 bronchial or tracheal infiltration, and 2 invasion to the aorta. Palliative surgical procedures were performed in 15 patients: 8 gastrostomies, 5 tubus insertion, and 2 by-pass. Three patients had a naso-gastric tube inserted for the needs of nutrition.

Performance status (Karnofsky) was as follows: > 70 in 106 patients, 50–70 in 33 patients and < 50 in 13 patients.

The length of esophageal stenosis was estimated in 120 patients: up to 5 cm in 26, 5–10 cm in 74, and over 10 cm in 20 patients.

The duration of dysphagia was as follows: 1 month in 15, 1–3 months in 61, 3–6 months in 36, and over 6 months in 24 patients. For 16 patients there were no reliable data on the duration of dysphagia.

Radiotherapy was performed by a linear accelerator (x ray, 8 or 10 MeV), daily doses ranged between 1.5 and 3 Gy with two opposite or three planned fields, and maximum equivalent TD 70 Gy/7 weeks, mostly in split course regimen.

Chemotherapy consisted of 5-FU 1.000 mg/m^2 in 24^h infusion, on days 1-4, and cisplatin 90 mg/m^2 on day 1, repeated 1–4 times.
Ninety-eight patients were treated by radiotherapy alone, 36 by radiotherapy and chemotherapy, and 18 symptomatically only.

Of 134 irradiated patients, 69 received "radical" TD > 45 Gy/weeks, 51 patients < 45 Gy, whereas in 14 patients radiation was started but had to be terminated before TD 15 Gy had been achieved because of worsening of the patient's condition. So, only 69 "radically" and 51 palliatively irradiated patients could be considered.

Results

One-, two- and five-year crude survival of all 152 patients was 18%, 7%, and 4% respectively; median survival was 5.5 months (Figure 1).

The survival of irradiated patients was better:

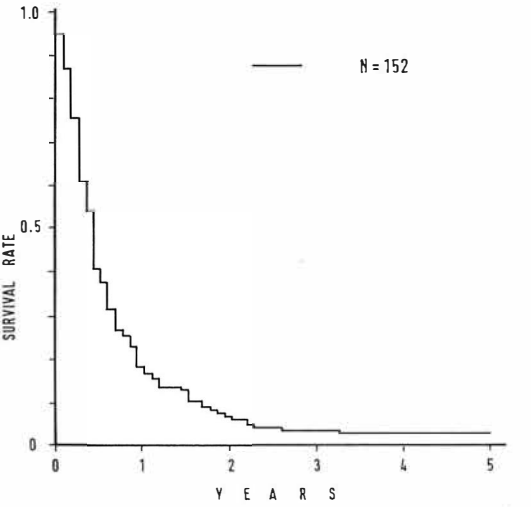

Figure 1. Crude survival of all treated patients.

in "radically" irradiated patients the rate was 32%, 13% and 5% respectively; median 8 months. The difference between "radically" and palliatively irradiated patients was significant (Figure 2).

There was no difference in the survival of our patients irradiated with palliative doses and those treated symptomatically (Figure 3).

Performance status and length of esophageal stenosis influenced the survival of irradiated patients (Figures 4 and 5).

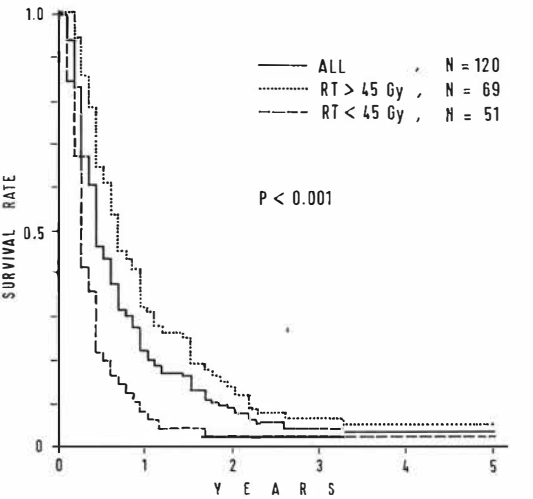

Figure 2. A comparison or irradiated patients by tumor dose.

Chemotherapy did not improve the survival of irradiated patients, irrespective of tumor dose (Figure 6), duration of dysphagia, tumor localisation and sex (all $p > 0.1$).

The influence of radio- and chemotherapy on dysphagia was poor: in only 21 of 101 evaluable patients the improvement lasted two months or more whereas in 39 of 101 patients swallowing ability worsened.

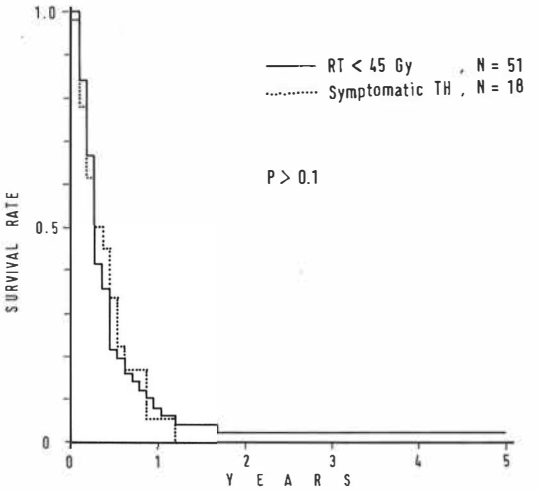

Figure 3. A comparison of survival by treatment method: radiotherapy with TD < 45 Gy and symptomatic therapy.

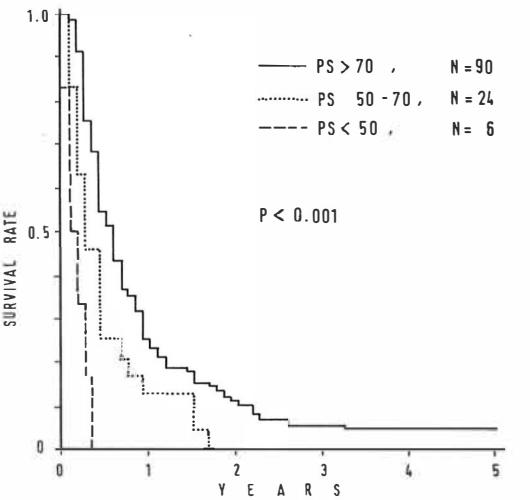

Figure 4. A comparison of irradiated patients by performance status.

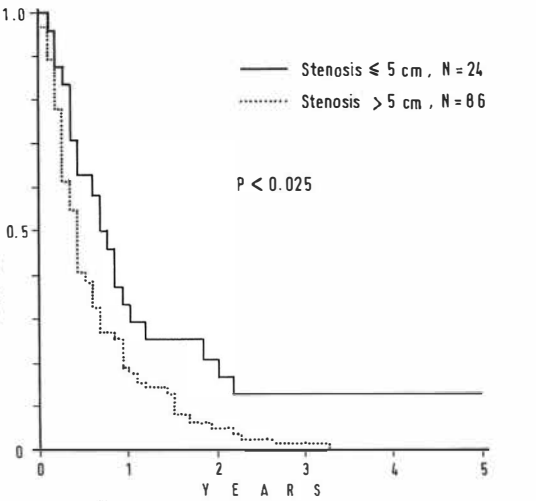

Figure 5. A comparison of irradiated patients by length of esophageal stenosis.

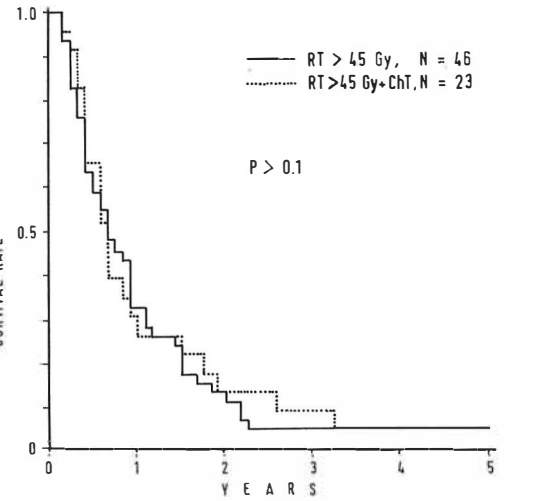

Figure 6. A comparison by treatment method: radiotherapy and radiotherapy + chemotherapy.

Our 14 selected patients with tumor stenosis up to 5 cm and performance status at least 70 were irradiated with TD > 45 Gy: their one-year survival was 50 % and five-year survival 21 % (Figure 7).

The survival of all patients with complications was very short: with fistulas maximum 10 months, with bronchial (& tracheal) infiltration and invasion of the aorta 18 months. All 15 patients with palliative surgery died within 8

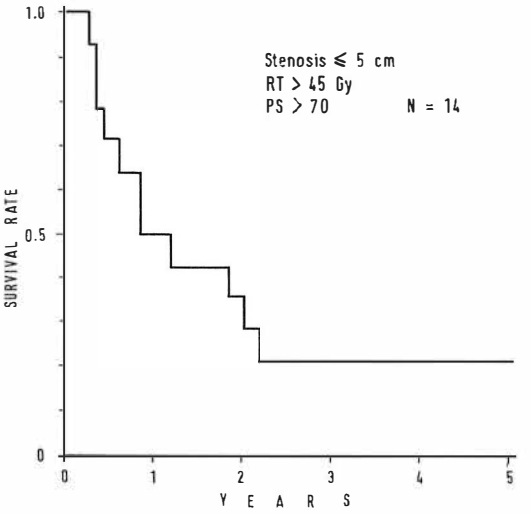

Figure 7. Crude survival of selected patients.

months, and 3 patients with naso-gastric nutrition tube within 3 months, despite all our therapy.

Discussion

Paterson[2] stated 30 years ago "that with more advanced oesophageal cancer anything we can offer gives poorer palliation than simple surgical measures, such as tube or gastrostomy. Even where obstruction is temporarily relieved by radiation the duration of such relief is short and the discomfort of achieving it considerable." Obviously we were not enough aware of that. Radiation after palliative surgical procedure which rendered feeding possible was ineffective: the swallowing did not improve and all patients died soon. Usefulness of our therapy in patients with complications due to local progression is questionable as well: in these patients radical radiation was not possible, and there was no difference in survival between palliatively irradiated and symptomatically treated patients at all.

Unfortunately, the therapeutic effect on dysphagia was poor: in 1/5 of the patients swallowing improved although 18 of 21 were irradiated with "radical" doses. However, it is difficult to draw a distinction between radical and palliative radiation doses at five-year survival about 5 %. In our patients radiation with TD over 45 Gy resulted in significant better survival than with TD bellow 45 Gy. This is in agreement with the results reported by Albertsson et al.[3]

Our survival results could be compared with the data of Earlam and Cunha-Melo:[4] 8489 irradiated patients reported in 49 papers, had one-, two- and five-year survival of 18 %, 8 %, and 6 % respectively.

Paterson[2] considered patients in good general condition and with lesions not exceeding 5 cm as suitable for radical radiation therapy. The survival of our selected patients conforms to this opinion. The shortening of stenosis improved the survival in the absence of metastases.[5] Tumor length served as a basis for staging according to TNM classification of 1978.[1] Okawa et al.[6] found a significant difference between the survival of patients with stenosis up to 5 cm of length, and over 10 cm. On the contrary, Slevin and Stout[7] did not esstablish statistical difference in survival between cases with stenosis of 5 cm or less compared with 6 to 10 cm long stenoses, and Albertsson et al.[3] did not find difference with tumors < 9 cm and tumors > 9 cm.

There was no relationship between tumor site and survival rate in our patients. This is in accordance with the observations of other authors.[3, 5, 6]

Chemotherapy did not improve the survival of our irradiated patients. Also in the case of "radical" radiation doses we could not achieve the results reported in literature.[8–11]

Hospitalization time of our patients treated by chemotherapy was longer because treatment on outpatient basis was not possible.

Our treatment results suggest that radiotherapy is reasonable only with radical intent in esophageal cancer patients in good general condition and with short tumor stenosis; for the time being, chemotherapy should be performed only with protocols.

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Breast tumor aspiration biopsy with a multihole needle

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In 36 patients, breast tumors or palpable breast masses were punctured with a standard fine needle and a multihole needle. Equal quality of cell material for cytologic investigation was found with both methods, but a significantly larger quantity of material was aspirated (in punctures) using the multihole.

Key words: breast neoplasms – methodology; biopsy, needle; cytology, aspiration biopsy, technique

Introduction

Breast tumor aspiration with a fine needle is a routine method without which it is difficult to organize the complete diagnosis of breast diseases. According to the data from the review article by Us-Krašovec et al. (1982), the percentage of correct diagnoses in breast cancer obtained by cytologic analysis of aspirates ranges from 77–92.3 %. The percentage of false positive (0.2–1.6 %) and false negative (3.2–11.5 %) results is within sufficiently low limits. Similar results were also registered at our institution.[1]

A serious drawback of cytologic diagnosis is a problem which is often not within the power of the cytologist to solve: (not enough) insufficient quantity of diagnostically relevant material. The cause may lie in inadequate collection or poor preparation of biopsy specimens, in greasy plates preventing fixation of specimens, or in the nature of the punctured lesion itself. This is often the case in cyst aspirates where there is little cell material, or in scirrhous carcinoma aspirates where the presence of the epithelial component of tumor is minimal. Thus, various authors report on 3.3–7.9 % of unsuccessful biopsies among carcinomas and on a significantly larger share among benign breast lesions (9.0–24.1 %).[1–4]

Aspiration biopsy of the suspicious breast area presents a special problem when there is no palpable tumor. Increased nodosity is not always the result of proliferation of the glandular component of breast tissue. The amount of glandular tissue varies strongly with regard to breast type and the woman's age. In premenopause it amounts up to 20 %, in postmenopause only up to 2–5 %. In this period of time the share is fatty (50–70 %) and connective tissue (30–40 %) is prevailing. Such transformation of the breast makes collection of representative cytologic samples for analysis difficult.

The aim of our study was to compare the success of puncture using a fine needle – fine

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needle aspiration cytology (FNAC) with that using a needle with several openings – multihole needle aspiration cytology (MHNAC). This would offer a greater possibility of obtaining an aspirate from a correct site and in a sufficient amount. The needle was made in the needle factory in Kobarid (TIK) according to description from literature.[5]

Some authors report that by using a fine needle with several side openings (a multihole or MH needle) they obtain more cell material for analysis and get better diagnostic results (5). It was our aim to establish whether biopsy specimens obtained by puncture with a MH needle contain an equal, larger or smaller amount of cell material than specimens obtained with a standard fine needle.

Material and methods

The multihole needle was made for research purposes in the TIK factory. For its fabrication a standard disposable needle was used, with three additional openings made at its distal end. Two openings were on the same level and one was on the opposite side.

The technique of aspiration using the MH needle was identical to that used in punctures with the fine needle. Since we were comparing the quality of smears obtained with two different needles, each lesion was punctured in the same manner through the same needle insertion site.

Before puncture, the skin was disinfected. The first puncture was done with a fine needle. A Cameco puncture pistol and a 10 ml syringe were used. The contents of the lesion were aspirated while moving the needle forwards and backwards in different directions through the lesion and simultaneously rotating the syringe. Then the puncture was continued with a MH needle. It was introduced through the same insertion point and the same puncture technique was used. The aspirate was squirted onto a specimen plate and larger pieces of tissue were crushed with the needle.

Cell material obtained by aspiration puncutre was smeared on 2–3 specimen plates, fixed and stained in the cytological laboratory according to three staining methods: May Grünwald-Giemsa, Papanicolaou and hematoxylineosin.

Every pathologic process which could be localized, irrespective of whether it was suspicious or not, presented an indication for aspiration puncture with a fine needle.

The cytologic findings were classified into negative, suspicious and positive. Negative cytologic findings mean the presence of normal glandular epithelium of the breast with or without cellular atypia and the presence of cells of benign breast dysplasia.

Cytologic findings are considered suspicious when according to their morphology and their distribution the cells give the impression of a malignant process, and for certain reasons the cytologist cannot take the responsibility for the subsequent radical therapy. Positive cytologic findings mean the presence of malignant cells in the smear of the tumor biopsy specimen.

Biopsy specimens with little or insufficient cell material for cytologic investigation are rather questionable. In view of the fact that cytodiagnosis is a subjective diagnostic method, it is often difficult to determine the limit at which the aspirate is still adequate for investigation and to decide whether a certain number of cells in the aspirate still gives a sample representative for cytologic investigation. In cytologically negative findings with little cell material it is therefore difficult to determine whether they really are negative, taking into account that a high percentage of false negative findings can follow as a result of misinterpretation. In such cases a repeated puncture and follow-up investigation are recommended.

Statistical significance was tested with the chi-square test.

Results and discusion

In our Breast Diagnostic Center, 37 MHNAC and 41 FNAC were carried out in 36 patients.

In 30 patients the same tumor was punctured with a fine and with a MH needle, in 6 patients the puncture was carried out only with the MH needle; 1–4 punctures were done in each patient.

In FNAC, the number of aspirates with an insufficient amount of cell material was larger (n = 18) than in punctures with the MH needle (n = 13), but in specimens obtained with FNAC, the number of positive cytologic findings was larger (n = 7) than in those obtained with the MH needle (n = 5). In both groups the difference was not statistically significant. These two positive cytologic results in aspirates obtained with FNAC we suspicious in aspirates with the MH needle (in one case the amount of cell material in the sample was smaller, in the second case the cell material was less representative – probably obtained by puncture from the tumor margin). The number of suspicous specimens was the same with both types of needle (n = 7). Negative findings were observed more frequently in MH needle group (n = 12 vs. 9)

In 30 patients the cytologic findings and the quantity of cell material obtained by FNAC and MHNAC were compared.

In one third of our cases (10 out of 30) an approximately equal quantity of cell material was found, meaning that the cell sample was equally representative in aspirates with the standard fine needle and with the MH needle.

A more representative cell sample was also found in about one third of cases in aspirates obtained with the MH needle (8 out of 30) and in those obtained with the fine needle (12 our of 30).

Factors affecting the sensitivity of FNAC of the breast include the aptitude of the aspirator, the experience of the cytopathologist, the size of the lesion and certain histological cancer types.

By means of MHNAC we wished to improve the sampling of the punctured lesions. We assumed that the quantity of the material would be larger while the number of inadequate samples would be smaller. This would enable safer application of aspiration cytology for the final definition of benign lesions and conservative treatment of benign tumors.

Today numerous authors speak in favour of a second benign FNAC sample before patients with palpable benign lesions can meet the criteria for conservative management.[6] The reason for this lies above all in the possibility of avoiding the risk of inadequate sample collection in eventual carcinoma.

We believe that the described technique can bi particularly successful in ultrasonically quided punctures as well as in punctures of benign palpable breast masses.

Conclusion

The comparison of puncture biopsy specimens obtained with the standard fine needle and the MH needle revealed approximately equal quality of cell material for cytologic investigation. The quality of the cell material itself did not differ essentially, in spite of the fact that a significantly larger quantity of material was obtained using the MH needle. It would only be possible to assess the value of MHNAC on the basis of a study comprising a larger number of aspirates from palpable and nonpalpable breast lesions.

Acknowledgement

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Stomach tumours following vagotomy and pyloroplasty

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During a 25-year period (1965–1989), 1571 patients underwent surgical treatment for ulcus diseases at the Surgical Clinic, Clinical Hospital Center Rijeka, using the method of vagotomy and pyloroplasty. A 30-year systematic follow-up of these patients revealed two cases of malignant and one case of benign tumours localized in the aboral part of the stomach. These results pointed to a rarer finding of malignant tumours following vagotomy and pyloroplasty compared with stomach resection.

Key words: stomach neoplasms-radiography; stomach ulcer-surgery; vagotomy; pylorus-surgery

Introduction

Scanty data on gastric cancer genesis following vagotomy have been reported by a small number of authors. Various reasons, such as potential precancerous factors (atrophic metaplastic gastritis, cancer at the ulcer site, malignant alteration of gastric ulcer, achlorhydria, duodenogastric reflux and surgical trauma) are quoted.[1, 2]

In literature, there are data about laboratory studies on animals where more frequent cancer occurrence following vagotomy and gastroenteroanastomosis and administration of carcinogens was proved. Greater frequency of gastric ulcers following vagotomy and pyloroplasty are mentioned.[3]

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Patients and methods

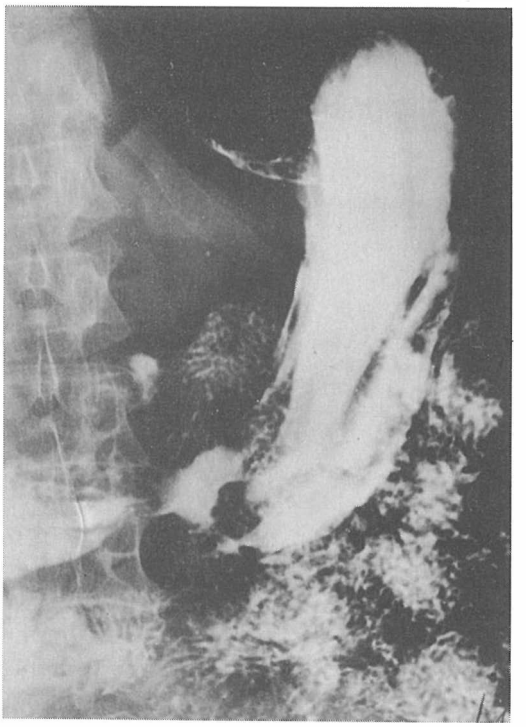
During the 25-year period from 1965 to the end of 1989, 1571 patients underwent surgical treatment for ulcus disease at the Surgical Clinic, the Clinical Hospital Center Rijeka, using vagotomy together with one of drainage methods. Anterior selective and posterior total vagotomies were used as a rule. Bilateral total vagotomy was applied in urgent cases, and older patients. Of drainage methods, Finney pyloroplasty was used, while Heineke-Miculicz pyloroplasty was applied in the earliest stage only.

All the operated patients who were re-examined because of various discomforts were treated systematically and their findings verified during a 30-year period, especially with regard to a peptic ulcer relapse and the occurrence of malignant and benign tumours.

Results

During a 30-year follow-up of these patients, two malignant tumours and one cherry-size

pedicled polyp were verified by classical radiography. The time lapse from the surgical intervention to the detection of malignant tumours was 12 and 18 years respectively, being 8 years at the time of benign tumour verification. Both patients with gastric cancer underwent vagotomy with Finney pyloroplasty. Malignant tumours were localized in the aboral part of the stomach, before the entrance into the surgically changed pylorobulbar area (Figure 1). A polyp of the same localization had a long pedicle enabling its mobility inside the pylorobulbar area (Figure 2).



Figirue 1. Irregular, partially poorly delineated defect of a mandarine-size contrast shadow in front of the entrence to the pylorobulbar area corresponds to an expansive malignant formation. Several folds of gastric mucous membrane stretch out to the defect border.

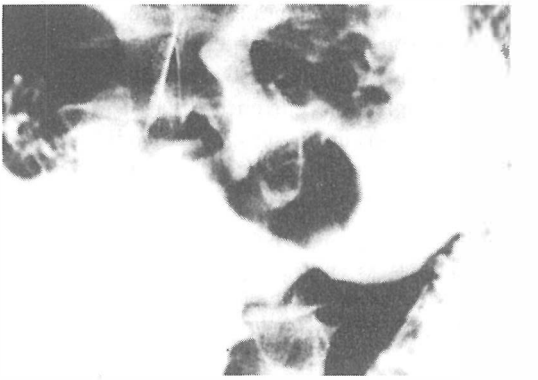


Figure 2. Sharply delineated, round and regular defect of a cherry-size contrast shadow continues to the linear lighting, up to the upper contour of the pylorobulbar area. The finding is consistent with a well movable pedicled polyp.

Discussion and conclusions

The comparison of these findings with one of our earlier studies on primary gastric pouch cancer, resected because of ulcer disease, reveals interesting results.[4] During a 10-year period (1959–1968) 14 primary cancers following stomach resection were found in the area of gastroesophageal junction and the gastric fornix. Postoperative time was approximately 18 years, being somewhat longer than at vagotomy with pyloroplasty. A group of German authors report on 13 primary cancers of the gastric pouch found among 1707 patients during a 10-year period.[5]

The main question here is whether the cancer appearance is more frequent in vagotomized or in resected patients?

In order to answer this question properly, all surgically treated patients should be followed up in the course of a few years accompanied by uniform files. Our patients also "came off" probably from various reasons, as the postoperative time wore on, being lost to (our) follow up. Starting from the fact that our 30-year surveys comprise a greater number of patients with surgery-related discomfort, and according to the comparison with our former study on resected patients and statements from literature, we should be able to conclude the finding of primary cancer in vagotomized patients to be rarer relating to the resected stomach, versus reported opinions in literature. This fact should be of great importance on the selection of surgery especially in younger patients.

Localization of tumour speaks for the presumed reasons for tumour appearance at vagotomy with pyloroplasty. Duodenogastric reflux and metaplastic occurrence because of chronic inflammations in the plastic area could take the first place.

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Primary leiomyosarcoma of the liver

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This report is on the case of a 42-year-old woman patient with whom the ultrasound scan revealed a 30 × 20 mm hypoechogenous focal lesion of the right liver lobe. The clinical workup resulted in the diagnosis of adenoma hepatis. The patient refused any further workup. Thirty-six months after that, additional workup confirmed the growth of the same hypoechogenous lesion in the size of 52 × 40 mm. Ultrasonographically guided cytological biopsy revealed a malignant tumor of the liver and the patient was operated. After the right liver lobectomy the patient was feeling well and had no complaints. The first workup of the patient had not been complete and there was no treatment. The correct diagnosis was established only 36 months later when a malignant tumor of the liver was established by cytological biopsy of the focal lesion, and radical surgery was carried out. The pathohistological diagnosis was: leiomyosarcoma.

Key words: liver neoplasms; leiomyosarcoma; liver

Introduction

Primary malignant mesenchymal tumors of the liver are extremely rare as compared with malignant epithelial tumors. They represent only 1–2 % of all primary malignant tumors of the liver.[1] Leiomyosarcoma of the liver is an extremely rare tumor. Up to the year 1991 only about thirty cases had been reported.[2–11] As this malignant tumor is very rare its histological characteristics have not yet been completely explained.

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A case of primary leiomyosarcoma of the liver in a young woman is presented.

Case report

The patient, P. G., aged 42, was for the first time admitted for clinical workup in January 1987. She was complaining of discomfort and strain under the right thoracic arch. On that occasion the ultrasound scan of the abdomen revealed a round, 32 × 30 mm hypoechogenous lesion of the right liver lobe.

The patient refused the recommended ultrasonographically guided cytological needle biopsy of the tumor, as well as the surgery suggested. Although there was no cytological or histological diagnosis of a tumor, a possible liver adenoma was suspected. The patient was

feeling well and throughout 1988 did not appear for a checkup. In January 1989 a follow up ultrasound scan of the abdomen was made and it showed progres of the tumor (39 × 40 mm). A year later she was hospitalized again and had percutaneous ultrasonagraphically guided cytological needle biopsy performed (Figure 1).

The cytological report gave evidence of numerous malignant tumor cells. The CT of the abdomen showed hepatomegaly with extended blood vessels in the parenchyma. Situated centrally in the cranial part of the right lobe, an expansive 46 × 53 mm formation with nonhomogenous colouring and a small central necrosis could be observed. No signs of pathological enlargements of the paraaortal and paracaval lymph nodes could be differentiated (Figure 2).

During this hospitalization, three years after the first diagnosis, the patient finally agreed to being operated on. Right lobectomy was performed. The tumor was of hard consistency and well delineated (Figure 3). The light microscopy showed interlacing fascicles of spindle-shaped cells containing elongated nuclei (cigar-like nuclei) and eosinophylic cytoplasm typical of a smooth muscle tumor. A delicate reticulin network between the tumor cells was revealed by silver impregnation. Between three and four mitoses per 10 high-power field (HPF) were found. These histological features were indicative of differentiated leiomyosarcoma (Figure 4).

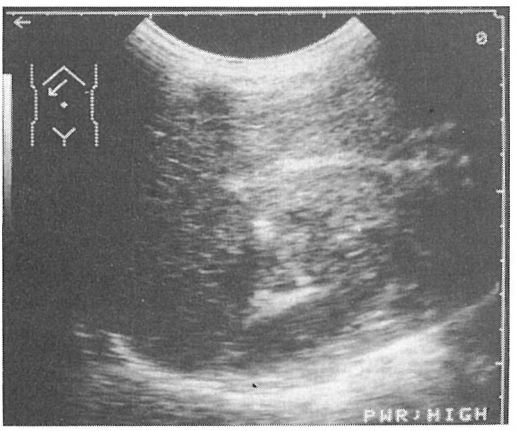

Figure 1. Ultrasonographically-guided percutaneous cytological needle biopsy of a hypogenous 52 × 40 mm round lesion in the centre of the cranial part of the right liver lobe.

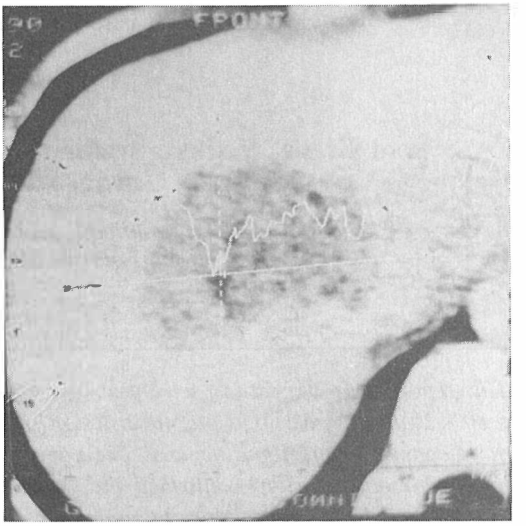

Figure 2. CT liver scan showed an expansive 46 × 53 mm formation situated centrally in the cranial part of the right lobe.

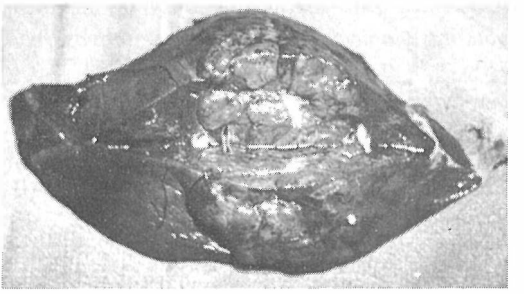

Figure 3. A 7 × 6 cm large grey tumor in the liver, well delineated, with small central necrosis.

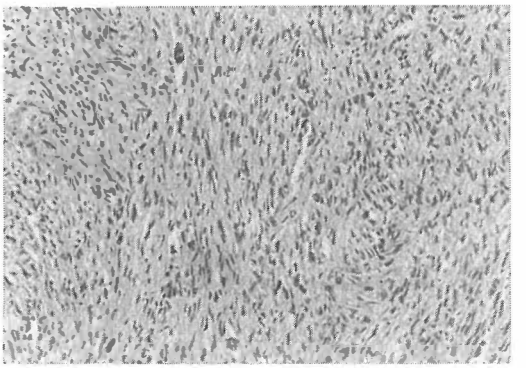

Figure 4. A hepatic tumor composed of uniform spindleshaped cells arranged in an interlacing pattern.

More than three years after surgery the patient is feeling well and is free of any complaint. During this period an ultrasound scan of the abdomen was made on several occasions, as well as scintigraphy of the liver and abdominal CT, all showing through regeneration of the liver, with no evidence of disease (Figure 5).

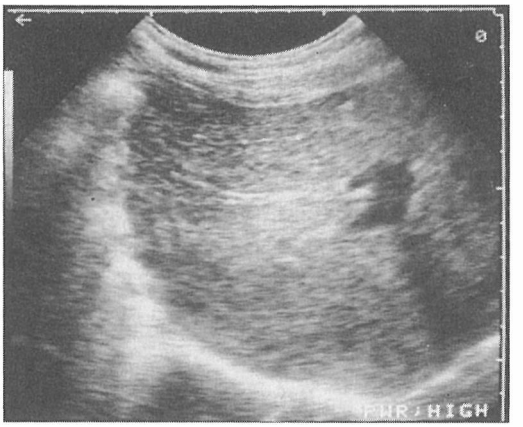

Figure 5. Ultrasound scan showing regeneration of the liver.

Discussion

Leiomyosarcomas of the liver are usually large, slowly growing tumors found in adults. The main symptoms usually include swelling of the abdomen and pains under the right thoracic arch, accompanied by a loss of body weight. If the tumor is small, pains of some intensity may occur without abdominal swelling. Hepatomegaly may also be observed, sometimes extreme and weighing even up to 11.200 g.[10] Now and then, ascites may also be present. Leiomyosarcoma is mostly solitary, but may also be multiple.

All the cases described so far had no specific symptoms, so that there was a clear-cut discrepancy between the findings of tumors and the hepatic functional tests. With smaller tumors all laboratory tests are usually normal, whereas with the bigger ones there are alterations of alkaline phosphatase, gammaglutamyl transpeptidase, transaminases or lactic dehydrogenase, which however are not specific.

It is most important to make the diagnosis as early as possible, since the prognosis of this tumor is much better than that of other primary malignant hepatic tumors, especially after an adequate surgical treatment.[12]

The only safe preoperative diagnostic method of this tumor is histologic analysis. In case there is any doubt as to the histologic finding obtained by means of routine methods, electronic microscopy is recommended.

In the diagnostics of this tumor the ultrasound examination of the abdomen, CT of the liver, angiography of the arteria hepatica propria, liver nuclear magnetic resonance (NMR) and laparsocopy with target biopsy of the tumor are also of great help. Of all these methods, the best results are provided by the CT of the liver, ultrasound guided percutaneous biopsy of the tumor and the laparoscopy with target biopsy of the tumor. These are the methods of choice. In particular cases, a percutaneous liver biopsy can also be made using the transjugular approach. This, of course, can be done only if the patient has no coagulation irregularities.[13] The findings of the liver ultrasound and CT in combination with arteriography will yield a good anatomic image of the tumor mass and local veinal structure, which can be of great assistance when planning surgery.

Laparoscopy with target biopsy of the tumor is also recommended.[2] This can yield additional information on the size, appearance and any possible spread of the tumor to an extrahepatic area.

The diagnosis of this tumor requires a careful search to ascertain that it originates from neighbouring structures,[14–18] and that it is not metastasized from another primary site. The clinical presentation and the results of the examination are not specific for the diagnostic of hepatic leiomyosarcoma.

Microscopically it consists of interwoven bundles of spindle cells with a variable amount of cytoplasm. Characteristic are the elongated cigar-like nuclei, as well as their mitotic activity.

Morales et al.[19] present ultrastructural criteria of leiomyosarcoma. According to these authors, leiomyosarcoma must meet the following electron microscopic criteria: presence of intra-

cytoplasmic myofilaments; dense bodies in both cytoplasm and plasma membrane; pinocytic vesicles and invaginations of plasma membranes; remnants of basal lamina or an excessive cell coat.

Histologically, hepatic leiomyosarcoma has to be distinguished from fibrosarcoma and malignant schwannoma, which are also built of spindle cells. The histologic diagnosis is made on the basis of: (1) proliferation of long spindle-shaped cells in interlacing bundles; (2) presence of cigar-shaped nuclei; (3) presence of intracytoplasmic thin filaments and marginal dense patches; (4) immunohistochemical positivity for vimentin and muscle-specific actin.

In response to the muscle-specific actin the antibodies react with both alpha and gamma actins within the skeletal, cardiac and smooth muscle cells, and are not reactive with other mesenchymal and epithelial cells.[20] This antibody is a much safer marker for differential diagnosis of mesenchymal malignant tumors than desmin, because of its high sensitivity for poorly differentiated muscle tumors.

When leiomyosarcoma of the liver is histologically confirmed, the degree of malignant potential has to be ascertained on the histological image. In order to achieve this, usually such criteria as the size of the tumor, cellularity, number of mitotic figures and the presence of necrosis within the tumor are used.

Enzinger and Weiss[21] tried to establish the gradation of malignancy of leiomyosarcoma. They have found that the retroperitoneal tumors of smooth muscle cells with only 5 mitoses/10 HPF have to be considered as malignant, while those tumors having between 1 and 4 mitoses/10 HPF should be considered as potentially malignant. In oposition to these authors, Wolf et al.[22] found tumors with smooth muscle cells of the soft tissue, which had mitotic activity of less than 1 mitosis/10 HPF, to be nevertheless metastasized.

On the basis of this it can be concluded that we have not yet found a reliable morphological criterion for the gradation of malignancy of the hepatic leiomyosarcoma. The reason for this is the absence of a precise analysis of morphological criteria and criteria of growth. It is not easy to determine the metastatic potential of this tumor. The mitotic index alone is not a sufficient indication. There are a number of morphological criteria such as e.g. the size of the tumor, degree of differentiation, as well as the characteristics of tumor growth, such as e.g. the mitotic index, frequency of cells in the growth fraction, that need to be taken into account.

The therapy of choice for this tumor is an extensive surgical resection. The role of the chemotherapy is not yet clearly understood[2, 9] as there is no safe attitude towards this question due to the insignificant number of cases reported so far. The patient could be treated also with the hepatic transplantation.[23]

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Radiol Oncol 1994; 28: 146-8.

Report from the joint meeting of European Society for Radiation Biology and European Society for Hyperthermic Oncology Amsterdam, June 1–4, 1994

For the first time European Society for Radiation Biology (ESRB) held the joint meeting with European Society for Hyperthermic Oncology (ESHO). More than 350 participants attended this meeting. Many investigators came from Eastern Europe; for the first time, scientists from Japan and India also presented their work.

Only the opening and the closing lecture (J. Denekamp and D. Bootsma) were given for all participants. Throughout the meeting, the program started at 8 a. m. in four parallel sections. It began with refresher courses, followed by workshops, symposia, proffered papers or poster viewing. With two coffee breaks and one hour for lunch, it finished at 6 p. m. The presentations were divided in the following sections: clinical hyperthermia, hyperthermia physics and technology, hyperthermia biology, photodynamic therapy and the heat shock proteins, X-rays, hyperthermia, apoptosis, tumor radiobiology, radiation and environment carcinogenesis, EULEP: genetic predisposition of radiosensitivity, cellular radiobiology, DNA and chromosome damage and repair, radiation damage to normal tissue, and biological basis for the clinical application of boron neutron capture therapy. In this report, I will point out some of the most important new data or some general conlusions that have both, basic and clinical implications.

Basic science

The newest basic data were presented by D. Bootsma (DNA repair: genes and syndromes). With his group (no doubt the best in this field in the world), he has made a tremendous progress since last year. His talk was concentrated on three genes involved in the repair of human genome. In collaboration with Japanese colleagues, HHR23A and HHR23B genes were cloned. These genes are located on human chromosome 3, and show great homology with yeast RAD10 and RAD23 genes. The defect in these genes affected the so-called "slow DNA repair" component, while the fast one was unaffected. (During fast repair, the active genes are repaired, while, during slow repair the lesions from rest of DNA are removed.) The defect in HHR23 genes is thought to be responsible for the genotypic and phenotypic characteristics of Xeroderma pigmentosum (XP) C type of patients: photosensitisation, characteristic pigmantation, proneness to cancer). The other gene mentioned was ERRC-6. This gene was cloned two to three years ago. It shows great homology with RAD 16 and RAD 54 genes. The deffect in this gene is expressed in the Cockney syndrome (the lack of pigmentation characteristic of XP patients, dysmyelinisation, short growth, "bird face", but no proneness to cancer). The product of ERCC-6 gene is thought to be a helycase, which is important in fast DNA repair. In his lecture, Bootsma also dealt with TFIIH(BTF2) gene, the first gene known today to participate in recombinational repair in eukaryotes. The product of this gene form a complex with several proteins (p34, p41, p44, p62, p80-from ERCC2 gene, p89-from ERCC3 gene, and two or more unknown proteins). This complex exerts helycase and phosphorylating activities, enabling that RNA polymerase II to transcribe DNA. Thus the deffect in this gene causes the deffect in DNA transcription and manifests itself clinically as "transcriptional syndrome" (neurodysmyelinisation, disturbance in physical and mental development). Not surprisingly, it is difficult to find a

patient with this syndrome, because such a defect is more or less incompatible with life. Other genes which have now been known to participate in the DNA repair include: 13 human, more than 10 rodent and more than 15 yeast genes involved in the repair of lesions induced by UV light or mitomycin C, and 5 human, 10 rodents and 10 yeast genes involved in the repair of X-rays induced lesions.

An attept to explain the cause of adaptive response of human keratocytes to N-mehyl-N-nitro-N-nitroso-guanidine (MNNG) was made by H. E. Kleczkowska and F. R. Althaus. Like rodent cells, human keratocyites, do not possess O^6-methylguanine DNA methyltransferase, which is otherwise specifically induced in bacteria following treatment with MNNG and which is specifically involved in the adaptive response to this drug. In keratocytes, the authors revealed the induction of poly-(ADP-ribose) synthesis after pretreatment with MNNG; this synthesis is thought to play an essential role in adaptive response. (The polymers are very efficient in removing histones from DNA, thus facilitating the DNA repair).

Basic-clinic data

Many presentations at the meeting dealt with the methods that could give the accurate answer to the question what happens in the cells after irradiation, and with the assays that could predict the cell sensitivity to irradiation. Variations in the initial level of DNA damage have previously been suggested as potential determinants of radiation sensitivity in both rodent and human cell lines. These studies were usually performed with the non-denaturating filter elution technicques, a method often suggesed to be influenced by factors other than DNA breakege. H. H. Kampinga gave a talk about the results obtained by some new techniques: Comet assay and pulse field gel electrophoresis (PFGE). Both these methods, however, failed to detect any significant difference in sensitivity of radioresistant and radiosensitive cell lines obtained by clonogenic assay. PFGE determines the retention of DNA on gel, depending on the number of double strand breaks (the main cause of cell death after irradiation). While smaller fragmets are released, more than 70% of larger fragments are retained. This could limit the capacity of this assay to distinguish between radiosensitive and radioresistant cells (J. Dalm-Daphi and E. Dikomey). In the case of Comet assay, the situation is even worse; moreover, it is not known what is really detected by this technicque (E. C. Woudstra). It is speculated that the features of chromatine structure interfere with the detection of damage by some assays. Indeed, it is disappointing, that during so many years of investigations, no simple and sensitive method was found that may replace the clonogenic assay. Obviously, the theoretical basis of new techniques is too simple and do not take all the relevant facts into consideration, beeing therefore inadequate in the detection of the final damage effect at the cellular level.

Clinical application

The results of three reports of ESHO trials, presented by J. Overgaard, will be briefly mentioned. The assessment of the efficacy of hyperthermia adjuvant to radiotherapy was determined in the treatment of neck and breast tumour and the metastatic melanoma. For metastatic malignant melanoma, 128 patients were treated from 1987 till now. They received either radiation alone (3 x 8–9 Gy) or this same radiation treatment was combined with hyperthermia (3 sessions, 43°C, 1 hour). The initial complete response was significantly higher in patients receiving hyperthermia. This was maintained during the two years period (the study is closed). 77 patients with neck tumours node metastasis received irradiation alone (60–70 Gy) or combined with hyperthermia (5–6 sessions, once weekly, 43°C, 1 hour). The preliminary analysis was given showing no difference in this group of patients (the study is still open). Similar results were obtained with the same treatment schedule involving 155 patients with

locally advanced breast cancer. However, collaborative phase III hyperthermia trials (C. C. Vernon) on 300 pacients with breast cancer (started in U. K. at 1989 and because of slow accural rate of this study, later also the data from ESHO patients were included and analysed together) shows better effects in pacients treated with hyperthermia. The disagreament in the results obtained with the breast cancer patients may depend on the different treatment schedules. In the workshop on clinical hyperthermia it was concluded that in future hyperthermia should continue to be used as the adjuvant to radiotherapy. The tumours, candidates for such treatments, should be accessible, high grade, pathologically deep (meaning that they are spread to muscles), with metastasis. That are breast, colon and rectal cancer and sarcomas. Also, more attention must be given to the adequate heating of tumour mass, because the rare and incomplate studies done so far indicate, that the expected temperature of 43° C is not reached in all parts of the tumor.

Clinical data provide a warning that the potential of these assays, and their predictive therapeutic power must be critically evaluated for specific endpoints. It is concluded that a more critical approach to experimental radiotherapy is required to avoid the rejection of potential improvements of the treatment, resulting from the falsy optimism. It was pointed out (S. M. Bentzen) that in the case when insufficient number of patients is taken into account, it is impossible to draw accurate conclusions (e. g., to prove that a new treatment protocol improves the success from 30 to 50 per cent, 124 patients are needed, while for the improvement of 30 to 40 per cent, 467 patients are needed). If it is not possible to have such a number of patients, than doing such clinical trials is not only a waste of time, but is also unethical to the patient. Therefore, it is recommended to clinicians to joint the ESHO program rather than to start their own trials with a low number of patients.

In this report only some of the presentations are mentioned from many interesting ones. The meeting was very well organized, giving all the participants the opportunity to talk with their colleagues. Finally, I must stress, that a lot of very young people attended the Meeting, thus clearly indicating that radiobiology has again come in the focus of interest.

Maja Osmak Ph. D.
Ruđer Bošković Institute, Zagreb

Notices

Notices submitted for publication should contain a mailing address, phone and/or fax number of a contact person or department.

Radiology

The European seminar (ESDIR) "Radiology of Gastrointestinal Tract Neoplasms: Diagnosis, Staging and Intervention" will be held in Iraklion, Crete, *September 22–24, 1994.*
Contact Public Relations Center LTD – 102, Michalakopoulou str., 11528 Athens, Greece; or call + 30 1 777 10 56 / 775 6336 / 771 1673; fax + 30 1 771 1289.

Breast cancer

The ESO refresher day will be held at *October 7, 1994.*
Contact Miss Gollubics, ESO-Vienna-Office, Arztekammer für Wien, Fortbildungsreferat Weihburggasse 10-12, A-1010 Vienna, Austria; or call + 43 1 51501 293; fax + 43 1 51501 240.

Lung cancer

The 1st international lung cancer conference "Non-small Cell Lung Cancer Management: Open Questions and Controversies" will be offered in Alba, Italy, *October 7-8, 1994.*
Contact Cuneo Lung Cancer Study Group, Via Romita 15, 12011 Borgo S. Dalmazzo, Cuneo, Italy; or call + 39 71 441 770 (hours: 12 a.m.–3 p.m., Monday through Friday); fax + 39 171 611 597.

Papillomavirus

The 13th international papillomavirus conference will be offered in Amsterdam, The Netherlands, *October 8–12, 1994.*
Contact Bureau PAOG, Mrc. C. M. Schoof / Mr. C. H. Walta, Tafelbergweg 25, 1105 BC Amsterdam, The Netherlands; or call + 3120 556 4801; fax + 31 20 696 3228.

IAEA Scientific meeting

The international symposium on spent fuel storage – safety, engineering and environmental aspects will be held in Vienna, Austria, *October 10–14, 1994.*
Contact International Atomic Energy Agency, P. O. Box 100, Vienna International Centre, A-1400 Vienna, Austria.

IAEA Scientific meeting

The seminar on radioactive waste management practices and issues in developing countries will be offered in Beijing, China *October 10–14, 1994.*
Contact International Atomic Energy Agency, P. O. Box 100, Vienna International Centre, A-1400 Vienna, Austria.

Radiology

The first congress of the Croatian Society of Radiology will be held in Opatia, Croatia, *October 11–15, 1994.*
Contact Congress secretariat, Mr. Berislav Budiselić or Mr. Stjepan Riman, Clinical Institute of Radiology, Clinical Hospital Center Rijeka, Tome Strižića 3, 51000 Rijeka, Croatia; or call + 385 51 216 899; fax + 385 51 536.

Radiobiology

ESTRO teaching course "Basic Clinical Radiobiology" will be held in Prague, Czech Republic, *October 16–20, 1994.*
Contact the ESTRO Secretariat, Radiotherapy Department, University Hospital St Rafael, B-3000 Leuven, Belgium; or call + 32 16 33-64-13; fax + 32 16 33 64 28.

IAEA Scientific meeting

The FAO/IAEA international symposium on nuclear and related techniques in soil/plant studies on sustainable agriculture and environmental preservation will be offered in Vienna, Austria, *October 17–21, 1994.*
Contact International Atomic Energy Agency, P. O. Box 100, Vienna International Centre, A-1400 Vienna, Austria.

ESTRO-AER PRE-MEETING TEACHING COURSE

THE USE OF MODERN DIAGNOSTIC IMAGING TECHNIQUES IN RADIOTHERAPY PLANNING

Granada 22–24 September, 1994

Teaching Staff: M. Brada, J. Britton, M.Goitein, G. Kantor, A. Neal, C. Raybaud, D. Ten Haken, A. Warrington.

Course aim:
This course is a joint venture of ESTRO together with the European Society for Radiology (AER). In the last year new radiotherapy techniques are becoming more and more important. The common aspect of these new techniques is the aim to apply higher doses to smaller volumes.This can be done both with brachytherapy as with external beam conformal radiotherapy. This development creates the need for radiotherapists to know how to use the modern imaging techniques such as ultrasound, computerized tomography and magnetic resonance imaging. In this course experts in the field of modern imaging techniques and radiotherapy will discuss and demonstrate modern treatment planning for different types of malignancies in the central nervous system making an optimal use of the imaging techniques. They will also demonstrate how to organize and structure the cooperation between the radiodiagnostic and radiotherapy departments. Although brain is chosen as a site to demonstrate the use of modern imaging techniques the principles demonstrated are also applicable to other sites.

Language: English

Programme:

Curent Status of Conventional Imaging
CT and MRI in the diagnosis of adult brain tumours (differential diagnosis, choice of imaging by sites and tumours, visualisation of the extent of tumour, diagnostic aspects of metastatic disease). CT and MRI in the diagnosis of paediatric brain tumours. Spinal imaging (primary and metastatic spinal tumours, techniques of imaging spinal seeding). Imaging in the follow-up of brain tumour patients (assessment of response, features of early and late toxicity of chemotherapy, radiotherapy and surgery, late vascular events, hydrocephalus). Angiography and MRA in the diagnosis of AVM's.

Imaging and Modern Radiotherapy Planning
Fixation and localisation devices for brain imaging. Problems of image distortion. 3D image reconstruction and visualisation and radiotherapy planning. Evaluation of 3D plans with dose volume histograms and other techniques. Physical aspects of small volume cranial irradiation.

New Imaging Modalities and Their Clinical Potential
PET scanning, Advances in MRI. MR Spectroscopy, Integration of multimodality into radiotherapy. PET imaging for radiotherapy.

Integration of Imaging into the Management of Brain Tumours
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Unabridged articles which should be submitted in triplicate to the Organizing Committee by the beginning of the Congress will be published in No. 4/94 of RADIOLOGY AND ONCOLOGY.

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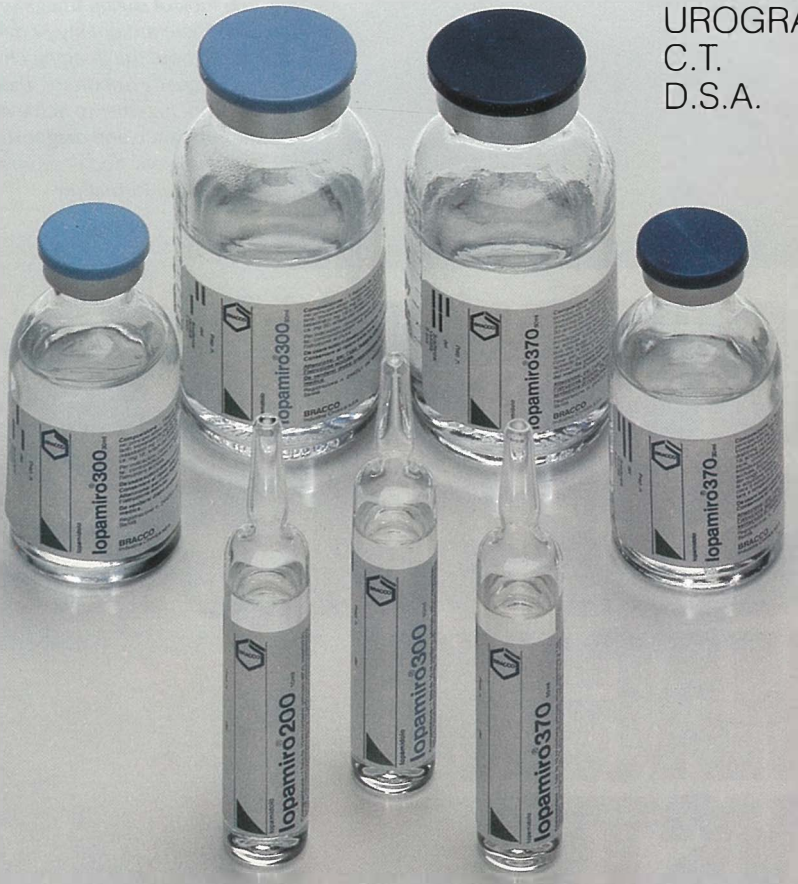

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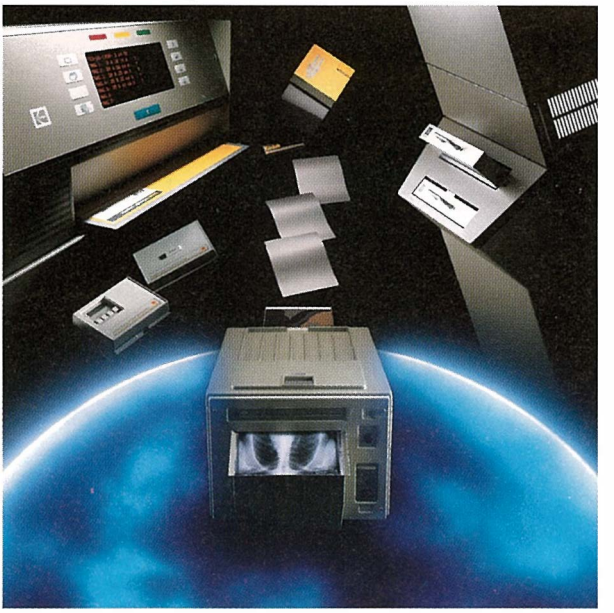

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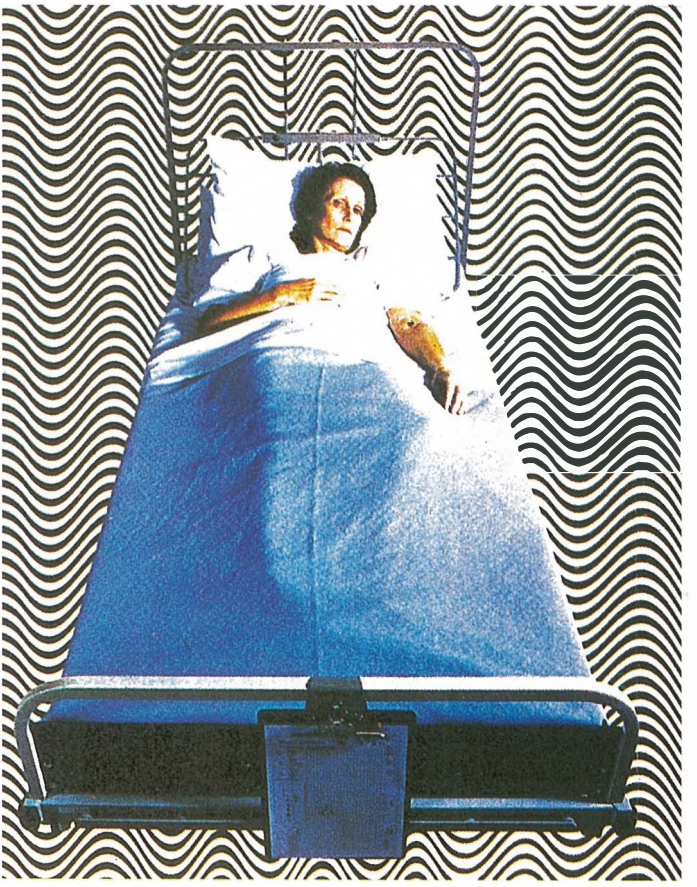

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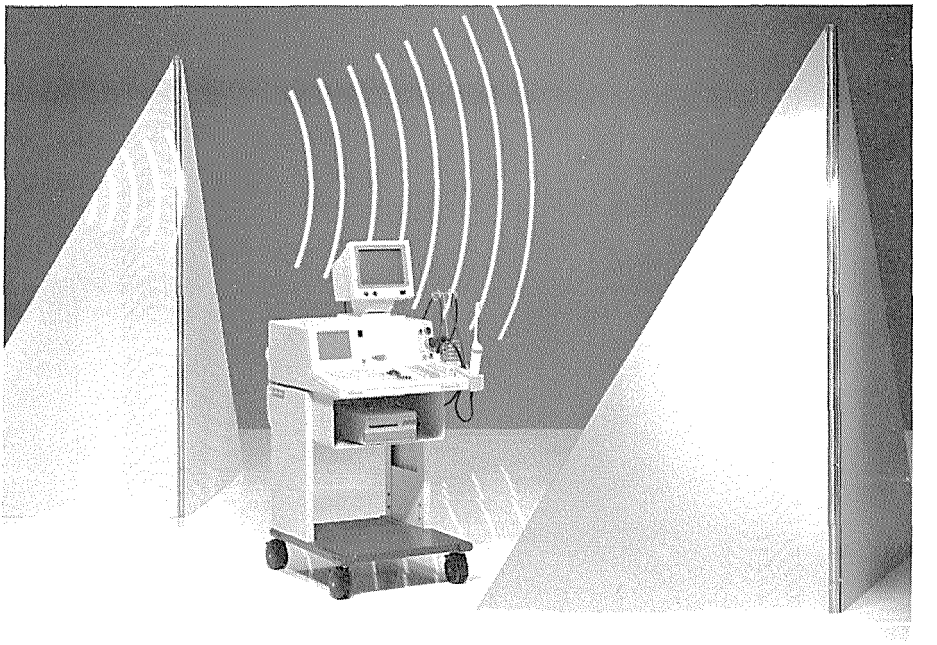

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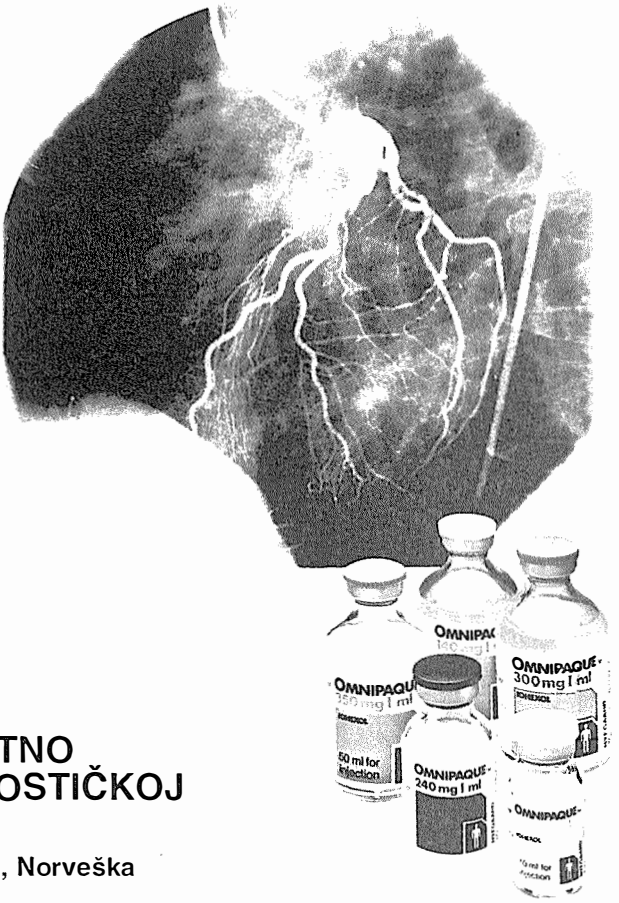

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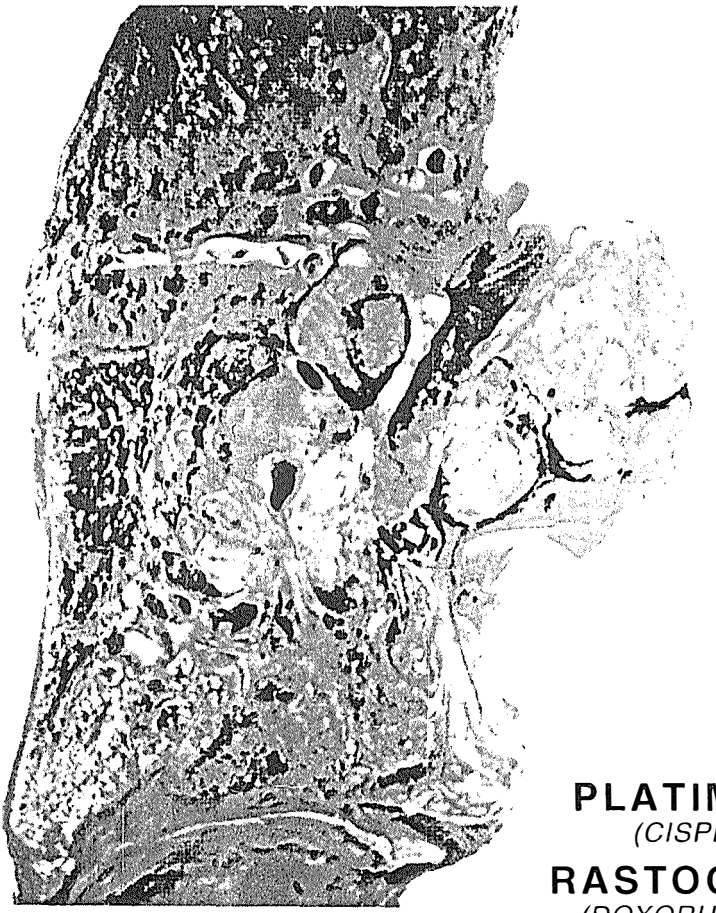

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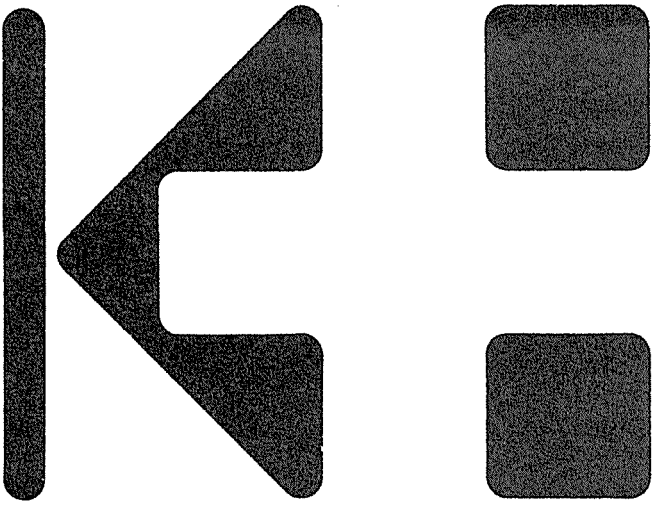

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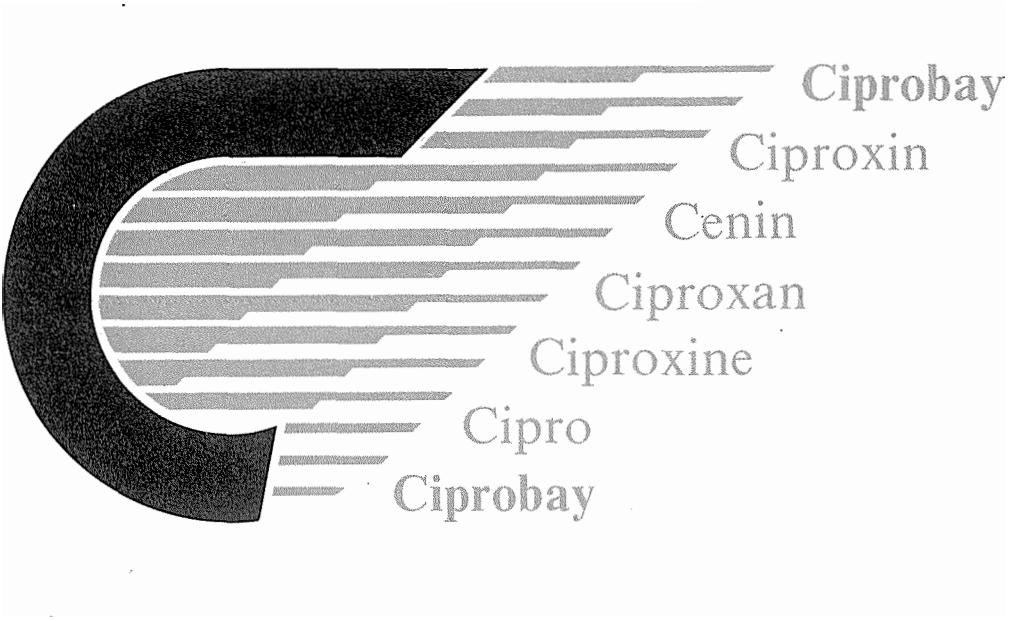

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