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Diagnosis and treatment of leiomyosarcoma of the oesophagus

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Leiomyosarcoma of the oesophagus is a rare tumour and its histological differentiation from that of benign leiomyoma is sometimes very difficult. The therapy of choice for leiomyosarcoma of the oesophagus is oesophagectomy in which a stomach tube (gastric transposition) is normally used to reconstruct the alimentary tract. If necrosis during the post-operative period occurs, then it is necessary to perform resection of the stomach tube with careful management of any subsequent complications such as infections. After an infection has been controlled, it is possible for parts of the large intestine (right or left hemicolon) or parts of the small intestine (jejunum) to be used as a replacement for the oesophagus. The decision as to which part of the intestine can be used for reconstruction of the alimentary tract can only be based on post-complication intraoperative findings. We report a case history of this rare type of malignancy.

Key words: leiomyosarcoma, oesophagus, oesophagectomy, alimentary tract reconstruction

Introduction

Leiomyosarcoma of the oesophagus is a rare tumour [1] and was first described in 1902 by Howard [2]. Almost a century later, only 165 cases have been reported in the literature [3]. This tumour represents less than 0.5% of all primary gastrointestinal sarcomas and only some 5% of all oesophageal tumours [4, 5]. Experience of this tumour, both diagnosis and treatment, is therefore extremely limited.

Growth pattern and incidence

Leiomyosarcoma is a tumour which originates from the mesenchymal smooth muscle cells. It grows submucously and in most cases is located inside the layers of the middle and lower parts of the oesophagus [3-5]. Its incidence is 45% for the lower-third of the oesophagus, 30% for the middle-third, and 25% for the upper-third [3, 5-7]. There is a distinction between the polyp and infiltrating types of this malignancy [3]. For both sexes, leiomyosarcoma of the oesophagus has its highest incidence in the age group 50-79 years [1, 3]. However, leiomyosarcoma is diagnosed 1.6 times more often in men than in women [3].

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Symptoms

The main symptoms of this malignancy are dysphagia (85%), loss of weight (58%) and pain (39%). More than one-third (35%) of the reported cases experience both dysphagia and loss of weight. Additional symptoms include reflux oesophagitis (17%), nausea combined with vomiting (7%) and acute bleedings (6%) [3, 8]. Leiomyosarcoma is almost never asymptomatic [3]. However, a definite diagnosis can often only be made a year after the appearance of the first symptoms [1, 3].

Diagnostic findings

A 69 year-old male patient complained about suffering for five months from dysphagia and relapsing post-prandial vomiting as well as experiencing a loss of weight of 13 kg during this period of time. Perianal bloody stool or melanemia were denied by the patient as nicotine addition and alcohol abuse. The family history did not show any malignant diseases.

Because of the dysphagia we performed a gastroscopy and this showed a semicircular, stenosing, exophytic growth which was suspicious of a malignancy. This was sited 25–32 cm from the superior aspect of the oesophagus, Figure 1. In-patient hospital admission took place for purposes of histological clarification and to obtain a definitive diagnosis.

On clinical examination, the patient's height was 1.83 m and weight 80 kg and he was assessed to be in good general and nutritional condition. The examination found no clinical abnormalities and no indications of a disease pathology. The common laboratory findings were all within normal ranges. The tumour markers

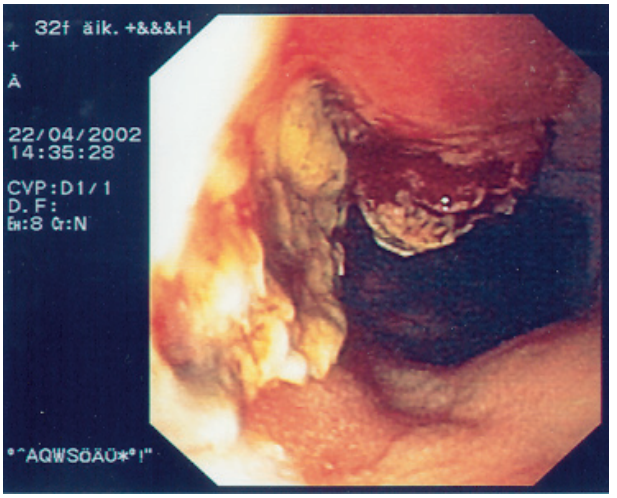

Figure 1. Endoscopic pre-treatment imaging

(CEA, Ca 19-9, Ca 50, Ca 72-4, PSA) except for a slightly higher NSE (29 ng/ml, normal range 12 ng/ml) were also all in their normal ranges.

During diagnostic investigative procedures including ECG, bronchoscopy and total body bone scanning, as well as sonography and computed tomography of the abdomen no abnormal pathological findings were observed. X-rays of the thorax in two planes and pulmonary function studies indicated in the images, the start of bronchial asthma with reversible obstruction. A barium study of the gastrointestinal tract, Figure 2, using water soluble contrast medium showed a 4-5 cm long stenosis of the middle-third of the oesophagus, with obviously delayed contrast medium outflow.

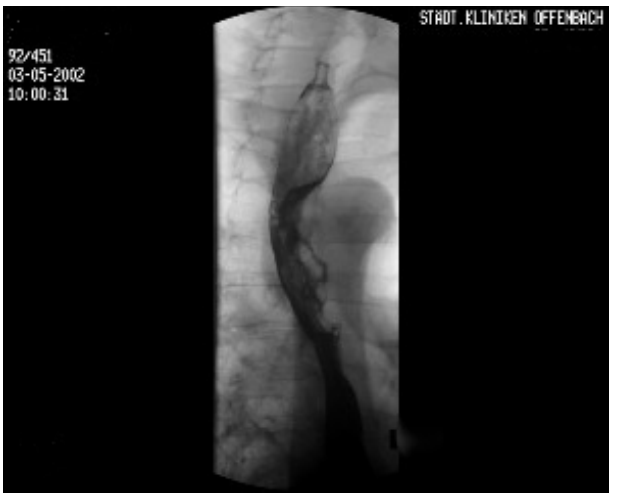

Figure 2. Pre-operative barium contrast imaging

In terms of diagnosis, a fistula could be excluded. The computed tomography (CT) imaging results showed a 3 cm x 4 cm space occupying mass at the height of the aortic arch with pre-stenotic dilatation of the oesophagus. In addition there were several small lymph nodes with a diameter of less than 1 cm but without any evidence of metastatically suspicious spherical lesions in the lungs.

To complete the pre-operative staging for this patient, an endosonoscopy was performed, Figure 3. This confirmed the earlier CT findings with a 2.5 cm x 3.7 cm echo-poor, inhomogeneous, semicircular stenosing tumour at 25-32 cm from the superior aspect of the oesophagus. Also indicated was penetration of the adventitia.

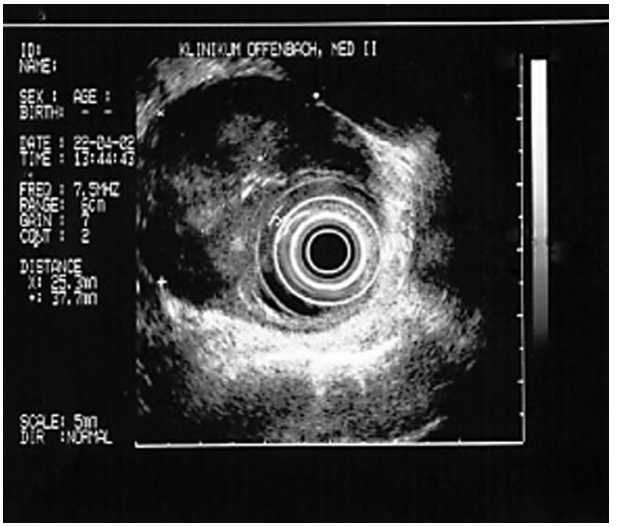

Figure 3. Endosonographic imaging for assessment of tumour staging

The images also suggested that the tumour abutted the thoracic aorta with the possibility of infiltration. It was possible to display up to 1 cm sized peri-tumoural lymph nodes. The histological analysis of the tissue samples were indicative of a spindle cell shaped sarcoma. After additional immunohistochemical testing (KI1, keratin 8, S100, actin, desmin) and a positive actin reaction, we suspected the existence of a leiomyosarcoma of the oesophagus of stage T4, N1, M0, G2.

Treatment strategy

After pre-operative preparation, including additive parenteral hyperalimentation, we performed a thoraco-abdomino-cervical en bloc resection of the oesophagus with a stomach tube as an oesophageal replacement. On the fourth post-operative day our patient developed clinical indications of an anastomosis insufficiency. We immediately performed a surgical revision. The cause of the complication was found to be stomach tube necrosis with incipient mediastinitis. After re-thoracotomy on the right side of the chest, we resected the stomach tube, occluded the remaining stomach stump and drained both pleural cavities and the mediastinum.

The disconnection of the stomach tube made necessary the implantation of a small intestine nutritional catheter. Subsequently, during the same surgical session, we performed a cervical resection of the remaining stomach tube as well as a hemi-thyroidectomy on the left side. This was due to a lack of space required in order to install a terminal salivary fistula. The further post-operative course was without pathological findings.

After eight weeks of anastasis, a temporary discharge was observed and the patient was re-admitted. We then performed an isoperistaltical colon interposition in order to reestablish the recontstructed oesophageal passage. Due to the vascular architecture, Figure 4, which was detected using angiography. Because of adequate mobility, the right hemicolon including the terminal ileum were chosen as interposition material after an appendectomy. It was demonstrated, intraoperatively, that the arterial blood supply was sufficient via the arteria colica media as well as its venous outflow.

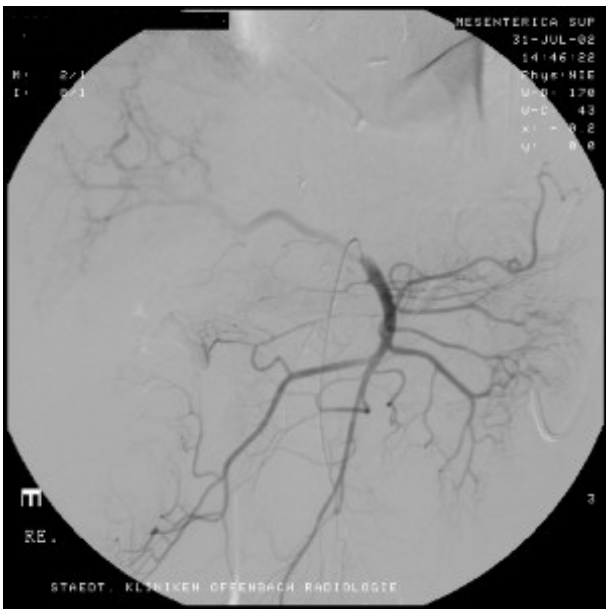

Figure 4. Angiographic imaging of the mesenteric vessels

Because of the expected late stage of the tumour, T4, and a planned post-operative irradiation, we decided to dislocate the colon interposition through a retrosternal path to the cervical level. The post-operative development was satisfactorily accomplished and an assessment of the anastomosis using water soluble contrast medium appeared to be sufficient. A gradual alimentation build-up was initiated on the fifth post-operative day and after three weeks the patient was discharged. Adjuvant radiotherapy of 50.4 Gy was given without any need for the patient to be hospitalised.

Post-operative histological findings on the surgical specimen showed a 7 cm diameter moderately differentiated leiomyosarcoma of the oesophagus with infiltration of the muscularis propria as well as of the adventitia, but without any evidence of affected lymph nodes, T2 N0 M0, G2, R0.

Follow-up

Currently, the patient is in very good general and nutritional condition. Since his discharge from in-patient treatment he has gained 7 kg in weight after initial additive parenteral hyperalimentation. He is now able to ingest nutrition of any kind, not dependent on its consistency. He has no post-treatment complaints.

Discussion and conclusions

Leiomyosarcoma of the oesophagus is a rare tumour and the space occupying mass does not necessarily cause immediate symptoms. It is essential to be able to differentiate between a benign leiomyoma and a malignant leiomyosarcoma in order to determine the therapeutic strategy. Histologically this is often quite complicated [1, 3, 5, 8]. The leiomyosarcoma consists of spindle-cell-like cells with long drawn-out nuclei and eosinophilic cytoplasm. The distinction between the malignant leiomyosarcoma and benign leiomyoma depends on the amount of mitosis, the cell concentration and the evidence of cellular atypia with or without necroses, in order to determine the grade of malignancy [5, 9] of which there are four, Table I [5].

A differentiation between the benign leiomyoma and malignant leiomyosarcoma solely through immunohistochemical studies does not work [3]. The detection of vimentin and actin characterises the mesenchymal smooth muscle cells and allows a distinction from tumours which arise from epithelial cells and show a positive reaction to cytokeratin, such as for example, spindle cell carcinomas [3]. A diagnosis of oesophageal carcinoma

Table I. Histological grading of leiomyosarcoma, after Pesarini et al [5]

Grade 1.	Only a small increase in the number of mitoses when compared to leiomyomas Only slightly higher concentration of cells as in leiomyomas No cellular pleomorphism
Grade 2.	An increase in the number of mitoses: at least in 1 of 5 high power fields A moderately higher concentration of cells as in leiomyomas A greater nucleocytoplasmatic ratio than leiomyomas
Grade 3.	A higher rate of mitoses: more than 1 in 5 high power fields An obviously higher concentration of cells as in leiomyomas Cellular pleomorphism
Grade 4	Numerous mitoses A very high concentration of cells Cellular pleomorphism with atypia of the nucleus

always needs to be ruled out before leiomyosarcoma can be diagnosed [1, 3].

Leiomyosarcomas can often grow intralumenally and as polyps but rarely intramurally and invasively [3]. If an invasively growing leiomyosarcoma leaves an intact mucous membrane of the oesophagus and if the tumour is not clearly recognisable, it is possible that a superficial tissue sample can falsely lead to a negative histology [10].

Clinical parameters which are required in order to fully estimate malignancy, include size increase over a period of time, infiltration grade, the presence of a displacing growth which cause the patient to complain [1, 3]. The major symptoms of leiomyosarcoma of the oesophagus are dysphagia and loss of weight, but they are not specific only to this disease [1].

The use of diagnostic endosonography is very important. This is because a leiomyosarcoma presents as echo-poor and usually inhomogeneous, arising from the lamina muscularis mucosae or lamina muscularis propria [12]. Sometimes, intratumoural necroses or calcifications are visible, and therefore it is not possible to distinguish the tumour from its surroundings [3, 5]. Pre-operative diagnostic imaging often indicates suspected tumour infiltration of the aorta or of other arterial blood vessels. However, intraoperative findings show in most cases that arterial vascular structures are normal and are not infiltrated by the neoplasm.

The pre-operative studies which are necessary include chest X-rays, abdominal sonography, gastroscopy with tissue sample biopsy, endosonography, barium radiographic studies of the oesophagus employing water soluble contrast medium and CT of the abdomen. These should be considered to be standard procedures in order to obtain an accurate diagnosis and to eliminate the possibility of distant metastases [3, 5]. Total body bone scanning and bronchoscopy are not considered by us to be essential.

A literature review reveals that at the time of the diagnosis already one-third of leiomyosarcomas have developed distant metastases [3, 10]. The most frequently affected organs are liver and lung, because of haematogenic dissemination. In rare cases a lymphogenic metastasis is possible [1, 3-5, 8].

Resection of the oesophagus with stomach tube replacement is the first choice treatment strategy [1, 3-5, 8, 11]. In spite of the surgical risk involved, which is not negligible, approximately 70% of the tumors can be curatively resected [5, 6] and a five-year survival rate can be achieved in the range 20–40 % [1, 3, 5, 12]. The most important prognostic factors are the grade of malignancy and tumour growth rate [1, 5, 12]. The existence of metastases is not a contraindication for surgery, because even in these cases a significantly improved survival can be achieved. Even though this is a palliative tumour resection or selective extirpation of metastases [11, 13].

The most severe complication after an oesophageal replacement procedure interposition-necrosis and is reported to be some 2% of all cases. The most reliable verification of a successful surgical procedure can be achieved by an early endoscopic examination of the interposition [20]. If post-operatively a patient develops a stomach tube necrosis, it is essential that a strict complication management is followed. This includes early revision with stomach tube resection, blind plugging of the stomach stump, generous thorax and mediastinum drainage, installation of a terminal salivary fistula and of a small intestine nutritional catheter. In addition there must be adequate convalescence in order to be able to accomplish later the recreation of the passage continuity among infection-free tissue [20].

After an extensive search of the literature we have come to the conclusion that internationally there is only very limited experience of the surgical procedure of colon interposition. For example, in 2002 in Germany only 22 centres reported any experience with this disease [15].

If a stomach tube as an oesophageal replacement is not possible, for example after gastrectomy, or after a two-thirds resection of the stomach or a stomach tube necrosis, it is still possible to either use the small intestine (the jejunum) [17, 18], the right hemicolon with the terminal ileum, the colon transversum or the left hemicolon as the interposition [16, 18, 19]. Experience has also been reported with dystopia of the right hemicolon [18].

If a long replacement tube is necessary to recreate oesophageal passage continuity, Furst et al [19] suggest the use of the left hemicolon including the oral part of the colon ascendens, with preservation of the arteria colica sinistra, the riolan-anastomosis and the arteria colica media. The blood supply of the left hemicolon via a few major supply branches and not via multiple small arcades, which often is the case in the area of the right hemicolon, is an advantage of the left hemicolon for interposition when compared to the right hemicolon. This permits a greater variability in length of the oesophageal replacement [21].

If a diverticulosis exists, which appears more often in the area of the colon descendens than inside of the colon ascendens, the left hemicolon cannot be used to recreate passage continuity. The creation of an isoperistaltic or anisoperistaltic colon interposition does not have clinical relevance for the transportation of the chyme through the oesophageal replacement, since this process is essentially influenced by gravity rather than by peristaltic movements [21]. The small intestine can be seen as an alternative organ, if the colon cannot be used because of previous surgery or colonic disease [17]. However, which method is applied, can only be decided intraoperatively.

We recommend the following considerations as important when involving the use of the right hemicolon, as was the case with our 69 year-old male patient. (1) After preoperative angiographic display of the mesenterial vessels, an adequate long arteria colica media for blood supply of the interposition should be verified and confirmed as haemodynamically sufficient in the intraoperative site via branching off of the blood vessels. (2) It is the nature of both oesophagus and terminal ileum that

they have the same kind of lumina. This is beneficial for the suture of the anastomosis. (3) If the right hemicolon is used as an interposition, an ileotransversostomy is necessary in order to recreate the passage continuity of the intestine. A small intestine-large intestine anastomosis allows more favourable healing than a colon anastomosis, which is necessary when favouring the left hemicolon as an oesophageal replacement. (4) The terminal ileum and the colon ascendens are less populated with germs and have a consecutively reduced foetor ex ore. (5) For the sake of completeness it must be mentioned that with this type of reconstruction the obligatory appendectomy with a consequent additional risk of insufficiency has been proved to be unfavorable.

Following our evaluation from the literature of an inevitably small number of cases we consider that an acceptable morbidity rate (general complications 37.1%, anastomosis insufficiency 14.8%, ischemic colitis 3.0%) and an acceptable operative mortality rate (5.9%) can be currently obtained using the strategies we have described [18].

Post-operative irradiation and chemotherapy are controversial because leiomyosarcoma is classified as relatively radiation resistant [3, 14], although tumour reduction after radiotherapy of a non-resectable leiomyosarcoma has been described [14]. There is also a relatively low response rate to chemotherapy of 10–30% when compared to other soft tissue sarcomas [14].

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