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Case Report

Giant Esophageal Liposarcoma – Multimodal Treatment Results in Long Term Survival: Case Report and Review of the Literature - @

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ABSTRACT

Background: Esophageal liposarcomas are notably rare mesenchymal malignant tumours. Due to their slow progress, well-differentiated sarcomas of the esophagus may remain asymptomatic for a long time resulting in an advanced diagnosed stage and, therefore, represent a significant challenge for treatment.

Case presentation: We report the case of a 66-year old male patient who presented with the second largest esophageal liposarcoma reported to date with involvement of the upper aerodigestive tract and the posterior mediastinum. Clinical, radiological and pathological findings, a detailed description of the multimodal treatment and long-term follow up data are presented. In detail, palliative tumour debunking with final histological confirmation and conformal radiation therapy resulted in tumour response with control of symptoms and a 55 months survival.

Conclusion: Multimodal treatment in patients with not curatively resectable esophageal liposarcoma may result in long-term survival, even in patients with very advanced tumours.

Keywords: Liposarcoma; Esophagus; Radiation; Resection

BACKGROUND

Although liposarcoma is the most common malignant soft tissue tumour in adults, it rarely develops in the hypopharynx, the gastrointestinal tract, and the mediastinum. The case of a liposarcoma of the esophagus [1]. Thus far, a total number of only 46 single case reports have been published in literature. Here, we report the case of a very advanced tumour. Clinical, radiological, endoscopic and pathological findings, a detailed description of the multimodal treatment and long-term follow up data are presented.

CASE REPORT

A 66-year-old male patient was admitted to our department because of dysphagia, odynophagia and loss of body weight of 7 kg within one year.

On flexible esophagogastroduodenoscopy, a large partially pedunculated submucosal soft tissue tumour, whitish-yellow in color, commencing at the proximal esophageal sphincter, and continuing down to the distal esophagus (Figure 1) was found. Flexible bronchoscopy revealed the proximal border of the tumour infiltrating both aryepiglottic folds (Figure 2) and a tracheal compression resulting in a tracheal stenosis of 30%. The right upper lobe bronchus appeared compressed with mucosal inflammation. However, the mucosa was not affected. Cytological examination of the bronchoalveolar lavage and repeated biopsies by flexible endoscopy failed to determine the diagnosis. Therefore, three consecutive rigid hypopharyngo-, microlaryngo- and esophagoscopies with multiple deep biopsies in different locations (hypopharynx, aryepiglottic folds and proximal esophagus) containing a total volume of more than 5 cc were performed. Pathological examination of these biopsies revealed a myxoid lesion, possibly a myxoid liposarcoma.

Diagnostic imaging was performed including a Computed Tomography (CT), a cine esophagography and a Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET). The multi-slice CT of the chest and abdomen was performed in 2 x 64 x 0,6 mm Collimation (Siemens Somatom Definition AS +), with oral and i. V contrast medium application. CT scan revealed a polylobulated mass (tumour size of 330x85x65 mm) of the esophagus with fatty and soft tissue density, extending from the thoracic inlet to the distal esophagus and causing a tracheal compression as well as a compression of the right main stem bronchus (Figure 3). There were no metastatic lesions detected in the CT. In the PET only the tumour masses in the middle part of the mediastinum showed a FDG uptake with a maximal Standard Uptake Value (SUV) of 7,4 (Figure 4).

A cine-esophagogram showed a dilated esophagus with a large, irregularly circumscribed contrast media filling defect mainly throughout the upper two-thirds of esophagus (Figure 5).

After repeated discussion of this patient in the interdisciplinary tumour board of the University Cancer Center (UCC), we performed an explorative right-sided dorsolateral thoracotomy in order to prove the malignant histology of this tumour and to relieve the patient of his symptoms. While technically feasible, a laryngo-pharyngo-



Figure 1: Esophagoscopic view: Submucosal soft tissue tumour of whitish-yellow color of the esophagus.



Figure 2: Bronchoscopic view: Proximal border of tumour infiltrating in both aryepiglottic folds.

esophagectomy as treatment with curative intent was not favoured by the patient. Intraoperatively, we discovered gross dilatation of the thoracic esophagus up to 8 cm in diameter caused by the intraluminal tumour mass (Figure 6). Via longitudinal esophagotomy, two large pedunculated tumours originating from the cervical esophagus and hypopharynx were protruded and (Figure 7) debulking of these intraluminal tumour masses was achieved with an Endo-GIA-Stapler device (Figure 8). The postoperative course was uneventful, and the patient was discharged from the hospital on day 13.

Histologically, the two resected lesions were composed of a paucicellular collagenous tissue with uniform spindle cells. In the two specimen mild nuclear atypia and scattered bizarre stromal cells associated with rare multivacuolated lipoblasts and adipocytes could be identified (Figure 9). The adipocytic component showed a significant variation in cell size with focal nuclear atypia and hyperchromasia. No mitotic activity was found. The tumour was covered by the esophageal epithelium (Figure 10). Although the fibrous component represented the majority of the lesion, the diagnosis of a well-differentiated liposarcoma was determined based



Figure 3: Computed tomography scan of the chest: large tumour mass with multiple circumscribed lobulations with fat and soft tissue density extending from the thoracic inlet to the lower mediastinum.

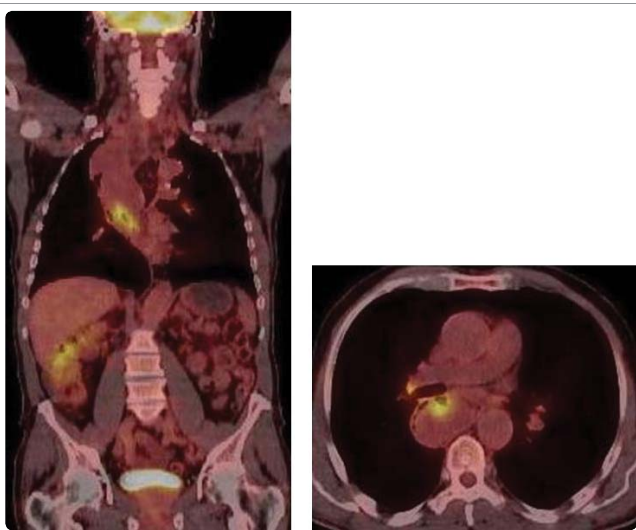


Figure 4: PET/CT: FDG positive mass in the middle part of mediastinum with a maximum standardized uptake value (SUVmax) of 7, 4.

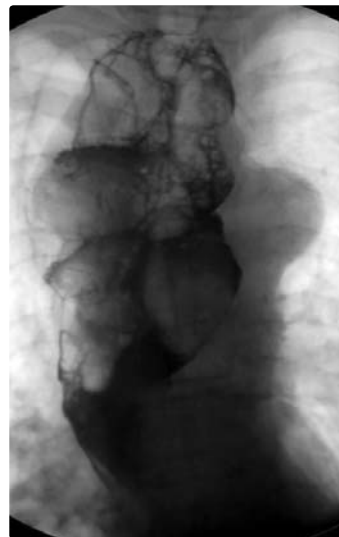


Figure 5: Cine esophagography: dilated esophagus with large contrast media filling defect throughout the esophagus.

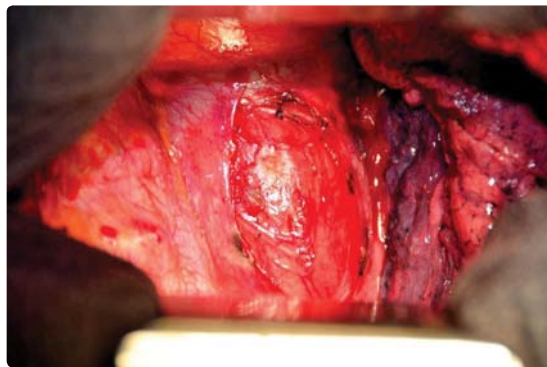


Figure 6: Right-sided thoracotomy: dilatation of the esophagus up to 8 cm in diameter due to intraluminal tumour mass.

on the presence of the scattered adipocytes and lipoblasts. This diagnosis was confirmed by a Fluorescence in Situ Hybridization (FISH), which revealed amplification in MDM2 (data not shown).

Postoperatively, the patient was once again discussed in the interdisciplinary UCC tumour board. Because of the patient's preference and the extent of disease, especially given the involvement of the upper aerodigestive tract, complete resection was not favoured. Therefore, the indication for radiotherapy was presented.

The patient was simulated in supine position with arms above the head and the previously acquired contrast-enhanced CT was fused to the planning CT. The Gross Tumour Volume (GTV) was defined as macroscopic tumour apparent in contrast-enhanced CT. Clinical Target Volume (CTV) was defined as the whole esophagus including GTV plus 5 mm margin. Planning Target Volume (PTV) was created by adding a margin of 10 mm to the respective CTV. The volume of the PTV was 957.5 cc. A 15 MV 3D-conformal photon plan with 8 irradiation fields was approved, delivering 2 Gy per fraction up to 50 Gy over 5 weeks. The minimum dose and maximum dose to the PTV were 76% and 108.2% of the prescribed dose. 3, 6 cc were > 107%. The maximum dose was within the PTV. The minimum of 76% was due to air in the PTV and the proximity of the spinal cord to the PTV.



Figure 7: Right-sided thoracotomy and esophagotomy: large pedunculated tumors originating with broad base in the cervical esophagus and hypopharynx protruding out of the esophageal lumen.

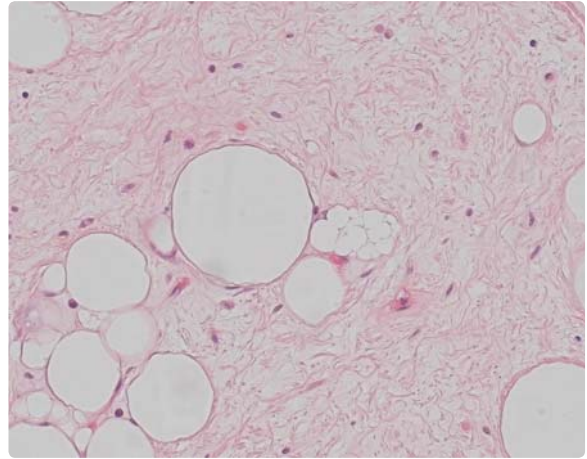


Figure 9: Tumour section (HE 20x): paucicellular collagenous tissue with uniform spindle cells with mild nuclear atypia and scattered bizarre stromal cells and associated with rare multivacuolated lipoblasts and adipocytes.



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Metric 1 2 3 4 5 6 7 8 9 10 11 12
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Figure 8: Specimen (tumour debulking): two palliative resected pedunculated tumors.

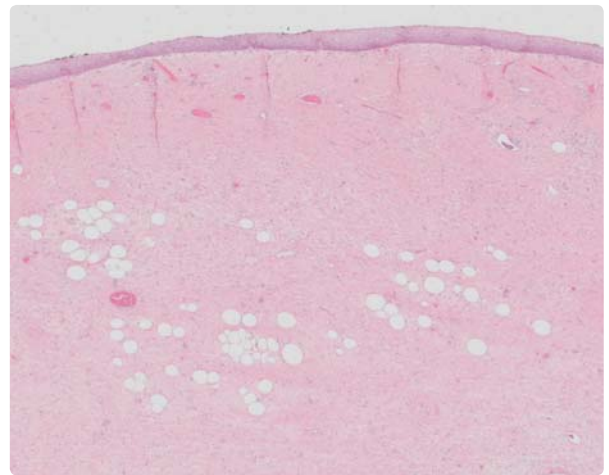


Figure 10: Tumour section (HE 20x): tumour covered by the keratinizing epithelium of the oesophagus.

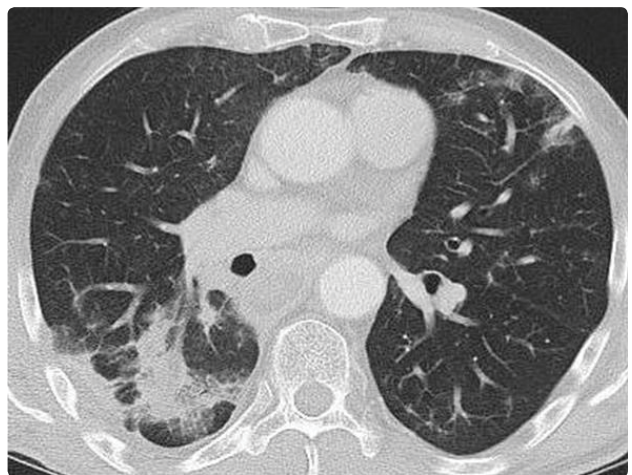


Figure 11: Follow up CT scan one year after tumour debulking and 10 months after radiation therapy: significant decrease in tumour size and pulmonary infiltrates in the right lower lobe and in the lingula, compatible with post-radiation changes due to fibrosis.

The boost volume was prescribed to the CTV only, due to the maximum tolerated dose of the spinal cord. A 15 MV 3D-conformal photon boost plan with 6 irradiation fields was approved, delivering 2 Gy per fraction up to 10 Gy over 1 week, resulting in a total dose of 60 Gy. The maximum dose to the spinal cord was 44.9 Gy and the mean lung dose was 17.9 Gy (whole lung V20Gy = 35%). Daily image guidance was performed with orthogonal kV-imaging.

After 38 Gy (4 weeks) a contrast-enhanced CT was performed to reevaluate the tumour response. No tumour regression was seen and the treatment was continued up to the approved total dose of 60 Gy.

Because the patient presented with a symptomatic esophagitis

after 38 Gy, a supportive therapy with tilidin was initiated. Hereby, sufficient oral nutrition with smooth foods until the end of the radiotherapy was possible. Four days after the end of treatment, the patient presented with a deterioration of the general condition, a grade 3 dysphagia and a suspicion of bipulmonary pneumonia. An in-patient treatment with levofloxacin and dipyron was initiated, and it was then possible for the patient to be discharged from the hospital after 10 days. A contrast-enhanced CT-scan was performed 6 weeks after the end of radiotherapy, showing radiologic signs comparable with radiation pneumonitis. The patient was in good clinical condition without clinical symptoms, therefore no specific therapy, despite respiratory exercises during rehabilitation, was initiated.

Nine months after the end of treatment the patient was presenting in good performance status (ECOG 0). A partial response was seen in a contrast-enhanced CT-scan and fibrotic changes due to the radiotherapy fields were observed in the lung parenchyma adjacent to the esophagus. An asymptomatic pericardial effusion was diagnosed and controlled by echocardiography.

A follow up one year after tumour debulking and 10 months after the radiation therapy showed a significant decrease of the tumour mass continuing to spread from the cricopharyngeal area down to the carina, but the transversal extent was reduced (from about 70 x 50 x 110 mm to 59 x 56 x 90 mm (width x depth x length)). In addition, new bipulmonary infiltrates compatible with postradiogenic changes due to fibrosis appeared, mostly localized in the right lower lobe (Figure 11). No metastatic lesions were detected. The last follow-up after 4 years displayed a stable disease in CT-scans (data not shown).

Despite a good clinical condition for more than 2 years, the patient had been admitted in hospital in bad physical condition, dysphagia and tumour cachexia after 4 years and succumbed to pneumonia 55 months after the end of multimodal treatment.

DISCUSSION

Here, we present the second largest esophageal liposarcoma reported to date with involvement of the upper aerodigestive tract and posterior mediastinum. After extensive diagnostics with multiple biopsies from different locations, we indicated an explorative thoracotomy with palliative tumour debulking. Only then was histological confirmation of a well-differentiated liposarcoma possible. From a surgical perspective, the option of a curative intended laryngo-pharyngo-esophagectomy as the procedure of choice was considered, however, it was favored neither by the surgical team nor by the patient due to the expectation of very poor postoperative functional results. The patient underwent radiotherapy with partial response, and a long term control of symptoms and a survival of more than 4 years could be reached.

Since Mansour et al. published the first case of a malignant pedunculated liposarcoma of the esophagus [1], a total number of only 46 cases have been reported [1-46]. The median diameter of the tumour was 12 cm (range 4 to 40 cm). The largest esophageal carcinoma (40x30x15 cm in size) [46].

The treatments performed were dependant on the tumour location, size and type of lesion as well as on the experience of endoscopists and surgeons. In selected patients, flexible or rigid endoscopic polypectomy or transoral surgical polypectomy was performed. In many cases, esophagotomy with polypectomy or wedge resection was accomplished via a cervical approach and

only occasionally via a thoracotomy or laparotomy. More extensive procedures included subtotal and total esophagectomy via a one-, two- or three-hole approach. Mandell et al. reported a case of giant liposarcoma involving the upper aerodigestive tract which was rejected by a laryngo-pharyngo-esophagectomy in 1999 [18]. One patient underwent palliative tumour debulking. Adjuvant radiation [47], neoadjuvant radiotherapy [45] or adjuvant chemotherapy [44] was applied very rarely. Histologically, most of the liposarcomas were surrounded by benign fibrolipomatous or fibrovascular tissue suggesting that sarcomatous transformation may occur within the primary benign submucosal tumour and may finally result in excessive tumour growth and infiltration. Pathological tumour grading was assessed as being low in most patients. Survival of more than 3 years was reported only in patients with "small" and completely resected tumours [42, 48]. A recurrence may develop even after decades [49]. However, few reports provided long-term follow-up information and therefore, comparative data concerning control of symptoms and survival are rare.

CONCLUSION

Although recurrent deep biopsies are not always sufficient for histological confirmation, malignancy has to be considered in accordance with the endoscopic and radiological findings. Therefore, complete resection of these sarcomas with clear resection margins should be aimed for histological examination. For very advanced tumours, tumour debulking combined with radiation is an ideal option, which results in symptom control and long-term survival.

COMPLIANCE WITH ETHICAL GUIDELINES AND CONFLICT OF INTEREST

S. Pistorius, D. Küpper, N. Kiria, J. Pablik, and C. Jentsch declare that they have no competing interests.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, in its most recently amended version. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

The authors state the accompanying manuscript is in compliance with ethical guidelines.

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