Case Report

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A rare case of giant oesophageal liposarcoma treated with oesophagectomy

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ABSTRACT

Background: Oesophageal sarcomas are extremely rare, constituting less than 5% of oesophageal tumours, with only 0.5% (10%) of these being liposarcomas.

Aim: Presentation of a rare case of an oesophageal liposarcoma and review of the literature.

Case Presentation: A 69-year-old man with a three-year history of voice changes and progressive dysphagia was referred to our department for consultation and treatment of a giant dedifferentiated oesophageal liposarcoma. The patient underwent hybrid McKeown oesophagectomy.

Conclusions: Multimodal management of such patients in specialised centers may spare these patients the discomfort while offering the best chances for cure.

Key Words: *Liposarcoma; spindle cell; oesophagectomy*

INTRODUCTION

Sarcomas are a heterogeneous group of malignant tumours of mesenchymal origin that more commonly affect soft and bone tissue. Their incidence is approximately 5 cases per 100.000 population, with a slight male predominance [1,2]. Gastrointestinal tract sarcomas, in particular, are a rare entity, with a published annual incidence of 0.07 cases per 100.000 population [1]. Primary oesophageal sarcomas are even more infrequent, with the majority of oesophageal tumours arising from the mucosal lining and only 5% being from mesenchymal origin. Only 0.5% of these are liposarcomas, thus representing a challenging diagnosis [3].

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We present the case of a 69-year-old man diagnosed with a giant oesophageal liposarcoma, initially misdiagnosed and managed as a lipoma.

Case Presentation

A 69-year-old man of Caucasian descent was referred to our department for surgical management of a dedifferentiated oesophageal liposarcoma.

The patient had a three-year history of progressive voice change with a characteristic "hot potato voice" and worsening nocturnal breathing difficulty, with no associated odynophagia, dysphagia, lump sensation, heartburn or weight loss. The patient was assessed at an ENT department in March 2019, and endoscopy revealed a mobile mass obstructing two-thirds of the laryngeal inlet without involvement of the mucosa. The endoscopic excisional biopsy revealed a spindle cell lipoma of the larynx.

Fourteen months later, the patient presented with symptom recurrence. A flexible micro-laryngoscopy revealed a tumour originating from the internal laryngeal

wall, extending from the left aryepiglottic fold to the corresponding apioid fossa. The supraglottic part of the tumour was excised, and CO2 laser ablation of the residual lesion was applied. The patient had an uneventful postoperative period and was discharged on the 5th postoperative day.

Sixteen months later, the patient presented with dysphagia to solid food and weight loss. A repeat endoscopy revealed significant narrowing of the entire length of the oesophageal lumen (Figure 1). A chest CT scan showed a 18 cm long, fat-density lesion along the oesophageal wall. No mediastinal lymphadenopathy was found (Figure 2). The patient underwent endoscopic ultrasound (EUS) and fine-needle biopsy (FNB). The EUS reported a partially obstructive submucosal tumour of the oesophagus, extending from 20 cm to 38 cm from the incisors without extension to the other layers of the oesophagus. In addition, the submucosa of the stomach was found thickened up to 4 cm below the gastroesophageal junction.

The histological report revealed a mesenchymal tissue neoplasm consisting of pleomorphic spindle cells with high-grade nuclear atypia, suggestive of a dedifferentiated esophageal liposarcoma. Subsequent immunohistochemical analysis further supported this diagnosis: MDM2 (+), CDK4 (+), Vim (+), CkAE1/AE3 (-), S100 (-), DOG-1 (-), CD117 (-), SOX10 (-), CD45 (-), Desmin (-), Ki-67 25%.

Further imaging was applied for investigation of the mediastinal extent of the lesion. A chest MRI ascertained the lesion's intramural spread with no evidence of invasion to adjacent structures (Figure 3), while a PET/CT revealed a moderately hypermetabolic esophageal wall (SUV max=3,9) and esophagogastric junction (SUV max=7.3) with no findings of distant metastases.

Surgical Management

A three-field hybrid McKeown oesophagectomy was performed. The resection consisted of a right thoracoscopy, a midline laparotomy and a left cervical incision (Figure 4). A hand-sewn single-layer end-to-side oesophagogastric anastomosis of the cervical esophagus to the gastric conduit was performed in the neck after radical resection. A feeding jejunostomy was also placed. An 18Fr chest tube was placed on each pleural space. The overall duration of

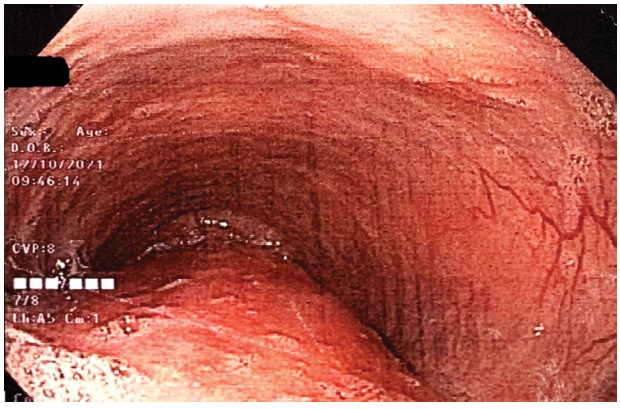

FIGURE 1. Endoscopic image showing the narrowed oesophageal lumen, with no signs of mucosal infiltration.

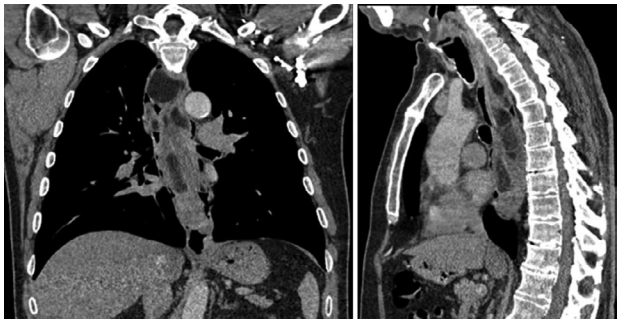

FIGURE 2. Coronal (a) and sagittal (b) chest CT images showing an 18cm long, fat-density lesion along the oesophageal wall. Neither direct invasion to adjacent structures nor mediastinal lymphadenopathy was noted.

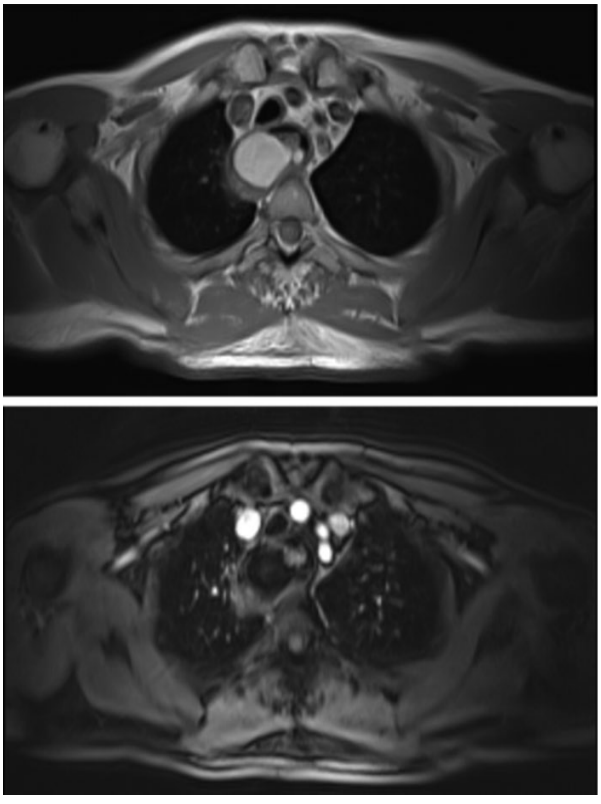

FIGURE 3. T1W (a) and T1W FS (b) chest MRI images showing the predominantly fatty composition of the intramurally spread of the oesophageal lesion. No evidence of invasion to adjacent structures is shown.

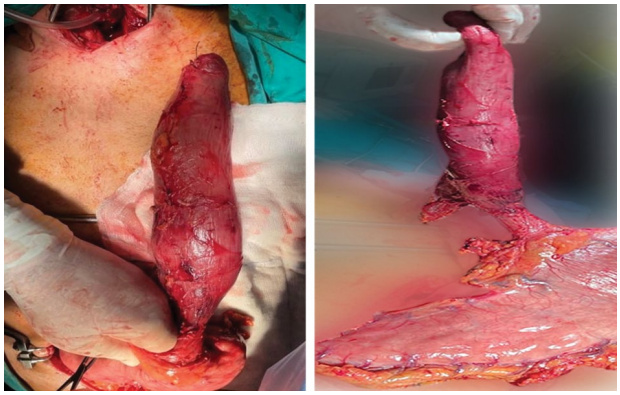

FIGURE 4. (a,b) Intraoperative images showing the dissected oesophagus, with prominent distention above the stenotic lesion.

the procedure was 5 hours and 45 minutes. The procedure was well tolerated without intraoperative complications and with minimal blood loss. The patient was successfully extubated and was admitted to the ICU for early postoperative monitoring during the 1st postoperative day (POD). On POD 2, the left chest tube was removed as there were no signs of pleural effusion or pneumothorax, and the patient was started on enteral feeding via the jejunostomy. On POD 4, oral feeding was initiated and the right chest tube was removed. Two days later, the patient presented mild swelling and redness in the cervical incision and an anastomotic leak was confirmed and drained bedside; a course of intravenous antibiotics was administered for 5 days and oral feeding was resumed during the second postoperative week. The patient remained hemodynamically stable with no systemic inflammatory signs during the hospital stay and was discharged on POD 14 on enteral feeding via the feeding jejunostomy tube.

Specimen's Histopathology Report

On macroscopic assessment, the length of the esophagus was 21cm. A 19x6x4 cm polypoid mass was developed intramurally. The microscopic examination revealed the presence of pleomorphic adipocytes with nuclear atypia and associated stromal cell atypia, and variable numbers of lipoblasts. The immunohistochemically analysis, was positive for MDM2, CDK4 and CD34, Ki67 expression was 30% (Figure 5). Retrieved lymph nodes had no signs of malignant infiltration.

Literature review

Materials and Methods

A search in PubMed was conducted aiming to identify cases of esophageal liposarcoma. Literature reviews, case

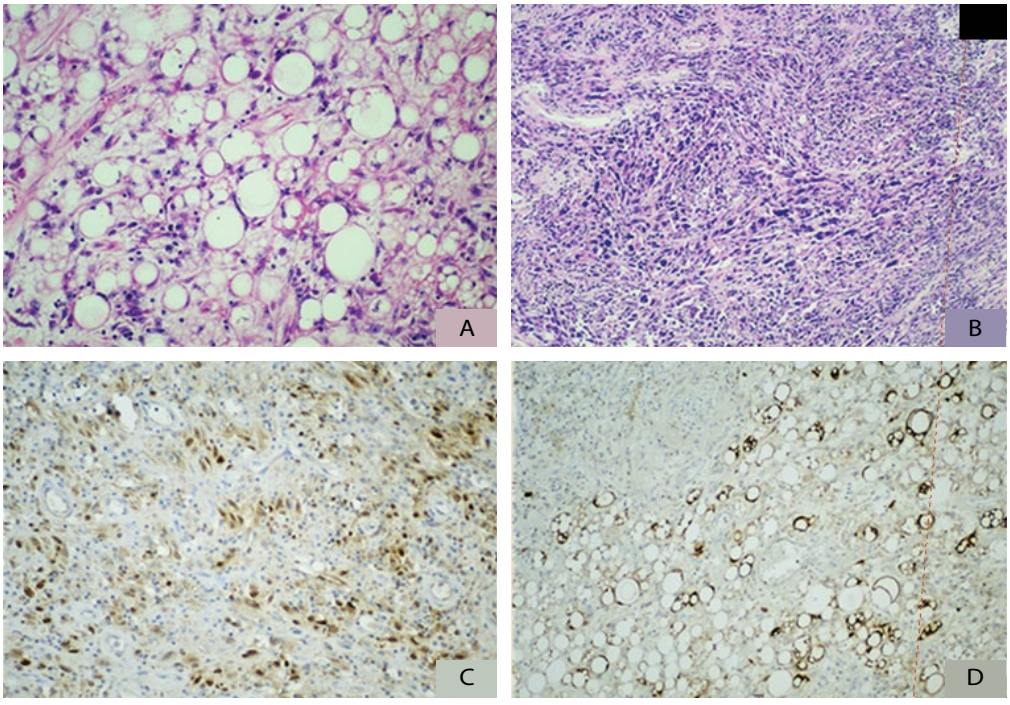

FIGURE 5. (a): Histological image of well-differentiated liposarcoma. Note the abundant lipoblasts, with hyperchromatic nuclei and lipid-rich droplets in the cytoplasm (Hematoxylin-Eosin x40). (b): Histological image of a dedifferentiated liposarcoma, composed of highly atypical cells (Hematoxylin-Eosin x20). (c): CDK4 immunohistochemical staining shows positive expression of the tumor. (d): S100 immunohistochemical staining highlights lipoblasts.

reports and one systematic review were also included in our analysis. Only English-language articles were included.

RESULTS

A total of 15 cases of esophageal liposarcoma ,including our case , were identified (Table 1) [4-17]. The mean patient age was 58.7 (42 - 83) years. 3 of the patients were female (20.0%) of the patients One patient was diagnosed with liposarcoma of the gastroesophageal junction; therefore, excision of the distal esophagus and a total gastrectomy were performed [17].

Progressive dysphagia was the most common complaint, being present in 13 out of 15 patients (86.6%). Other common symptoms were weight loss (5 patients, 33.3%) and dyspnea (4 patients, 26.6%). In addition, 2 patients (13.3%) complained of either nausea, chest discomfort, vomiting, or voice change. Less common symptoms included anorexia, palpitations, throat discomfort, foreign body sensation, night sweats, cough, and retrosternal pain.

The duration of symptoms before treatment varied significantly among the patients, ranging from 1 month to 17 years [11,17]. This variation is explained by the fact that many patients had undergone other less invasive treatments prior to esophagectomy, and the decision for radical resection was taken to achieve complete resection after local recurrence.

Regarding the tumours' location, the majority extended from the cervical part of the esophagus towards the middle or even the distal part of the organ. Interestingly, most patients had either a dedifferentiated liposarcoma or a well-differentiated liposarcoma with a dedifferentiated component (6 patients, 40.0%) [6,9,12,13,17].

Following the operation, 2 patients (13.3%), including ours, developed an anastomotic leakage, and one of them required a reoperation [4]. Moreover, two patients developed a benign anastomotic stricture 7 and 12 months after esophagectomy, with both being treated with endoscopic dilatations [10,11]. No deaths occurred in the early postoperative period.

DISCUSSION

Soft-tissue sarcomas (STS) are rare tumours accounting for 1% of all adult malignancies, occurring predominantly in the trunk, the extremities, and the retroperitoneum. They comprise more than 100 histologic subtypes. The most common subtypes are the liposarcoma, the leiomyosarcoma, and the undifferentiated pleomorphic sarcoma [18]. The 2020 WHO Classification of Soft Tissue Tumours classified the malignant adipocytic tumours into five categories: well-differentiated liposarcoma, dedifferentiated liposarcoma, myxoid liposarcoma, pleomorphic liposarcoma and myxoid pleomorphic liposarcoma [19].

Liposarcoma of the esophagus is extremely rare. Since the first report by Mansour in 1983 [20], less than 70 reports have been published in the literature, with the largest series of 13 patients coming from Graham et al [21]. In 2020, Ferrari et al. [22] published a systematic review about esophageal lipomatous tumours, including 65 case reports and two reviews. The total number of patients was 239, including 176 diagnosed with lipoma and 63 with liposarcoma. The median age was 66 years for the latter patient group, and the majority were men (73%). Furthermore, most of the tumours (73.0%) were found in the cervical part of the esophagus and protruded intraluminally (85.7%). Only 6 out of the 63 patients had a dedifferentiated liposarcoma on histology.

Ferrari also proposed an algorithm for the diagnosis, treatment, histopathological assessment, and surveillance of esophageal lipomatous tumours. According to this, an intraluminal lipoma that is larger than 15cm should be excised, either through a left cervicotomy or abdominal esophagectomy. In case that routine histology and MDM2 amplification on FISH confirm the diagnosis of liposarcoma, evaluation of the resection margins will guide the necessity for further excision or surveillance with CT imaging and endoscopy. We applied this algorithm to our patient, though already been subjected to two incomplete resections in the previous two years.

The mainstay of treatment is clear margin resection. This being said, several endoscopic or surgical techniques have been developed. Endoscopic techniques entail the endoscopic placement of a retraction suture followed by division of the tumour's stalk using either knife, ultrasonic shears, or electrosurgery snare, with or without hemoclip placement [23]. In cases where endoscopic resection is not feasible, surgery would be the standard resection mode. Surgical resection and reconstruction may include esophagostomy, esophagectomy and laparotomy for resection and retrieval of the tumour 23. In a systematic review by Dowli et al, including 40 cases of esophageal liposarcomas, the main reason for esophagectomy was the presence of a large, sessile submucosal tumor in need of clear resection margins [3].

Our patient was referred to our department after a histological diagnosis of esophageal liposarcoma was attained.

Here, the initial diagnosis two years before esophagectomy was spindle-cell lipoma, a benign lipomatous tumour, whereas the definitive histological diagnosis of the surgical specimen was WDLPS with a dedifferentiated component. Dedifferentiated liposarcoma (DDLPS) can

TABLE 1. Demographics, clinical presentation, histology, treatment immunohistochemistry and complication in 15 cases treated with oesophagectomy.

Author	Age	Gender	Presenting Symptom	Duration of symptoms until esophagectomy	Histology	Treatment	Type of lesion	Dimension (cm)	Location	Immunohistochemistry	Complications
Vouros (Greece)	69	M	voice change, dyspnoea, Dysphagia (recurrence)	34 months	Well-differentiated with dedifferentiated component	Mc Keown oesophagectomy (recurrence)	Polypoid mass	19x6x4	Upper, middle	CDK4(+) CD34(+) S100p(+) MDM2(-) SMA(-) Ki67=30%	Anastomotic Leakage/ Conservative management
Bak[4] (S. Korea)	49	F	Dysphagia, weight loss, anorexia, nausea, palpitation, chest discomfort	3 years	Well- differentiated	Total oesophagectomy	Polypoid mass	20x7	Upper, middle, lower	NA	Anastomotic Leakage/ Reoperation 8th POD
Chung [5](S. Korea)	56	M	Dysphagia, voice change, throat discomfort, foreign body sensation	13 months	Liposarcoma	Total laryngo-pharyngo-oesophagectomy	Polypoid mass	21x6x2	Upper, middle	NA	NA
Czekajska-Chehab [6] (Poland)	56	F	Dyspnoea	9 months	Well-differentiated with dedifferentiated component	Thoracotomy/ oesophagectomy	Polypoid mass	21x18x15 (Recurrence)	Upper, middle	NA	NA
Garcia [7] (USA)	42	M	Dysphagia, weight loss, vomiting, nausea, bleeding	3 months	pleomorphic	Transhiatal total oesophagectomy	Ulcerated, friable transmural mass	10,5x7x5,5	lower	S100 (+) in the better-defined lipoblasts. C-Kit(-), HMB-45(-), Melan A(-) and desmin (-) The more pleomorphic areas: CD68(+) and showed rare cytokeratin-positive cells.	Pulmonary oedema, bilateral pleural effusions, and pneumonia secondary to Klebsiella pneumoniae and Candida albicans.
Nakazawa [8] (Japan)	83	M	Chest Discomfort, vomiting	NA	Liposarcoma	partial oesophagectomy	Submucosal	12	middle	spindle cells: CD34(+) Adipocytes and lipoblasts: S100(+)	NA
Watkin [9] (France)	50	M	Dysphagia, weight loss, dyspnoea, night sweats, cough	NA	Dedifferentiated	subtotal oesogastrectomy	Submucosal lesion with exophytic component	10x8x6	lower	AE1/AE3 (-), CD34(-), desmin(-), S100(-), CD117(-), ALK1(-), CD21(-), CD23(-), CD35(-), CD30(-), EMA(-), MDM2(+), CDK4(+) (PCR), MDM2 amplification (FISH)	NA

TABLE 1. Demographics, clinical presentation, histology, treatment immunohistochemistry and complication in 15 cases treated with oesophagectomy *(continued)*.

Author	Age	Gender	Presenting Symptom	Duration of symptoms until esophagectomy	Histology	Treatment	Type of lesion	Dimension (cm)	Location	Immunohistochemistry	Complications
Yates [10] (U.K.)	49	M	Dysphagia, retro-sternal pain, weight loss	6 1/2 years	Myxoid	oesophagectomy (recurrence)	polypoid, intraluminal mass	NA	upper, middle, lower	NA	mild anastomotic stricture-dilations 7 months postop
Cooper [11] (U.K.)	68	M	Dysphagia	1 month	Myxoid	subtotal oesophagectomy	intraluminal, polypoid mass	7	lower	NA	benign anastomotic stricture 1 year postop
Lin [12] (China)	51	M	Dysphagia	6 months	Well-differentiated with dedifferentiated component	Mc Keown oesophagectomy	Submucosal	14x7x6,5	upper, middle	Vimentin (+), S100(+), CD34(+), CD117(-), CDK4(+), MDM2(+) (weak expression)	Uncomplicated
McCarthy [13](Canada)	61	M	Dysphagia	3 months	Well-differentiated liposarcoma (ALT/ WDL), with a focus of low-grade dedifferentiation.	Mc Keown oesophagectomy	Polypoid	21	upper, middle, lower	MDM2 (+) (FISH), CD34(-), S100(-), SMA (-)	Uncomplicated
Mehdorn [14] (Germany)	75	M	Dysphagia, weight loss	NA	Well- differentiated	Thoracotomy, oesophagectomy	Polypoid	25x10	upper, middle	MDM2 (+) (FISH), CD34(+), S100(+), SMA(+)	Uncomplicated
Sui [15] (China)	49	F	Dysphagia	3 years	Well- differentiated	Subtotal ooesophagectomy	Transmural ellipsoid mass	12x6x4	middle, lower	NA	Uncomplicated
Rui Li [16] (China)	52	M	Dysphagia, dyspnoea	NA	Liposarcoma	Laparoscopic and thoracoscopic oesophagectomy	Polypoid mass	21x5,1 cm	upper, middle	adipose cells: CDK4(+), S100 (+) Discrete spindle cells: Desmin (+), CD34(+), S100(-), DOG1(-), SMA(-), STAT(-)	Uncomplicated
Askan [17] (Turkey)	71	M	Dysphagia	17 years (reccurence X2)	Dedifferentiated	Total gastrectomy with distal oesophagus	solid mass protruding into the lumen	3X2,5X11,1	lower (GEJ)	MDM2 (+) (FISH), CDK4 (+), CD34(-), CD117(-), DOG1(-), SMA(-), S100(-), pan cytokeratin(-), desmin (-), HMB45 (-), SOX10(-)	NA
Sum	58,7	M:12, F;3									

M: male, F: female, NA: not applicable, POD: postoperative day, SMA: smooth muscle actin

either occur de novo (90%) or during a recurrence of a preexisting well-differentiated liposarcoma (10%) [17]. If this is the case, dedifferentiation of WDLPS will occur at 20% during the first recurrence and 44% during the second recurrence [17].

In addition, it is relatively common for an oesophageal liposarcoma to be initially misdiagnosed as a "giant fibrovascular polyp" or a "lipoma." Graham et al. reexamined the clinicopathologic features and MDM2 amplification status of 13 cases initially diagnosed as: "lipoma" (n=1), "giant fibrovascular polyp" (n=5), "WDLPS" (n=3) and "DDLPS" (n=3)4. Interestingly, a woman with a 7cm tumour initially diagnosed as a lipoma exhibited MDM2 amplification and was finally identified as a well-differentiated liposarcoma. In the same study, five patients with "giant fibrovascular polyp" had differentiated liposarcoma as their final diagnosis [21].

Although surgical resection is the cornerstone in the treatment of esophageal liposarcoma, a close long-term follow-up is strongly recommended since approximately 40% of DDLPS tend to recur locally and 17% tend to metastasize distantly. Eventually, 28% of the patients die as a result of distant spread [24]. Our patient remains disease-free, with no signs of local or distant recurrence, five months following esophagectomy.

CONCLUSION

The present study presents the unusual case of an oesophageal liposarcoma initially misdiagnosed and treated as a benign lipomatous tumour. A significant difficulty in diagnosing such lesions stems from its rarity, with less than 70 cases published in the international literature. Furthermore, accurate assessment of subtle histological characteristics and specific immunohistochemical testing are mandatory, , whereas multimodal assessment in specialized centers and meticulous assessment through endoscopic and imaging studies might improve the overall prognosis of this rare entity.

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Ethical Standards: *1) This case report has been approved by the hospital's ethics committee (Hippokrateion General Hospital) and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. 2) All persons gave their informed consent prior to their inclusion in the study.*

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