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【 CASE REPORT 】

Large Inflammatory Myofibroblastic Tumor of the Esophagus: A Case Report and Literature Review

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Abstract:

Inflammatory myofibroblastic tumor (IMT) is a rare tumor composed of myofibroblasts with inflammatory blood cell infiltration. It commonly occurs in the lungs and rarely in the esophagus. We herein report a valuable case of IMT originating in the esophagus. A 60-year-old Japanese woman with dysphagia had a large subepithelial lesion (SEL) in the cervical esophagus, which was 15 cm in length. Surgical resection was performed to confirm the pathological diagnosis and improve the symptoms. The postoperative diagnosis was IMT composed of multiple nodules. There was no recurrence or metastasis within one year after surgery.

Key words: inflammatory myofibroblastic tumor, esophagus, subepithelial lesion

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Introduction

Inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal tumor. It is seen mainly in children and young adults but can occur at any age (1). In children, approximately one-third of IMTs are reported to be pulmonary, and two-thirds are extrapulmonary (2). Although IMT was once regarded as an inflammatory lesion mimicking malignancy (1), it is currently considered an intermediate-grade tumor with potential for recurrence and metastasis (3). Pathologically, IMT is defined as a distinctive lesion composed of myofibroblastic spindle cells accompanied by an inflammatory infiltrate of lymphocytes, plasma cells, and eosinophils (1).

We herein report a rare case of IMT derived from the cervical esophagus that was resected surgically and had a good outcome without recurrence during follow-up.

Case Report

A 60-year-old Japanese woman with dysphagia and weight loss for 2 months visited our hospital. Computed tomography (CT) showed a long mass occupying the cervical and middle thoracic esophagus. Esophagogastroduodenoscopy (EGD) revealed a large, rod-like lesion covered with normal mucosa that occupied most of the lumen of the esophagus 19–32 cm from the dental arch (Fig. 1A).

Probe-type endoscopic ultrasound (EUS) was performed, but it was difficult to visualize the base of the lesion because the water did not fill the cervical esophagus. Sixteen biopsy samples acquired with forceps showed only stratified squamous epithelium without atypia, which failed to yield a diagnosis. Esophagography revealed a large mass lesion, 15 cm in length and 3 cm wide, attached to the anterior wall of the cervical esophagus and occupying the cervical to the middle thoracic esophagus (Fig. 1B). Contrast-enhanced computed tomography (CT) showed a mass extending cephalocaudally into the esophagus (Fig. 1C). An intense

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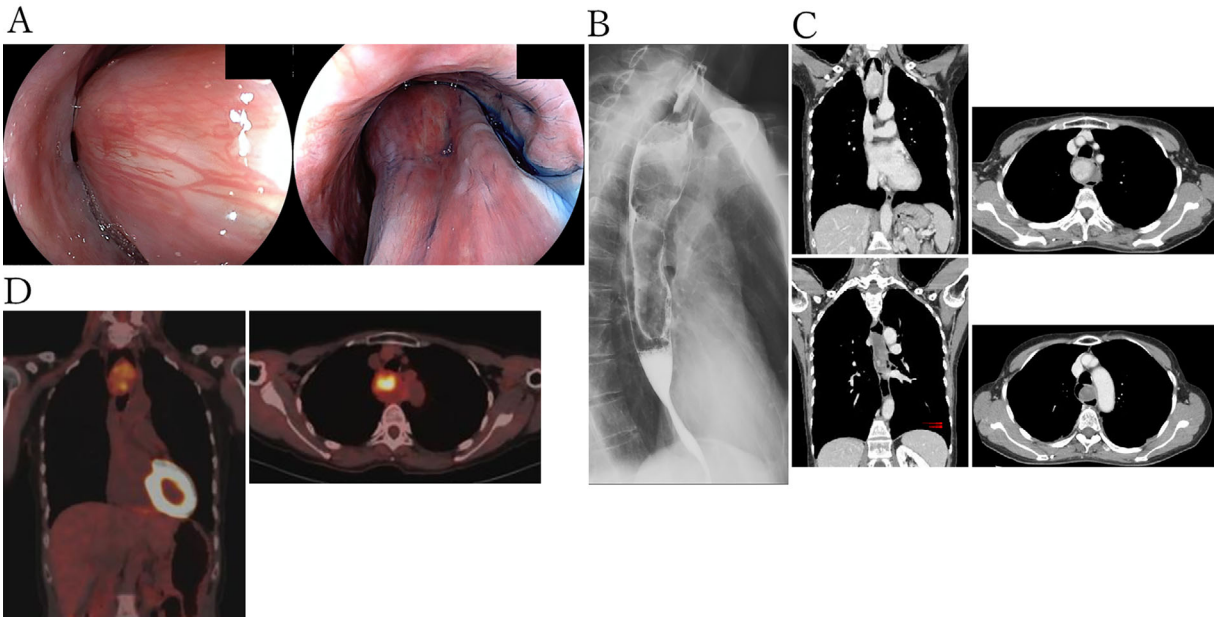

Figure 1. **A: On endoscopy, a large, rod-like lesion covered in normal mucosa occupied most of the lumen in the esophagus 19-32 cm from the dental arch. B: On esophagography, a large mass lesion 15 cm in length and 3 cm wide was attached to the anterior wall of the cervical esophagus and occupied the cervical to mid-thoracic esophagus. C: On contrast-enhanced CT, a mass extending cephalocaudally into the esophagus. An intense enhancing effect was seen on the cephalic side (upper image), whereas the caudal side was less strongly enhanced (lower image). D: Positron emission tomography (PET)/CT revealed increased tracer uptakes at the upper to middle thoracic esophagus.**

enhancing effect was seen on the cephalic side, whereas the caudal side was less-markedly enhanced. No extramural extension was evident. Based on these findings, hemangioma or leiomyoma was suspected.

Barium contrast passed through the lesion with a slight delay. Positron emission tomography (PET)/CT revealed an increased tracer uptake from the upper to middle thoracic esophagus (Fig. 1D). The maximum standardized uptake value (SUVmax) was 6.1 on the proximal side of the lesion. There was no abnormal uptake in any other organs.

Based on several examinations, we suspected a subepithelial lesion (SEL) originating from the cervical esophagus and growing into the lumen. However, it was impossible to obtain tissues with EUS-guided fine-needle aspiration because of the tumor location in the cervical esophagus. As esophageal SEL was the cause of chronic dysphagia, we recommended surgical removal to improve the symptoms and confirm the pathological diagnosis.

Enucleation of the esophageal submucosal tumor was performed via a left cervical approach. A large, rod-shaped tumor appeared in the lumen after making a 5-cm longitudinal incision in the left wall of the cervical esophagus. The tumor was removed by cutting at its base. The tumor was approximately 160 mm long and covered with normal squamous epithelium. The macroscopic secant specimen showed a white, solid nodule with scattered small nodules, consistent with the findings regarding the 18F-fluorodeoxyglucose uptake on PET/CT (Fig. 2). Microscopically, the tumor was located in the subepithelial region of the esophageal squamous epithelium. The tumor border was relatively well demarcated. The tumor consisted of spindle cells with atypical and hyperchromatic nuclei with occasional bizarre cells, suggesting an inflammatory myofibroblastic tumor (IMT).

Immunohistochemical analyses unexpectedly revealed that the tumor was reactive not to ALK (ALK1; DAKO, Glostrup, Denmark) but to MDM2 (IF2; ThermoFisher Scientific, Invitrogen, Waltham, MA, USA), CDK4 (DCS-35; Santa Cruz Biotechnology, Dallas, Texas), and p16 (E6H4; Roche Diagnostics, Basel, Switzerland) and partially to desmin (DE-R-11; Leica Biosystems, Novocastra, Newcastle upon Tyne, United Kingdom). The Ki-67 (MIB-1; DAKO) staining index was approximately 10%. Although these results suggested the possibility of dedifferentiated liposarcoma, the tumor controversially lacked adipose and lipoblastic cells. The possibility of IgG4-related disease was denied due to a lack of IgG4 (MRQ-44; Roche Diagnostics)-positive cells. In addition to the pathological image of hematoxylin and eosin staining, by referencing previous reports noting that MDM2 and CDK4 were positive in ALK-negative IMTs (4, 5), we finally diagnosed this tumor as IMT. Fortunately, there has been no recurrence for one and a half years since surgery.

Discussion

The lesson from this case report is that an IMT should be considered as an SEL in the esophagus. Most SELs, such as

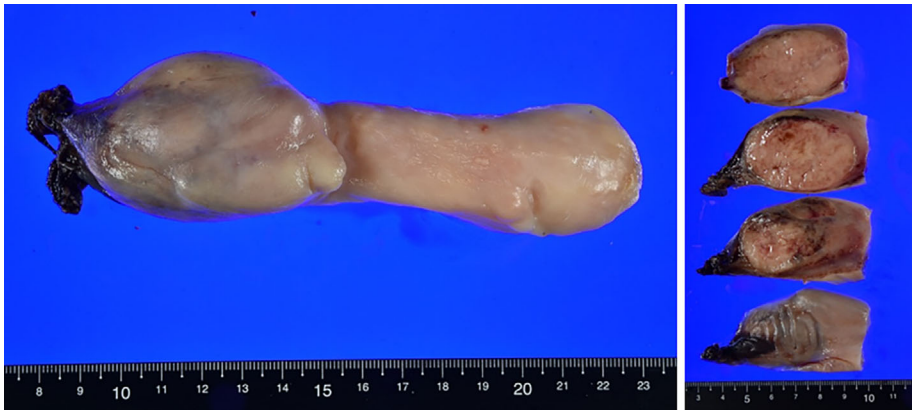

Figure 2. **A macroscopic secant specimen showed a white solid nodule with scattered small nodules, which was consistent with the 18F-fluorodeoxyglucose uptake on PET/CT.**

Table. **REPORTS OF INFLAMMATORY MYOFIBROBLASTIC TUMORS IN THE ESOPHAGUS FROM 2001 TO 2020.**

Author	Sex	Age	Symptoms	Location	Maximal diameter (mm)	Possible etiology	Treatment	Outcome	Follow-up (month)
Saklani *et al.* (2001)[14]	F	23	Dysphagia	Cervical	large (NS)	UD	Esophagectomy	Favorable	6
Marchi *et al.* (2001)[15]	F	49	Substernal pain Dysphagia	Proximal	20	Trauma	None	Favorable	2
Kurihara *et al.* (2001)[16]	M	54	Dysphagia	Upper thoracic	large (NS)	Acid reflux	Subtotal esophagectomy	Favorable	33
Goldin *et al.* (2007)[17]	F	12	Substernal pain Dysphagia	Middle thoracic	110	EB virus	Esophagectomy	NS	Yearly
Privette *et al.* (2008)[18]	M	43	Dysphagia Odynophagia	Distal	100	UD	Esophagectomy	Favorable	12
Cao *et al.* (2009)[19]	F	55	Dysphagia Weight loss	Thoracic	160	UD	Esophagectomy	NS	NS
Li *et al.* (2010)[20]	F	45	Dysphagia Weight loss	Thoracic	120	UD	Enucleation	Favorable	10
Chen *et al.* (2010)[21]	F	55	Dysphagia Weight loss Substernal pain Fever	Middle-lower thoracic	200	UD	Enucleation	Favorable	6
Stelow *et al.* (2010)[22]	F	39	Dysphagia	NS	30	UD	Esophagectomy	NS	NS
Cruz - Ruiz *et al.* (2010)[9]	F	47	Dysphagia Weight loss	Upper	40	UD	Endoscopic resection	Favorable	NS
Umesh Jayarajah *et al.* (2017)[3]	M	33	Hematemesis Melena	Upper	70	UD	Enucleation	Favorable	20
Douseket *al.* (2015)[1]	M	13	Dysphagia	Upper	30	UD	Esophagectomy	Favorable	10
Fangusaro *et al.* (2004)[23]	M	5	NS	NS	NS	UD	NS	NS	NS
Kirk *et al.* (2000)[24]	M	2	NS	NS	NS	UD	NS	NS	NS
SantaCruz *et al.* (2002)[25]	F	14	NS	Esophago-gastric junction	NS	UD	NS	NS	NS

M: male, F: female, NS: not specified, UD: undetermined

lipoma, inflammatory fibroid polyp, leiomyoma, and granular cell tumor in the esophagus, belong to the benign category, and malignant tumors, such as gastrointestinal stromal tumor, leiomyosarcoma, and liposarcoma, are thought to be rare (6, 7). In the present case, endoscopy revealed that the SEL was attached to a narrow area of the esophagus and grew like a polyp, occupying the lumen of the cervical esophagus. These findings were similar to those of a fibrovascular polyp (FVP) (8). Therefore, an FVP would be the most significant differential diagnosis based on endo-

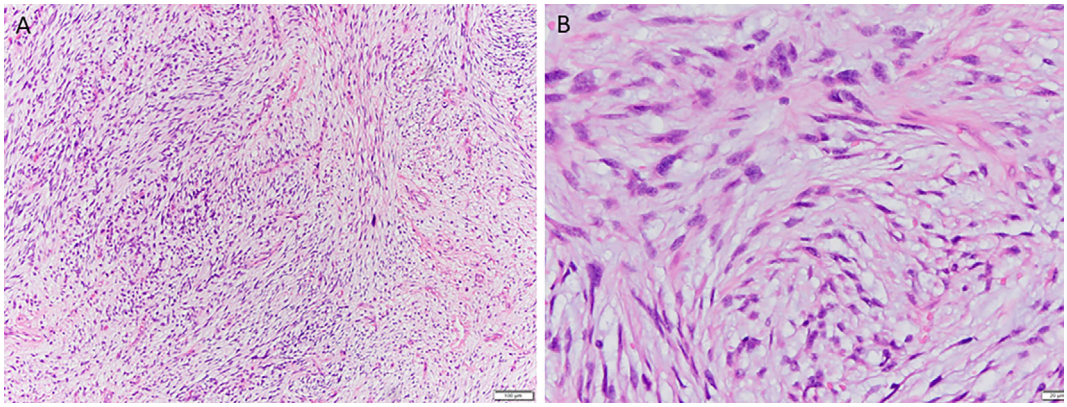

Figure 3. **Numerous spindle-shaped cells with various morphologies, including nodular bundle, spiral, full, and irregular arrangements, were seen. The presence of inflammatory cells, such as lymphocytes and plasma cells, was also noted (A: ×100, B: ×400).**

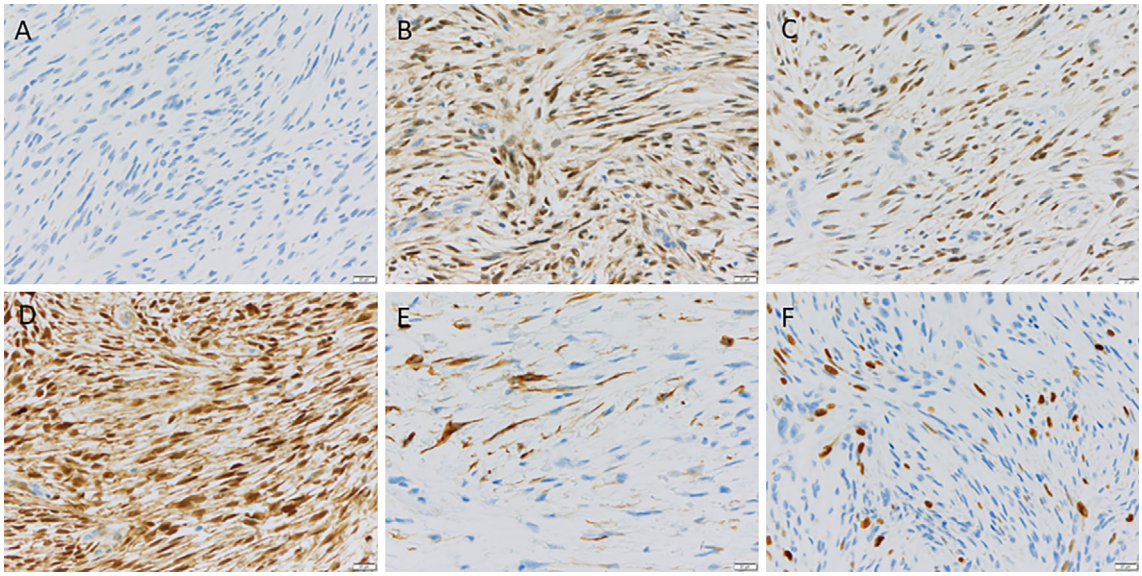

Figure 4. **An immunohistochemical analysis of the esophageal tumor. Spindle-shaped tumor cells were unexpectedly negative for ALK1 (A) but positive for MDM2 (B), CDK4 (C), and p16 (D) and partially desmin (E). The Ki-67 staining index was approximately 10% (F). Original magnification 400×.**

scopic findings.

In general, complete differentiation of SELs is difficult using imaging techniques, such as endoscopy, EUS, and CT. Therefore, a pathological diagnosis is essential for determining the treatment strategy (6). However, because the large tumor was located in the cervical esophagus and occupied the internal lumen, a definitive diagnosis could not be made preoperatively. Therefore, we ultimately diagnosed the lesion as an IMT based on the pathology of the surgically resected specimen.

IMTs are characterized by spindle cell proliferation with inflammatory infiltration of lymphocytes, plasma cells, and eosinophils (9). The cause of IMT remains unknown. However, the involvement of an abnormal response to tissue damage, such as viral infection (Epstein-Barr virus, human papillomavirus type 8), acid reflux, trauma, and overexpression of interleukin-6 (3), has been hypothesized. IMT has substantial histopathological diversity and is sometimes called plasma cell granuloma, inflammatory fibrosarcoma, and inflammatory pseudotumor (1).

Immunobiologically, Makhlouf et al. reported that smooth muscle actin and vimentin were positive in 86% and 77% of IMTs, respectively, whereas cytokeratin, desmin, CD34, and S100 were less frequently positive (1). Although ALK is considered a key molecule for the diagnosis of IMT, only 50%-70% of tumors have ALK gene rearrangement (11). Of note, two previous reports have shown immunopositive findings for MDM2 and CDK4 in ALK-negative IMTs that developed in the stomach (4) and mediastinum (5). Our case might therefore have been included in this rare category of IMT.

The most common organs affected by IMT are the lungs

of children or young adults, and uncommon organs are the brain, trachea, breast, spleen, kidneys, liver, stomach, colon, and ampulla of Vater (9). IMT in the esophagus is extremely rare, with only 15 case reports published in the past 20 years. Ten patients were adults, and five were pediatric patients (aged 15 years or younger). Esophagectomy, tumor enucleation, and endoscopic resection were performed in nine, three and one, respectively (Table). Complete surgical resection was performed for localized IMT as the standard therapy. Endoscopic resection may be considered for smaller tumors as a less-invasive treatment (9). Although IMT has been recognized as a benign tumor in the past, Kindblom et al. reported recurrence after resection in 10 of 27 cases (12). Risk factors for recurrence are polynodularity, irregular margins, and unclear borders (12, 13). Unlike apparently malignant tumors, metastasis is rarely observed. Therefore, IMT is now considered to have intermediate malignant potential (1). In the present case, since polynodularity was observed pathologically, this IMT has a risk of recurrence. Therefore, careful follow-up using CT should be performed annually.

Conclusion

We herein report a 60-year-old Japanese woman with dysphagia due to a rare IMT originating from the cervical esophagus. While IMT in the esophagus is rare, it should be considered as a cause of dysphagia.

The authors state that they have no Conflict of Interest (COI).

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