Case Report

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Successfully treated esophageal gastrointestinal stromal tumor by minimally invasive esophagectomy followed by imatinib therapy: a case report

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Introduction: Gastrointestinal stromal tumor (GIST) is a common malignancy of the gastrointestinal tract, but rarely occurs in the esophagus, composing approximately 0.7% of all GISTs. Surgery is a mainstay treatment for this disease. We herein report a case of a 68-year-old male patient treated by thoraco-laparoscopic esophagectomy followed by imatinib therapy for a large esophageal GIST, and also review a literature regarding this disease.

Case report: A 68-year-old male was admitted to our hospital due to dysphagia. After the initial investigations, the patient was diagnosed with esophageal GIST and underwent thoraco-laparoscopic esophagectomy. Final immunohistochemistry (IHC) was positive with CD117, CD34, DOG-1, Ki67 without the expression of SMA, S-100 that confirmed GIST. The patient was referred to adjuvant therapy with imatinib and there was no recurrence at 16 months after surgery.

Discussion: Due to the rarity of esophageal GISTs, diagnosis and treatment remain challenging. Without immunohistochemistry, this disease may be misdiagnosed as esophageal leiomyoma, or with other mesenchymal tumors such as sarcoma or schwannoma due to similar clinical, endoscopic and radiographic characteristics. Surgery is the cornerstone treatment, the choice of enucleation or esophagectomy depends on the comprehensive evaluation of clinical and pathologic factors of the specific case. Neoadjuvant or adjuvant treatment with imatinib is an effective therapy for selective patients.

Conclusion: GISTs are rare neoplasms of the esophagus. Currently, surgical resection is the cornerstone treatment, adjuvant or neoadjuvant therapy with imatinib may be indicated for selective patients. Clinical trials are expected with longer follow-ups to develop concrete guidelines for this disease.

Keywords: case report, esophageal GIST, esophagectomy, minimally invasive surgery

Introduction

GISTs are mesenchymal neoplasms that are commonly in the gastrointestinal tract, including the stomach (60-70%), small intestine (20-30%), colon, and rectum (5-10%). However, esophageal GISTs are extremely uncommon and only reported as individual case reports or case series[1,2]. Soleide summarized 13 550 cases of GIST in the gastrointestinal tract and reported that the incidence of esophageal tumors accounts for only 0.7%[3]. Treatment of esophageal GIST is predominantly surgery. Neoadjuvant or adjuvant therapy with imatinib is indicated for selective patients. We herein report a case of esophageal GIST that was initially treated by minimally invasive esophagectomy followed by imatinib therapy in our hospital. This work has been reported in line with the SCARE 2023 criteria[4].

HIGHLIGHTS

- Gastrointestinal stromal tumors (GISTs) are rare neoplasms of the esophagus.
- Surgery is the mainstay treatment, the choice of enucleation or esophagectomy depends on the specific case.
- Adjuvant or neoadjuvant treatment with imatinib may be indicated for selective patients.

Case report

A 68-year-old male patient was a regular smoker of 30 pack-years and had a lengthy history of alcohol use. As for the medical history, he had no known medical diagnosis. He was referred to our hospital with dysphagia for 6 months. At the time, the patient denied any symptoms of nausea, vomiting, or hoarseness. Upper gastrointestinal endoscopy showed a large rough lesion with an uneven ulcerated surface that was located about 29 to 35 cm from the upper dental arch and blocked half of the lumen (Fig. 1a).

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The patient was biopsied twice, the first result showed low-grade squamous epithelial dysplasia, and the second result revealed spindle cells. Immunohistochemistry confirmed esophageal GIST with positive immunostaining for CD117, CD34, DOG-1 and negative for SMA, S-100.

Upper gastrointestinal endoscopic ultrasound showed a mixed echoic lesion in the muscularis mucosa layer that grew to the muscularis propria layer with the intact adventitia (Fig. 1b). There was imaging of the middle-lower third esophageal wall thickening on the chest CT scan with a maximum thickness of 23 mm and length of 62 mm blocking the lumen (Fig. 1c). Abdominal CT scan and ear, nose, throat (ENT) endoscopy did not find any abnormalities, pre-op lab was within normal range, and SCC level was not elevated (0.8 ng/mL).

The patient was diagnosed with esophageal GIST and underwent minimally invasive surgery. Intraoperative exploration revealed a tumor was 4 × 6 cm in size with intact adventitia (Figs. 1d and 2). The thoraco-laparoscopic esophagectomy with gastric tube placement was performed due to the tumor size and its invasion to the mucosa. Initially, the total esophageal mobilization was carried out. The lymph node dissection was not indicated as GIST rarely metastasize via lymphatic vessels. Then, the gastric mobilization was performed, the left and right gastric artery and the left gastroepiploic artery were ligated. The next step was the esophageal resection and afterward the stomach was pulled up through the posterior mediastinum and was connected in the neck area to the remaining esophagus in anastomosis by the 25 mm circular stapler. The total duration of surgery was 4 hours with minimal amount of blood loss (about 200 mL). Final pathology (Fig. 3) and IHC (Fig. 4) one more time confirmed the diagnosis of esophageal GIST. The postoperative course was uneventful, so patient was referred to adjuvant imatinib with dosage of 400 mg QD for 3 years. Patient has been treated for 16 months, and the recent CT scan shows no recurrent lesions.

Discussion

GIST is a common malignant disease of the digestive system, that occurs predominantly in the stomach, small intestine, and rarely in the esophagus. Esophageal GIST accounts for less than 1% of all gastrointestinal tumors[3,5]. In comparison to gastric GIST, esophageal GIST occurred more frequently in males as well as in patients younger than 60 at diagnosis and primary tumor sizes were significantly larger[6]. The most common tumor location is the lower third esophagus, followed by the middle third esophagus, GIST in the upper third esophagus is uncommon. The frequent symptoms are dysphagia (36-51%), weight loss (20%), chest pain (8-15%), and bleeding (1-10%)[7].

Because of the rarity of esophageal GISTs, the diagnosis and treatment remain challenging. This disease may be misdiagnosed with esophageal leiomyomas, which are more common benign tumors, or with other mesenchymal tumors such as sarcomas or schwannomas due to the similar clinical, endoscopic and radiographic characteristics. Immunohistochemistry (IHC) is essential to differentiate GIST from other mesenchymal tumors, with positive immunostaining for CD117 and negative for SMA, S100[8]. However, preoperative diagnosis is difficult because we cannot take specimens from the subepithelial lesion using a conventional endoscopic biopsy method[9].

Endoscopic ultrasound (EUS) allows observation of the location, size, shape, and tumor deepness of invasion, and guides fine needle aspiration (FNA) or core biopsy. Nevertheless, EUS-

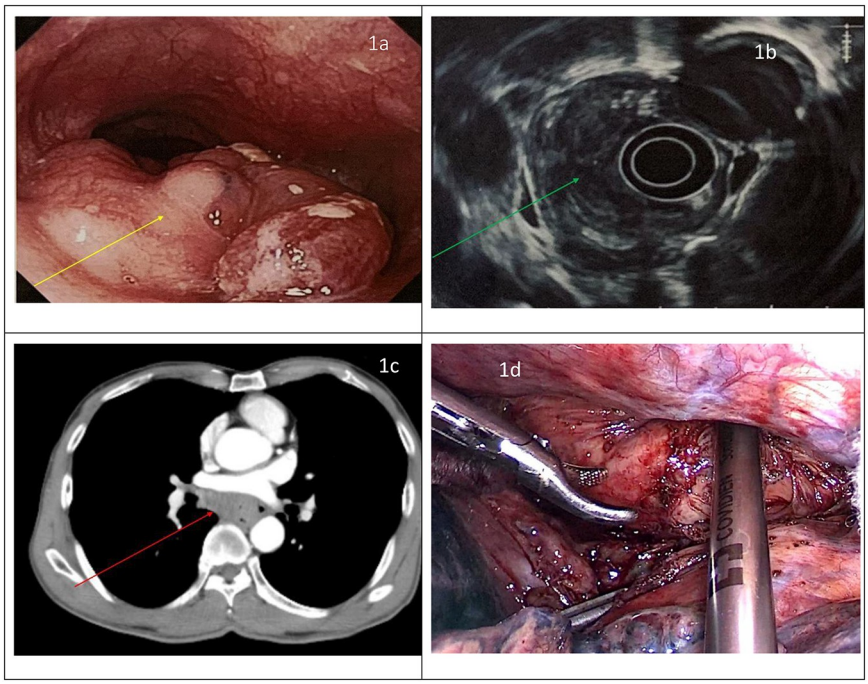

Figure 1. (a) A rough tumor in the middle thoracic esophagus by endoscopy (yellow arrow). (b) Endoscopic ultrasound: the imaging of a mixed echoic structure in the muscularis mucosa layer that grew to the muscularis propria layer with the intact adventitia (green arrow). (c) Wall thickening totally occluding the lumen of the middle thoracic esophagus on CT scan (red arrow). (d) A tumor in the middle thoracic esophagus during surgery.

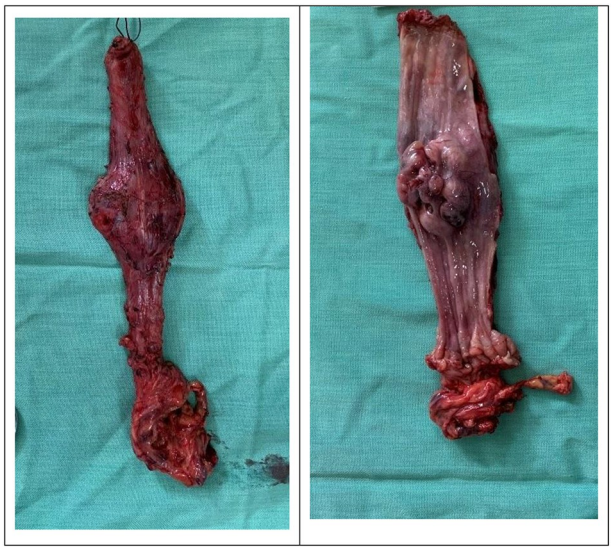

Figure 2. A specimen of the tumor with rough mucosa and intact adventitia.

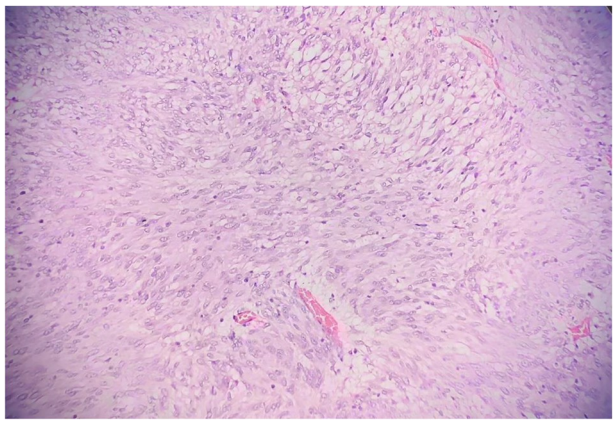

Figure 3. HE staining revealed that spindle tumor cells were crowed into bunches with elongated nuclei and had many mitotic activities (>5 mitoses/ 50 high-powered fields).

guided biopsy is a complex procedure in high-specialized centers. Typically, biopsy is not indicated for smooth submucosal tumors with regular borders, because scarring might cause mucosal adhesion and contraction, which can make enucleation more difficult, and there is a risk of tumor dissemination by capsule destruction as well.

Lee reported seven cases of esophageal GIST, among which there was no EUS-guided biopsy. Endoscopic biopsy was performed for two cases with a large mass of over 10 cm invading into the mucosa. According to the author, a preoperative biopsy may not be necessary if the submucosal tumor is less than 5 cm with regular borders, and suitable for enucleation. Tumors sized 5 to 10 cm might require biopsy followed by esophagectomy depending on the invasion status, tumor location, and the PET/CT result. For tumors over 10 cm in size preoperative biopsy is recommended, followed by esophagectomy[10]. Blum recommended that EUS with FNA should be performed for cases of over 2 cm tumors with growth during follow-up or FDG uptake on PET/CT, all considered clinically malignant features[11].

CT scan is valuable in defining the tumor's location, size, and deep of invasion, but still it is still difficult to differentiate GIST from other esophageal tumors. The maximum standardized uptake value on PET/CT is found to correlate with the degree of malignancy of GIST, however, it is important to be aware of benign tumors as esophageal leiomyoma has also a wide range of FDG uptake. PET/CT is more frequently utilized in the assessment of relapse and metastasis of esophageal GIST after the primary definitive treatment[7].

Positive c-kit (CD117) and CD34 markers by IHC are the most important diagnostic criterion of GIST. Without these markers, GIST can be misdiagnosed with leiomyoma, leiomyosarcoma, or schwannoma… Since using CD117 and CD34, the GIST diagnosis rate increased relatively while the total number of mesenchymal tumors remained the same[11]. In our clinical case, the patient presented with dysphagia, a long alcohol and cigarette consumption history, and the upper gastrointestinal endoscopy showed a large rough lesion with an uneven ulcerated surface, all are suggestive of esophageal carcinoma. However, IHC result was positive with CD117, CD34, and DOG-1, without the expression of SMA, S-100 that confirmed GIST, and subsequent endoscopic ultrasound showed the lesion suitable to pathology conclusion.

Surgery is the mainstay treatment for esophageal GIST, the choice of enucleation or esophagectomy depends on specific case and surgeon's experience. Optimal surgical therapy should aim to achieve complete resection without injury to the pseudocapsule surrounding the tumor[12]. Tumor enucleation is generally recommended for small tumors, while esophagectomy is indicated for larger GISTs, and routine lymphadenectomy is unnecessary because GISTs rarely metastasize to lymph nodes. Blum recommended that radical esophagectomy should be preferred due to the poor integrity of esophageal GISTs, especially for tumors over 2 cm in size. Tumor enucleation with warranted negative margins can be performed in tumors less than 2 cm, limited on the wall of the esophagus, especially in patients unable to tolerate esophagectomy[11]. Regarding this clinical case, a large esophageal GIST (4 × 6 cm) is shown as a rough lesion with mucosa invasion on endoscopy. The tumor enucleation was unfeasible during the surgical assessment; therefore, we decided to perform radical esophagectomy and gastric-tube reconstruction.

Imatinib is a promising therapy for esophageal GISTs, but the efficacy of routine imatinib treatment is unclear. Kang suggested that neoadjuvant imatinib therapy can be indicated in patients with high mitotic rates and/or larger tumor sizes to achieve clear margins and to reduce the risk of intraoperative complications including tumor rupture[13]. Lee suggested that adjuvant imatinib is not necessary if the tumor is localized and completely resected, preoperative imatinib therapy is also not indicated for patients with resectable tumors[10]. In our case, the patient was referred to adjuvant therapy with imatinib for 36 months considering the high mitotic rate and the large size of the tumor. No recurrence was found at 16 months after surgery.

The data about the prognosis of esophageal GIST are limited; some reports with small sample sizes showed that esophageal GIST has a bad prognosis and the relapse rate is much higher than other GISTs[5,6]. According to Lott's analysis, 5-year overall survival is 48.3%,[6] while Feng demonstrated about 65.1% of 5-year survival. The most common metastatic site is liver, followed by lung, mediastinum, pleura, and peritoneum[14].

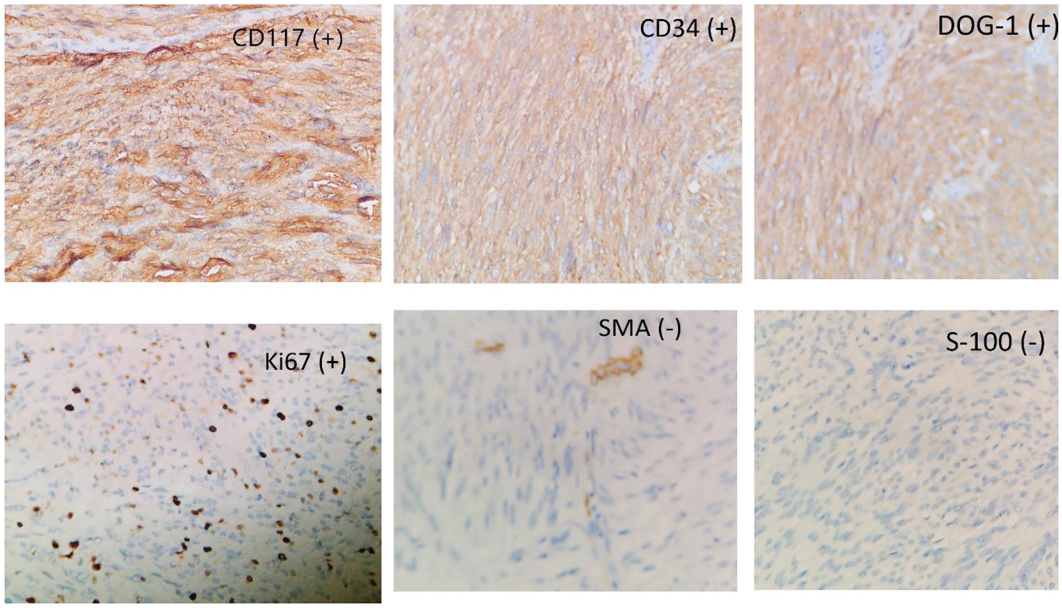

Figure 4. Immunohistochemistry result of tumor with CD117 (+), CD34 (+), DOG-1 (+), Ki67 (+), and SMA (–), S-100 (–).

Tumor size and mitotic rate are the important prognostic factors of GIST. Kang analyzed 25 cases with esophageal GIST and showed that a large tumor size (>10 cm), high mitotic rate (>5 mitoses/5 mm^2), presence of a deletion mutation in KIT exon 11 or microscopic positive margin are the poor prognostic factors of recurrence and metastasis[13]. Lee found that tumor size, mitotic activity, and surgical method are the important factors affecting the recurrence postoperatively. Clear margin is also a paramount factor, especially for tumor enucleation cases. Finally, accurate dissection to preserve the tumor capsule is necessary to reduce the risk of local recurrence[10].

Conclusion

Esophageal GIST is a rare disease and the diagnosis remains challenging. The cornerstone treatment is surgical resection, the choice of enucleation or esophagectomy depends on the specific case and the surgeon's experience. Adjuvant or neoadjuvant treatment with imatinib may be considered for selective patients. Nevertheless, studies in large numbers of patients with longer follow-ups are expected to develop concrete guidelines for this disease.

Ethical approval

The manuscript was approved by ethical committee of Vietnam National Cancer Hospital.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author's contributions

T.T.D.: the main doctor conceived the original idea and operated the patient, revised manuscript; D.T.P.: operated the patient, followed up, wrote manuscript; C.V.N.: operated the patient, followed up, revised manuscript; T.T.T.: followed up, revised manuscript; H.V.N.: followed up, revised manuscript.

Conflicts of interest disclosure

The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this paper. All authors read and approved the final manuscript for publication.

Research registration unique identifying number (UIN)

This is not a first-in-human study, thus it is not needed.

Guarantor

Tu Trong Doan, MD.

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