Esophagus (2010) 7:219–224
DOI 10.1007/s10388-010-0243-7

CASE REPORT

Kazuo Koyanagi · Motohito Nakagawa · Soji Ozawa
Takeshi Nagase · Ryou Seishima · Toshio Kanai

Thoracoscopic enucleation for small-sized gastrointestinal stromal tumor of the esophagus: report of two cases

Received: June 22, 2010 / Accepted: August 6, 2010

Abstract Gastrointestinal stromal tumors (GISTs) rarely occur in the esophagus. Surgical approaches for such tumors have not been established, since the standard wedge or segmental resection that is used for intra-abdominal GIST is not possible in the esophagus. We report two cases of small esophageal GIST in which thoracoscopic enucleation was performed. Both patients underwent the thoracoscopic surgery using four trocars. The tumor size was 43 and 32 mm in patients 1 and 2, respectively. The operating time was 240 and 238 min. The final diagnosis was as low-risk GIST in both patients. Postoperative course was uneventful and both patients have been disease-free at a follow-up of 40 and 32 months. Considering the special case of the esophagus and the very good prognosis of low-risk tumors, enucleation under the thoracoscopic technique may be feasible for small-sized esophageal GIST as a minimally invasive surgery. We also review the literature in this report.

Key words Esophagus · Gastrointestinal stromal tumor · Thoracoscopic surgery · Enucleation

Introduction

Gastrointestinal stromal tumors (GISTs) are defined as c-KIT-positive, spindle cell, or epithelioid mesenchymal tumors of the gastrointestinal (GI) tract. More than half of all GISTs are located in the stomach with the small intestine being the next common site; GISTs derived from the esophagus are very rare [1]. A wedge or segmental resection with adequate safety margins, which is recommended by certain guidelines as the essential surgical management for the GIST [2–4], is practically impossible for GIST of the esophagus. Tumor enucleation is not always recommended because the risk of tumor dissemination increases when the tumor capsule is destroyed. However, the high morbidity and mortality rates associated with an esophagectomy may favor tumor enucleation when the possibility of tumor recurrence is very low. Although thoracoscopic surgery has been introduced as a minimally invasive surgery, the usefulness of this technique for esophageal GIST has not been adequately demonstrated. We herein report two patients in whom small (less than 5 cm) esophageal GISTs were successfully enucleated during thoracoscopic surgery, and also review the literature.

K. Koyanagi (✉)
Department of Gastroenterological Surgery, International Medical Center, Saitama Medical University, 1397-1 Hidaka, Saitama 350-1298, Japan
Tel. +81-42-984-4111; Fax +81-42-984-4741
e-mail: koyanagi@saitama-med.ac.jp

M. Nakagawa · T. Nagase · R. Seishima · T. Kanai
Department of Surgery, Hiratsuka City Hospital, Hiratsuka, Japan

S. Ozawa
Department of Gastroenterological Surgery, Tokai University School of Medicine, Isehara, Japan

Case reports

Case 1

A 44-year-old woman was referred to Hiratsuka City Hospital for the treatment of a submucosal tumor (SMT) of the esophagus in July 2003. She initially had no symptoms. Barium swallow revealed a smooth and rounded defect on the right wall of the lower third of the esophagus (Fig. 1). An endoscopic examination showed a tumor with an apparently normal mucosa located 34–37 cm distant from the incisor teeth. A chest computed tomography (CT) scan also revealed a 3-cm tumor without associated mediastinal lymphadenopathy. An endoscopic ultrasonography (EUS) examination showed a well-circumscribed, hypoechoic, and homogeneous tumor originating from the muscular layer. Pathological examination of a biopsy specimen obtained using endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNA) diagnosed the lesion as a benign neurogenic tumor, since immunohistochemistry showed positive reactions for S-100 and vimentin, and negative reactions for c-KIT and CD34 as well as the absence of mitosis.

Fig. 1. Barium swallow of case 1. Smooth and rounded defect on the right wall of the lower third of the esophagus was shown (*arrow*)

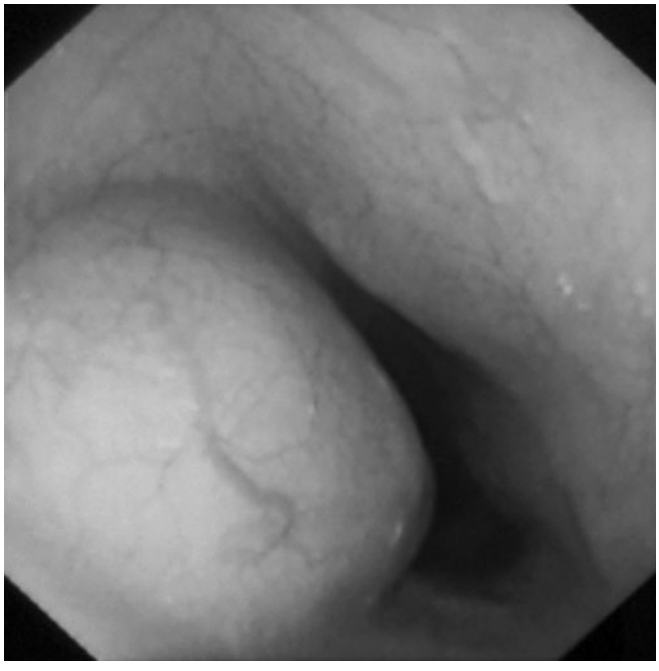

Fig. 2. Endoscopic examination of case 1. A tumor with a normal-appearing mucosa was located 34–37 cm distant from the incisor teeth

Because she had no complaints and no findings suggesting a malignant tumor, she refused surgery at that time; the patient was followed using periodic examinations.

In February 2007, she suffered dysphagia when ingesting solid food. An endoscopic examination revealed that the SMT had enlarged and narrowed the lumen of the esophagus (Fig. 2). A chest CT showed that the size of the SMT had increased to 4 cm in diameter. Because of the onset of symptoms and the increase in the tumor size, we decided to perform surgery and selected a thoracoscopic enucleation of the tumor. While the patient was in a left lateral position, the right lung was collapsed using a double-lumen endotracheal tube. After an initial exploration with flexible fiberscope through the first trocar located at the seventh intercostal space on the posterior axillary line, three other trocars were placed as follows: sixth intercostal space on the anterior axillary line, sixth intercostal space on the middle axillary line, and eighth intercostal space on the middle axillary line. Intraoperative endoscopy assisted in identifying the proximal and distal margins of the tumor. The mediastinal pleura overlying the tumor were divided, and the muscle layer was split to expose the surface of the tumor. The tissues adjacent to the tumor were easily dissected, and the tumor was totally enucleated without disrupting the pseudocapsule. The integrity of the mucosa was confirmed using intraoperative endoscopy, and the proper muscle layer was reapproximated with six interrupted sutures intracorporeally [5]. The tumor was placed in a specimen bag and retrieved through the trocar site. A chest drainage tube was inserted through the eighth intercostal space site, and the other trocar sites were closed.

Macroscopically, the tumor measured $4.3 \times 3.8 \times 2.8$ cm. Microscopically, the tumor showed a predominantly epithelioid pattern without necrosis, and the immunohistochemistry was positive for c-KIT, S-100, and vimentin (Fig. 3). The mitotic index was less than 5 per 50 high-power fields (HPF). The final pathologic diagnosis was a low-risk GIST according to the Fletcher risk classification [6]. The patient was discharged on postoperative day (POD) 7, and has been disease-free for 40 months.

Case 2

A 58-year-old man was referred to Hiratsuka City Hospital for the treatment of an esophageal SMT in April 2004. Although barium swallow, endoscopic examination, and chest CT scan revealed a 2.5-cm esophageal SMT located 34–36 cm distant from the incisor teeth, the patient refused to undergo further examination and any therapy because he had no symptoms at that time.

In October 2007, he suffered dysphagia when ingesting solid food. An endoscopic examination revealed that the lumen of the esophagus had narrowed as a result of tumor enlargement. A chest CT examination showed that the size of the SMT had increased to 3.5 cm in diameter. Endoscopic ultrasonography showed a well-circumscribed, hypoechoic, and homogeneous tumor originating from the muscular layer. Pathological examination of a biopsy specimen obtained using EUS-FNA resulted in a diagnosis of a benign leiomyoma, and no mitosis was found in the specimen. Because of the onset of symptoms and the increasing tumor size, we decided to perform a thoracoscopic enucleation of the tumor. Since the SMT was located on the left wall of the esophagus, we approached the tumor through the left pleural cavity. After an initial exploration with flexible fiberscope through the first trocar located at the seventh intercostal space on the middle axillary line, three other trocars were placed as follows: sixth intercostal space on the

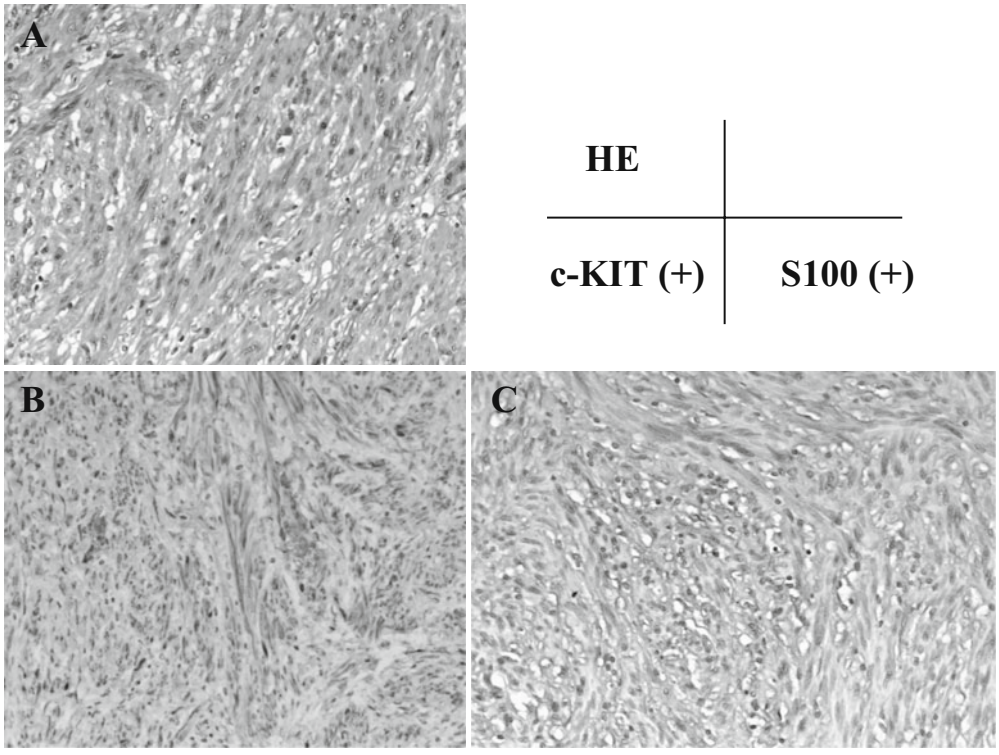

Fig. 3. Pathological findings of case 1. (×100) **A** Hematoxylin–eosin staining shows an epithelioid pattern. **B** c-KIT immunohistochemistry was positive. **C** S-100 was positive

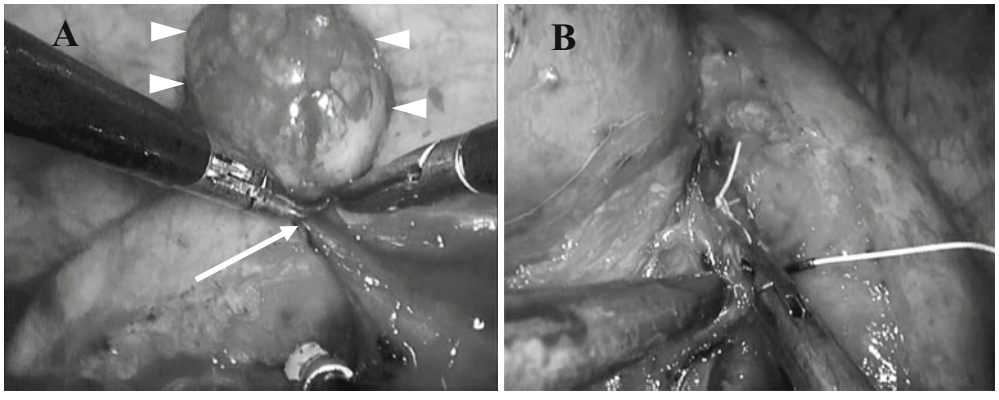

Fig. 4. Thoracoscopic enucleation of case 2. **A** A slight adhesion (*arrow*) between the esophageal mucosa and the tumor (*arrowheads*) was recognized and then dissected using a vessel sealing system. **B** The proper muscle layer was reapproximated intracorporeally

middle axillary line, ninth intercostal space on the middle axillary line, and ninth intercostal space on the anterior axillary line. Surgical procedures were performed as in case 1. However, when the tissues adjacent to the tumor were dissected, a slight adherence of the esophageal mucosa was observed at a site proximal to the tumor, and this area was dissected using a vessel sealing system and the proper muscle layer was reapproximated with six interrupted sutures intracorporeally (Fig. 4A,B). The tumor was placed in a specimen bag and retrieved through the trocar site. A chest drainage tube was inserted through the ninth intercostal space site, and the other trocar sites were closed.

Macroscopically, the tumor measured $3.2 \times 2.4 \times 1.2$ cm. Microscopically, the tumor showed a predominantly spindle cell pattern without necrosis, and the immunohistochemistry was positive for c-KIT and CD34. The mitotic index was less than 5 per 50 HPF. The final diagnosis was a low-risk GIST. The patient was discharged on POD 6, and has been disease-free for 32 months.

Discussion

The majority of esophageal SMT lesions consist of benign tumors, such as leiomyoma, while GIST of the esophagus is very rare [7]. Distinguishing GIST from other esophageal mesenchymal tumors prior to operation used to be difficult, and a definite diagnosis was usually made using immunohistochemistry of the resected specimens. EUS-FNA can be used to obtain the tissue materials of gastrointestinal SMT, and evidence for the usefulness of EUS-FNA for the diagnosis of the gastric GIST has been accumulating [8,9], while its use for esophageal GIST has been described in few

reports [10,11] and not been well defined because of, in part, the low incidence of these tumors. Some investigators have reported that the sensitivity of EUS-FNA for the diagnosis of GIST is influenced by size and location; the sensitivity correlates with increasing tumor size, and is higher when the GIST is located in the stomach [12,13]. The false-negative results may be attributable to sampling errors and/or low cellularity; the fibrosis and firmness of GIST cause the difficulty in obtaining sufficient material for immunohistochemistry, and the aggregates of spindle-shaped cells from GIST are sometimes misinterpreted as benign tissue, especially when cellularity is low. To improve the sensitivity, the presence of an on-site cytologist may be needed to confirm whether the material is sufficient for immunocytochemistry or immunohistochemistry. Heterogeneity of the tumor also has to be considered [8]. We were unable to diagnose the GIST prior to the operation; however, pathological examination revealed no mitosis in the specimens obtained using EUS-FNA. The mitotic rate and the tumor size are the main factors in the risk classification, reflecting the possibility of tumor recurrence. In the present cases, EUS-FNA suggested that the tumors had a low malignant potential, which prompted us to choose thoracoscopic enucleation as a less invasive method.

Recent advances in endoscopy have enabled the detection of relatively small GISTs. The size of a tumor is an important prognostic factor and influences the selection of the therapeutic strategy for treating GIST [6]. Because previously reported esophageal GISTs were extremely large at the time of their detection, they required an esophagectomy for resection and exhibited a poor outcome [1,7]. The surgical guidelines for GIST are based on tumors of the intra-abdominal gastrointestinal (GI) tract, especially the stomach, whereas the surgical strategy for esophageal GIST may differ from those of the intra-abdominal GI tract, because a wedge or segmental resection of the esophagus is impossible and the risk of morbidity and mortality after an esophagectomy is higher than that after gastric or colorectal surgery. Considering these special issues and the relatively good prognosis of low-risk GIST, we believe that the enucleation of small esophageal GIST might be acceptable. The surgical technique must be gentle and precise so as not to disrupt the pseudocapsule, since the exposure of the tumor could result in tumor dissemination. If a pathological examination reveals the tumor to be an intermediate or high risk, an esophagectomy or the administration of tyrosine kinase receptor inhibitor (imatinib mesylate) might be necessary, as is the case for a large GIST [11].

Otani et al. demonstrated the feasibility of using laparoscopic surgery for the resection of relatively small-sized (2–5 cm) GISTs of the stomach [14]. In previous reports, however, almost all esophageal GISTs have been resected using a transthoracic approach because the tumors were relatively large and because thoracoscopic surgery had not been widely adopted. A literature search of the PubMed database was performed using "esophagus," "GIST," and "gastrointestinal stromal tumor" as key words within a publication range of between 1980 and 2009. The individual clinicopathological characteristics of patients with esophageal GIST who underwent thoracoscopic enucleation are listed in Table 1 [15,16]. Of the four patients including our two cases, three patients had no initial symptoms and an endoscopic examination performed for some other reasons revealed the presence of the esophageal SMT. The tumor size of our patients was less than 5 cm, whereas that of the others was more than 5 cm. Consequently, the risk was classified as low in our patients and intermediate or high in the other patients. None of the patients received adjuvant therapy and none of them suffered a tumor relapse during the follow-up period. We also summarized the patients with

Table 1. Reported cases of esophageal gastrointestinal stromal tumors that underwent thoracoscopic enucleation

Patients' characteristics	Study			
	Ertem et al. (2004) [16]	Blum et al. (2007) [15]	Our case 1	Our case 2
Age (years)	46	75	44	58
Sex	Male	Female	Female	Male
Symptom	Dysphagia	No	No	No
Endoscopic tumor distance from incisors (cm)	22–30	Lower third	34–37	34–36
EUS-FNA	No	Yes (KIT(+))	Yes	Yes
Operation time (min)	NA	NA	240	238
Intraoperative bleeding (ml)	NA	NA	120	58
Postoperative complications	No	NA	No	No
Tumor size (cm)	$8.5 \times 3.5 \times 1.5$	$7.2 \times 2.1 \times 2.0$	$4.3 \times 3.8 \times 2.8$	$3.2 \times 2.4 \times 1.2$
Cellular pattern	Spindle	Spindle	Epithelioid	Spindle
Mitotic index/50 HPF	0	5	<5	<5
Necrosis	No	No	No	No
c-KIT	Positive	Positive	Positive	Positive
Risk classification[†]	Intermediate	High	Low	Low
Imatinib mesylate	No	No	No	No
Follow-up (months)	48	17	40	32
Recurrence	No	No	No	No

EUS-FNA, endoscopic ultrasound-guided fine-needle aspiration; HPF, high-power fields; NA, not available
[†] Classification by Fletcher et al. [6]

Table 2. Reported cases of esophageal gastrointestinal stromal tumors that underwent enucleation through thoracotomy

Patients' characteristics	Study			
	Lee et al. (2002) [17]	Chang et al. (2005) [19]	Portale et al. (2007) [18]	Blum et al. (2007) [15]
Age (years)	64	36	66	74
Sex	Male	Male	Female	Female
Symptom	No	Dysphagia	Hemoptysis	No
Endoscopic tumor distance from incisors (cm)	Lower third	Lower third	Lower third	26–36
EUS-FNA	No	No	No	Yes (KIT(+))
Tumor size (cm)	9×8	6.5	3.0	$12.5 \times 10 \times 6.5$
Operation time (min)	NA	NA	NA	NA
Intraoperative bleeding (ml)	NA	NA	NA	NA
Postoperative complications	No	No	No	NA
Cellular pattern	Spindle	Spindle	Spindle	Spindle
Mitotic index/50 HPF	NA	<5	<5	>10
Necrosis	Yes	No	No	No
c-KIT	Positive	Positive	Positive	Positive
Risk classification[†]	Intermediate or high	Intermediate	Low	High
Imatinib mesylate	No	No	No	Yes
Follow-up (months)	26	12	12	49
Recurrence	No	No	No	Yes

[†] Classification by Fletcher et al. [6]

esophageal GIST who underwent enucleation via a thoracotomy (Table 2) [15,17–19]. No obvious differences in the patient characteristics or short-term results were observed between the thoracoscopic and open thoracic groups. One patient who had a large tumor size and a high mitotic index suffered a tumor relapse. These findings suggest that thoracoscopic enucleation, rather than open thoracic surgery, might be favorable in patients with small esophageal GIST, because of the less invasive nature of thoracoscopic surgery. To perform thoracoscopic surgery, the early detection of tumors is necessary and an endoscopic examination is very important for confirming that the tumors are small. Thoracoscopic enucleation of esophageal GIST allows patients to have less surgical stress and a better quality of life. Although further analysis is needed to clarify the appropriate surgical management of esophageal GIST, thoracoscopic enucleation might be a possible therapeutic approach for small (less than 5 cm) esophageal GISTs.

References

1. DeMatteo RP, Lewis JJ, Leung D, Mudan SS, Woodruff JM, Brennan MF. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival. Ann Surg 2000;231:51–8.
2. Demetri GD, Benjamin RS, Blanke CD, Blay JY, Casali P, Choi H, et al. NCCN Task Force report: management of patients with gastrointestinal stromal tumor (GIST)—update of the NCCN clinical practice guidelines. J Natl Compr Canc Netw 2007;5 suppl 2:S1–29; quiz S30.
3. Nishida T, Hirota S, Yanagisawa A, Sugino Y, Minami M, Yamamura Y, et al. Clinical practice guidelines for gastrointestinal stromal tumor (GIST) in Japan: English version. Int J Clin Oncol 2008;13:416–30.
4. Blay JY, Bonvalot S, Casali P, Choi H, Debiec-Richter M, Dei Tos AP, et al. Consensus meeting for the management of gastrointestinal stromal tumors. Report of the GIST Consensus Conference of 20–21 March 2004, under the auspices of ESMO. Ann Oncol 2005;16:566–78.
5. Ozawa S, Morikawa Y, Oguma J, Kitagawa Y, Asada H, Kitajima M. Development of a new flat needle and a reduced surface coating thread for endoscopic suturing. J Surg Res 2008;145:266–71.
6. Fletcher CD, Berman JJ, Corless C, Gorstein F, Lasota J, Longley BJ, et al. Diagnosis of gastrointestinal stromal tumors: A consensus approach. Hum Pathol 2002;33:459–65.
7. Miettinen M, Sarlomo-Rikala M, Sobin LH, Lasota J. Esophageal stromal tumors: a clinicopathologic, immunohistochemical, and molecular genetic study of 17 cases and comparison with esophageal leiomyomas and leiomyosarcomas. Am J Surg Pathol 2000; 24:211–22.
8. Ando N, Goto H, Niwa Y, Hirooka Y, Ohmiya N, Nagasaka T, Hayakawa T. The diagnosis of GI stromal tumors with EUS-guided fine needle aspiration with immunohistochemical analysis. Gastrointest Endosc 2002;55:37–43.
9. Vander Noot MR 3rd, Eloubeidi MA, Chen VK, Eltoum I, Jhala D, Jhala N, et al. Diagnosis of gastrointestinal tract lesions by endoscopic ultrasound-guided fine-needle aspiration biopsy. Cancer 2004;102:157–63.
10. Arakawa S, Ozawa S, Yoshida R, Atsuta K, Kawase J, Oshima H, et al. Two resected cases of esophageal leiomyoma diagnosed with preoperative endoscopic ultrasound-guided fine-needle aspiration biopsy (EUS-FNAB). Esophagus 2008;5:149–54.
11. Matsumoto S, Takayama T, Watatsuki K, Enomoto K, Tanaka T, Migita K, et al. An esophageal gastrointestinal stromal tumor with regional lymph node metastasis. Esophagus 2010;7:115–8.
12. Philipper M, Hollerbach S, Gabbert HE, Heikaus S, Bocking A, Pomjanski N, et al. Prospective comparison of endoscopic ultrasound-guided fine-needle aspiration and surgical histology in upper gastrointestinal submucosal tumors. Endoscopy 42:300–5.
13. Sepe PS, Moparty B, Pitman MB, Saltzman JR, Brugge WR. EUS-guided FNA for the diagnosis of GI stromal cell tumors: sensitivity and cytologic yield. Gastrointest Endosc 2009;70:254–61.
14. Otani Y, Furukawa T, Yoshida M, Saikawa Y, Wada N, Ueda M, et al. Operative indications for relatively small (2–5 cm) gastrointestinal stromal tumor of the stomach based on analysis of 60 operated cases. Surgery 2006;139:484–92.
15. Blum MG, Bilimoria KY, Wayne JD, de Hoyos AL, Talamonti MS, Adley B. Surgical considerations for the management and resection of esophageal gastrointestinal stromal tumors. Ann Thorac Surg 2007;84:1717–23.

16. Ertem M, Baca B, Dogusoy G, Erguney S, Yavuz N. Thoracoscopic enucleation of a giant submucosal tumor of the esophagus. Surg Laparosc Endosc Percutan Tech 2004;14:87–90.
17. Lee JR, Anstadt MP, Khwaja S, Green LK. Gastrointestinal stromal tumor of the posterior mediastinum. Eur J Cardiothorac Surg 2002;22:1014–6.
18. Portale G, Zaninotto G, Costantini M, Rugge M, Pennelli GM, Rampado S, et al. Esophageal GIST: case report of surgical enucleation and update on current diagnostic and therapeutic options. Int J Surg Pathol 2007;15:393–6.
19. Chang WC, Tzao C, Shen DH, Cheng CY, Yu CP, Hsu HH. Gastrointestinal stromal tumor (GIST) of the esophagus detected by positron emission tomography/computed tomography. Dig Dis Sci 2005;50:1315–8.