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ABOUT COVER

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CASE REPORT

Total removal of a large esophageal schwannoma by submucosal tunneling endoscopic resection: A case report and review of literature

Yu-Zhu Mu, Qi Zhang, Jing Zhao, Yan Liu, Ling-Wei Kong, Zhong-Xiang Ding

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Abstract

BACKGROUND

Primary schwannoma is a rare submucosal tumor of the esophagus, which is most often benign, and surgery is the only effective treatment. So far, only a few cases have been reported. Herein, we reported a single case diagnosed with primary esophageal schwannoma that was totally removed by submucosal tunneling endoscopic resection (STER).

CASE SUMMARY

A 62-year-old man presented to the hospital with a history of resection of a malignant gastric tumor and mild dysphagia. Endoscopic examination revealed a large submucosal elevated lesion in the esophagus 25-30 cm from the incisors. Endoscopic ultrasonography detected a 45 mm × 35 mm × 31 mm hypoechoic lesion; chest computed tomography showed a mass of approximately 55 mm × 35 mm × 29 mm. A preliminary examination showed features suggestive of a stromal tumor. Pathological findings indicated esophageal schwannoma. Next, STER alone was performed to completely resect the mass, and the patient recovered

well post-surgery. Afterward, the patient was discharged and showed no tumor recurrence at 33 mo of follow-up.

CONCLUSION
Endoscopic resection is still an effective treatment for large esophageal schwannomas (> 30 mm) under meticulous morphological evaluation.

Key Words: Esophageal schwannoma; Submucosal tunneling endoscopic resection; S100; Submucosal; Case report

Core Tip: Primary esophageal schwannoma is a rare esophageal submucosal tumor that is usually benign. The final diagnosis requires histopathological and immunohistochemical examinations. The surgical method depends on the morphology and size of the lesion. Submucosal tunneling endoscopic resection appears to be a feasible treatment for a subset of large esophageal schwannomas with large supero-inferior diameter but the smaller antero-posterior diameter and left-right diameters, which may benefit patients intolerant to surgical treatment.

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INTRODUCTION

Primary esophageal schwannomas are very rare tumors. In most cases, they are benign, while only a few malignant cases have been reported[1,2]. Imaging findings can reveal the specific location of the lesion, blood supply, and the relationship between the mass and the surrounding tissues, which are useful to determine whether the tumor is benign or malignant, and subsequently choose the appropriate treatment[3]. As one of imaging tools, endoscopic ultrasonography (EUS) can clearly display the layers of the esophageal wall[3] as well as reveal the location and origin of lesions[4,5]. Preoperative diagnosis of schwannoma is difficult[6,7], and the final diagnosis requires histopathological and immunohistochemical examinations[7]. Immunohistochemical staining is currently the only reliable diagnostic method and S100 protein is a specific molecular marker of schwannomas[7,8].

Esophageal schwannoma is insensitive to medical treatments such as radiotherapy and chemotherapy. Hence, resection remains the only effective treatment, especially if the tumor is detected in the early stage[8]. The maximum diameter of most endoscopically resected masses over the past 12 years was less than 30 mm[1,2,6-36], but these cases only discussed endoscopic resection according to the maximum diameter of the tumor and did not analyze the three diameter lines of the mass. In this paper, we reported single submucosal tunnel endoscopic resection for an esophageal schwannoma with 55 mm in supero-inferior diameter.

CASE PRESENTATION

Chief complaints

A 62-year-old Asian male presented with mild dysphagia lasting for five months.

History of present illness

The patient suffered from mild dysphagia for five months when swallowing solid food. There was no associated chest pain, nausea, vomiting, or abdominal pain.

History of past illness

The patient underwent Billroth II subtotal gastrectomy six years ago due to the presence of stomach cancer, as well as exploratory laparotomy, intestinal adhesiolysis, and inguinal hernia repair two years ago. The patient also completed eight cycles of XELOX adjunctive therapy. His blood pressure was elevated for about one year, and he regularly took oral nifedipine 10 mg daily.

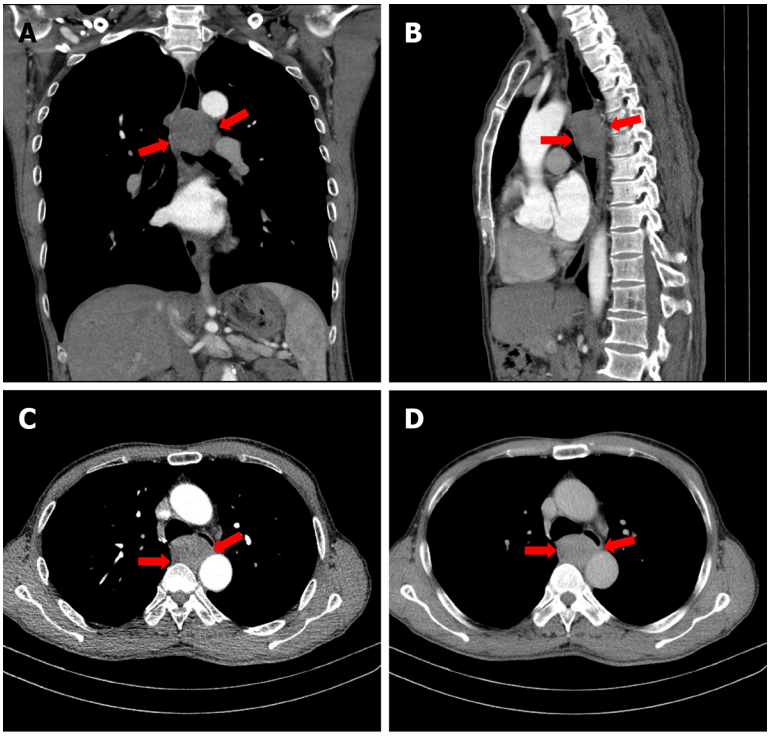

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Figure 1 Plain and contrast-enhanced chest computed tomography. A: Coronal view of chest computed tomography (CT) showed that the tumor in the middle and upper esophagus had clear boundaries and homogeneous density; B: Sagittal view of the CT scan revealed the mass was located in the posterior mediastinum, and the upper and lower diameters were larger than the anterior and posterior diameters; C and D: Axial view of CT demonstrated the tumor presented homogeneous enhancement.

Personal and family history

There was no clinically significant family history; the patient had no smoking or drinking habits, and neither did he have a history of exposure to toxic substances.

Physical examination

The patient was 177 cm tall and weighed 63.1 kg. His temperature was 36.1 °C, heart rate was 61 beats per minute, respiratory rate was 17 breaths per minute, and blood pressure was 153/84 mmHg. Lung and abdominal tests were normal. Neurological examination revealed no obvious abnormalities. There was no edema in the bilateral lower limbs.

Laboratory examinations

Levels of anti-thyroid peroxidase antibodies were elevated. Glycosylated hemoglobin level (7.1%), total bilirubin (21.2 μmol/L), and indirect bilirubin (14.2 μmol/L) were increased, while aspartate aminotransferase (11 U/L) was decreased. Tumor markers CYFRA21-13 (40 ng/mL) were elevated. All other laboratory tests were within normal range.

Imaging examinations

Plain and contrast-enhanced chest computed tomography revealed a round lesion of 55 mm × 35 mm × 29 mm in the middle and upper esophagus, with homogeneous enhancement and esophageal lumen stenosis (Figure 1). Upper gastrointestinal endoscopy indicated a lesion in the esophagus about 25-30 cm from the incisor, and the esophageal mucosa was intact (Figure 2A). EUS demonstrated a hypoechoic and homogeneous mass originating from the muscularis propria (MP), with a diameter of about 41 mm. It was provisionally diagnosed as a stromal tumor.

FINAL DIAGNOSIS

Microscopy showed a dense proliferation of spindle cells without mitosis and atypia. In addition (Figure 3A), immunohistochemical staining was positive for S-100 protein (Figure 3D), the expression level of Ki-67 was < 5% (Figure 3B), and negative for CD34, Desmin, CD117 (Figure 3C), DOG-1, and SMA. These findings were strongly suggestive of a benign esophageal schwannoma.

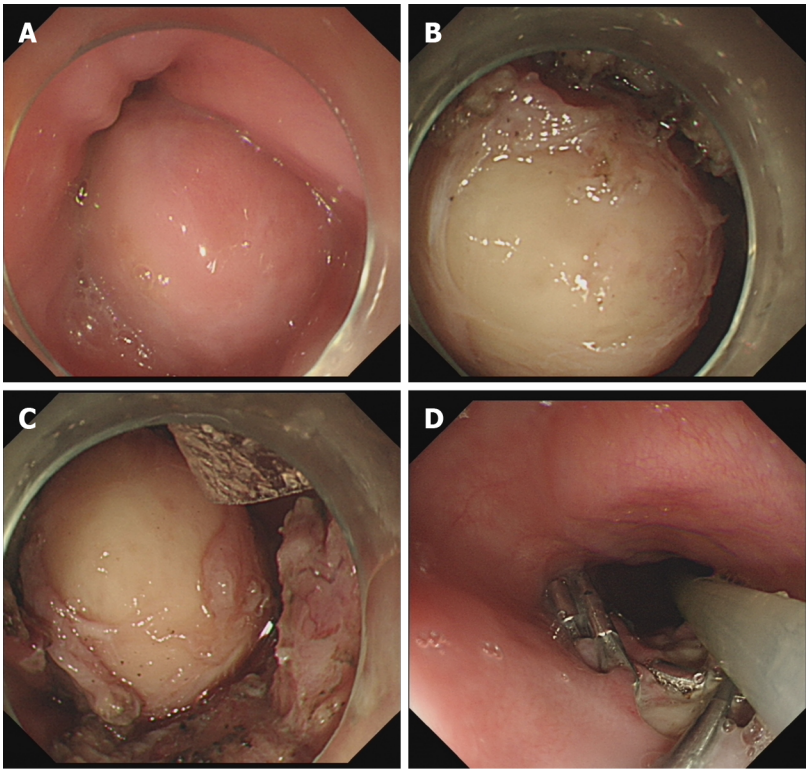

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Figure 2 Steps of submucosal tunneling endoscopic resection. A: Upper gastrointestinal endoscopy showing smooth elevated lesion; B: Submucosal tumor; C: Peeling the lesion; D: Closing the mucosal incision site with clips.

TREATMENT

The patient underwent submucosal tunneling endoscopic resection (STER). The tumor with the size of 45 mm × 35 mm × 31 mm was finally resected with the intact fibrous capsule. The entire procedure lasted for about five hours. STER was performed under general anesthesia with intravenous propofol (2 mg/kg). Intraoperative findings showed that the lesion was located in the esophagus about 25-30 cm from the incisor, and the esophageal mucosa was intact (Figure 2A). EUS demonstrated a hypoechoic and homogeneous mass originating from the MP, with a diameter of about 41 mm.

The STER procedure was as follows: after the submucosal injection of glycerol fructose, a submucosal tunnel was created, and a 20 mm longitudinal mucosal incision was made with a Hook knife. Then a submucosal tunnel was created with an IT knife between the mucosal and muscular layers. The tunnel was continued downwards with the dual knife until the tumor was exposed. Within the submucosal tunnel, the tumor was separated from the MP layer as much as possible. Next, circumferential full-thickness MP resection was performed using the IT knife and snare for the tumor involving the deep layer of MP. The tumor was finally resected with the intact fibrous capsule. Hot hemostatic forceps were applied to treat blood vessels in surgical wounds. IT knife was used to incise the mucosal surface of the tumor that was difficult to remove, and multiple snares and stone extractors were used to completely remove the lesion (Figure 2B-D). The mucosal entry incision was closed with 16 vascular clips and 10 tissue clips.

OUTCOME AND FOLLOW-UP

After surgery, the patient's dysphagia disappeared. On follow-up endoscopy at three months, the wound was fully healed. Follow-up did not reveal local tumor recurrence or metastasis at 33 mo post-operation.

DISCUSSION

Primary schwannomas are rare esophageal submucosal tumors accounting for less than 2% of all esophageal tumors[5,7,9]. Most of these tumors are benign, but a few malignant cases have been

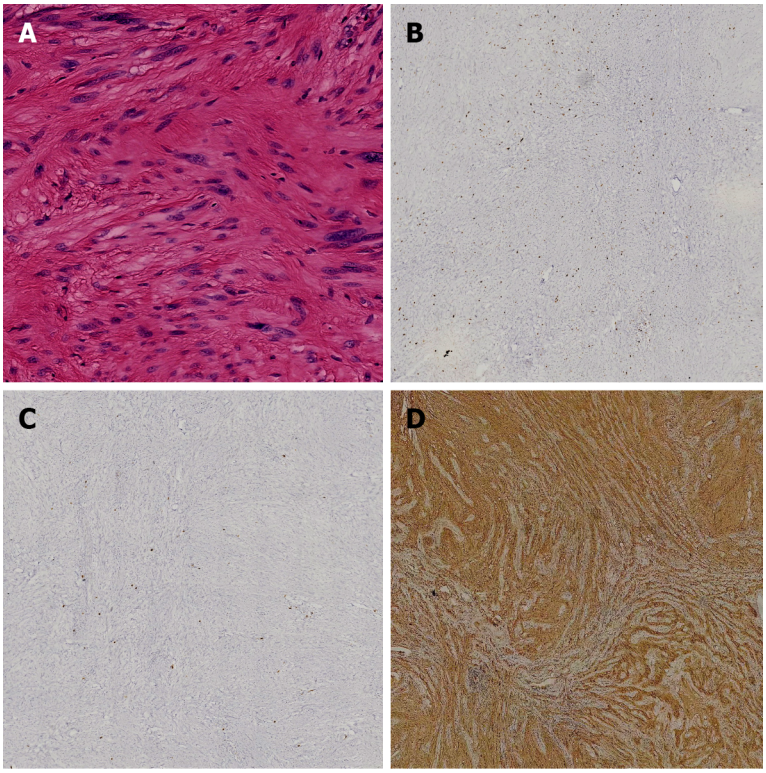

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Figure 3 Histology and immunohistochemistry of the tumor. A: Histopathologic findings revealed spindle-shaped cells in a fasciculated and disarrayed architecture, and no pathologic mitosis was observed (hematoxylin and eosin staining; (magnification, × 400); B: The mitotic activity rate was < 5% on Ki-67 staining (magnification, × 80); C: Immunochemical analysis revealed no staining with CD117 (magnification, × 80); D: Immunohistochemical examination revealed S-100 protein positivity (magnification, × 200).

reported[1,2]. Typically, dyspnea and dysphagia are the most common complaints; other reported signs and symptoms include chest pain, stridor, hematemesis, cough, and palpable neck mass[10]. A literature search in the PubMed database identified 40 reported cases[1,2,6-36] published between 2011 and October 2022, which are listed in Table 1. Statistical analysis of baseline information, clinical symptoms, tumor size, and management methods are shown in Tables 2-4.

Tables 1 and 2 show that the mean age of schwannoma patients was 52.92 years, with a standard deviation of 2.17 years, the minimum age was 22 years, and the maximum age was 78 years. The male-to-female ratio was 1:2 in the adult population. Of the 40 esophageal schwannomas, 2 (5%) were malignant, and 38 (95%) were benign. Of these, 28 (70%) tumors were located in the upper or middle esophagus, while 7 (17.5%) were in the lower third of the esophagus. In middle-aged women, tumors were located in the middle and upper esophagus and were mostly benign, in accordance with the description of the esophageal nerve mentioned in the previous literature[11].

The clinical symptoms are summarized in Table 3. Some patients had corresponding clinical symptoms, so we analyzed 40 patients with esophageal schwannoma, 31 (88.6%) of whom had dysphagia, which appears to be the most important symptom that may be caused by the expansive growth of the tumor in the esophagus. Five (14.29%) patients presented with dyspnea, perhaps due to tracheal compression by a tumor, and another patient presented with loss of consciousness. In addition, some patients presented with symptoms of dyspnea, chest pain, palpitation, chest tightness, abdominal distention, *etc.* A sore throat was observed in 2 patients, a cough in 1 patient, and hemoptysis in 1 patient. These findings are consistent with previous reports[10].

Most cases of esophageal schwannoma are found incidentally during a physical examination and are commonly misdiagnosed[6,24]. Previous reports on esophageal schwannoma have failed to correctly diagnose the tumor preoperatively[6,7]. We believe that the two main reasons for the misdiagnosis are the following: first, diagnosing esophageal schwannoma using imaging alone remains a challenging task; the tumor is often misdiagnosed as other submucosal tumors, such as esophageal leiomyoma and esophageal, gastrointestinal stromal tumors. Second, since esophageal schwannomas are very rare, most physicians do not consider it as the first diagnosis or differential diagnosis, highlighting the need to improve doctors' understanding of esophageal schwannoma.

Hence, meticulous radiographic evaluation of esophageal schwannoma is necessary. This can help identify the lesion's specific location, blood supply, relationship with surrounding tissues, and esophageal layer in which the lesion originated, which provide a crucial reference for distinguishing benign from malignant tumors and the choice of surgical methods.

Table 1 Esophageal schwannoma case reports in PubMed during the last 12 years

Case	Ref.	Year	Age	Sex	Location	Tumor size (mm)	Symptoms	Management	Malignant findings
1	Choo *et al*[10]	2011	22	M	Ut	80 × 60 × 30	Cough, dyspnea and dysphagia	Enucleation	Benign
2	Wang *et al*[2]	2011	44	F	Lt	55 × 44	Progressive dysphagia	Surgical enucleation	Malignant
3	Liu *et al*[16]	2013	62	F	NA	90 × 40 × 30	Dysphagia and dyspnea	Partial esophagectomy and esophagogastrostomy	Benign
4	Liu *et al*[17]	2013	NA	NA	NA	< 30	NA	STER	Benign
5	Kitada *et al*[6]	2013	55	F	UM	75 × 57 × 80	Palpitations and dysphagia	Mini thoracotomy	Benign
6	Gu *et al*[18]	2014	39	M	UM	35 × 32 × 12	Obstructive sensation	VATS	Benign
7	Jeon *et al*[19]	2014	63	M	Ut	94 × 89	No symptoms	Thoracotomy	Benign
8	Jeon *et al*[19]	2014	32	F	Ut	60 × 85 × 40	Intermittent chest pain	VATS	Benign
9	Tomono *et al*[20]	2015	59	M	Mt	109 × 72 × 71	Dysphagia, dyspnea, disturbed	Subtotal esophagectomy	Benign
10	Wang *et al*[21]	2015	53	F	NA	NA	NA	Surgical excision	Benign
11	Wang *et al*[21]	2015	52	F	NA	NA	NA	Surgical excision	Benign
12	Zhang *et al*[22]	2015	67	F	NA	NA	Dysphagia	Surgical excision	Benign
13	Mishra *et al*[1]	2016	27	F	Mt	120 × 100 × 101	Dysphagia and palpitations	Surgical enucleation	Malignant
14	Watanabe *et al*[23]	2016	39	F	Ut	55 × 45 × 24	Epigastric pain, difficulty swallowing	Surgical excision	Benign
15	Chen *et al*[24]	2016	46	M	Mt	30 × 20 × 17	Discomfort during swallowing	VATS	Benign
16	Chen *et al*[24]	2016	42	F	Ut	30 × 40 × 40	Dysphagia	Enucleation	Benign
17	Chen *et al*[24]	2016	58	F	Ut	80 × 60 × 60	Dysphagia	Enucleation	Benign
18	Onodera *et al*[12]	2017	47	F	Ut	60	Dysphagia	Thoracoscopic + endoscopic excision	Benign
19	Moro *et al*[25]	2017	66	M	Ut	52 × 40 × 31	Dysphagia	Surgical excision	Benign
20	Zhang *et al*[13]	2018	48	F	Mt	69 × 36	Dysphagia	Robot-assisted enucleation	Benign
21	Iwata *et al*[26]	2018	74	F	Ut	80 × 42	Loss of consciousness	Surgical excision	Benign
22	Zhu *et al*[27]	2019	55	F	Mt	25 × 25 × 20	Dysphagia and chest pain	Left thoracotomy with subtotal esophagectomy	Benign
23	Souza *et al*[28]	2019	43	M	Ut	70	Pharyngitis, odynophagia, hemoptysis	Surgical excision	Benign
24	Ramos *et al*[29]	2019	40	F	Ut	80 × 45 × 20	Pharyngitis, odynophagia, dysphagia	Surgical excision	Benign
25	Degheili *et al*[30]	2019	50	F	Ut	78 × 54 × 105	Dyspnea and dysphagia	Surgical excision	Benign
26	Matteo *et al*[31]	2020	22	M	Lt	37 × 28 × 70	Dysphagia	Subtotal esophagectomy	Benign
27	Wu *et al*[7]	2020	67	F	Ut	61 × 46 × 60	Dysphagia and dyspnea	Surgical excision	Benign
28	Li *et al*[11]	2020	59	M	Lt	14 × 5	Upper abdominal distension	Endoscopic submucosal excision	Benign
29	Li *et al*[11]	2020	51	F	Mt	18 × 20	Heartburn	STER	Benign
30	Li *et al*[11]	2020	49	M	Lt	28 × 22	Dysphagia	STER	Benign

31	Wang *et al*[8]	2021	62	M	Lt	53 × 39 × 50	Severe dysphagia	VATS	Benign
32	Matsui *et al* [32]	2021	50	M	Lt	20	Asymptomatic	VATS	Benign
33	Khalayleh *et al*[33]	2021	61	F	Ut	50 × 30	Dysphagia	VATS	Benign
34	Zackria *et al* [15]	2021	78	F	Ut	30	Dysphagia	FNA	Benign
35	Khan *et al*[34]	2021	60	F	Lt	76 × 46 × 66	Dysphagia	Right-sided VATS	Benign
36	Wang *et al*[35]	2022	70	F	Ut	32 × 40 × 54	Dysphagia	VATS	Benign
37	Froiio *et al*[14]	2022	55	F	Ut	65 × 47	Dysphagia	Robotic enucleation	Benign
38	Gupta *et al*[9]	2022	62	F	Mt	51 × 31	Dysphagia	FNA	Benign
39	Nashed *et al* [36]	2022	72	F	Mt	29 × 29 × 21	Dysphagia	STER	Benign
40	Current article	2022	62	M	Mt	55 × 35	Dysphagia	STER	Benign

NA: Not available; F: Female; M: Male; Ut: Upper thoracic esophagus; Mt: Middle thoracic esophagus; Lt: Lower thoracic esophagus; STER: Submucosal tunneling endoscopic resection; FNA: Fine needle aspiration; VATS: Video-assisted thoracoscopic surgery.

Table 2 Clinical characteristics of schwannomas

Characteristics		*n* (%) s (Total 40)	Characteristics		*n* (%) s (Total 40)	mean ± SD
Location	Upper/middle	28 (70)	Sex	Male	13 (32.5)	
	Lower	7 (17.5)		Female	26 (65.0)	
	NA	5 (12.5)		NA	1 (2.5)	
Malignant findings	Benign	38 (95)	Age (yr)			55.92 ± 2.17
	Malignant	2 (5)				

NA: Not available.

Table 3 Clinical symptoms

Symptoms	*n* (%) s (Total 40)
Dysphagia/odynophagia	31 (88.57)
Epigastric pain/upper abdominal distension	3 (8.57)
Palpitations/chest pain	4 (11.43)
Dyspnea	5 (14.29)
Cough	1 (2.86)
Hemoptysis	1 (2.86)
Loss of consciousness	1 (2.86)
Pharyngitis/pharyngodynia	2 (5.71)
Asymptomatic	2 (5.71)
NA	5 (14.29)

NA: Not available.

Esophageal schwannomas are mainly treated by surgical resection[13]. Literature reports published in the past 12 years (Table 4) revealed that the average maximum diameter of all 40 tumors was 67.25 (± 4.72) mm, of which 29 (72.5%) cases underwent surgical resection or thoracoscopic resection, and the largest diameter reached 120 mm, the smallest was 20 mm, and the average maximum diameter was

Table 4 Management and tumor size

		n (%) s	Maximum diameter (mm)		
Total		40	mean: 67.25 (± 4.72)		
			The largest	The smallest	mean ± SD
Management	Surgical excision/VATS	29 (72.5)	120	20	67.25 ± 4.72
	Endoscopic excision/STER	5 (12.5)	29	14	22.75 ± 3.54
	Current article (STER)	1 (2.5)	55		
	Robot-assisted excision	2 (5)	69	65	
	FNA	2 (5)	51	30	
	Thoracoscopic + endoscopic excision	1 (2.5)	60		

STER: Submucosal tunneling endoscopic resection; FNA: Fine needle aspiration; VATS: Video-assisted thoracoscopic surgery.

67.25 ± 4.72 mm. Five (12.5%) esophageal schwannomas were resected *via* endoscopic surgical approach (including STER), with a maximum diameter of 29 mm, a minimum of 14 mm, a mean maximum diameter of 22.75 ± 3.54 mm, and maximum diameters of these masses were less than 30 mm. In our reported case, complete resection of esophageal schwannoma was performed using STER alone, and the size of this tumor exceeded the maximum size of esophageal schwannomas in all previously reported cases. Only one reported mass with a maximum diameter of 60 mm[12] was larger than our case; however, that case was managed by using thoracoscopy combined with endoscopic surgery rather than endoscopic surgery alone. In addition, there were other management methods, including robot-assisted resection of tumors with maximum diameters of 69 mm[13] and 65 mm[14] in two cases, and no further treatment measures were taken in the other two cases[9,15] after FNA puncture to obtain pathology.

Surgery may be performed by open thoracotomy or video-assisted thoracoscopy[13]. Small lesions in a suitable location can be removed endoscopically by experienced endoscopists using endoscopic submucosal excision or STER[11]. Compared with the first two surgeries, endoscopic resection causes less trauma and fewer complications and reduces the risk of anesthesia, leading to faster recovery and shorter hospitalization[11]. Although no specific cutoff for size could be identified, most tumors > 70 mm were removed by thoracotomy[7,37]. Most of the reported endoscopically resectable submucosal tumors were < 30 mm[11].

However, in all these reports, including cases of esophageal schwannomas treated endoscopically over the past 12 years[11,12,17,36], the size discussed was the maximum diameter of the tumor, while the supero-inferior diameter, antero-posterior diameter, and left-right diameter of the tumor were not analyzed separately. Due to the narrow structure of the esophagus, many schwannomas are limited by the wall of the esophagus and typically have a narrow shape, which often leads to smaller antero-posterior diameter and left-right diameters of the masses although the long diameter is very large, and gives more operating space for endoscopic surgery.

In the present case, the maximum diameter of the lesion was > 50 mm, and postoperative esophageal fistula and pneumothorax may have occurred if endoscopic surgery had been performed. Hence, we recommended thoracoscopic surgery or an open surgical approach[11]. However, the patient refused to undergo surgery again and requested endoscopic minimally invasive resection. After carefully examining the morphology of the mass, we found that this tumor had a large supero-inferior diameter but also smaller antero-posterior and left-right diameters, which meant that the mucosal tunnel only needed to withstand a width of > 30 mm, not 50 mm. Hence, we concluded that there is a certain but controllable risk in treating this patient by endoscopic surgery, and then proposed STER for this patient under the premise of controllable risk and fully considering the possible complications and corresponding solutions.

To the best of our knowledge, this is the first report of using STER alone for the successful removal of an esophageal schwannoma > 30 mm. It is also the first report on the specific analysis of the relationship between the shape of esophageal schwannoma, different diameter lines, and surgical options. Therefore, if the morphological factors of the mass are included, endoscopic treatment could be used for esophageal schwannomas with a maximum diameter of > 30 mm. Hence, risk-controlled STER appears to be a feasible and effective treatment for a subset of large esophageal schwannomas with large supero-inferior diameter but smaller antero-posterior and left-right diameters, which may benefit patients intolerant to surgical treatment.

CONCLUSION

Primary schwannoma is a rare submucosal tumor of the esophagus. Imaging findings can provide useful information, including the location, size, morphology, density, and relationships with the surrounding tissues, particularly the size and morphology, which could influence the treatment choice. We reported a successful resection of the esophageal schwannoma by STER, with a maximum diameter of 55mm and a minimum diameter of 29 mm. In our case, the tumor's small antero-posterior and left-right diameter were important factors for successful removal by STER. Therefore, the morphological features of a mass, especially the three diameters, should be meticulously analyzed. STER appears to be an effective treatment method for a subset of large esophageal schwannomas with large supero-inferior diameter but smaller antero-posterior and left-right diameters, thus benefiting the patients intolerant to surgical treatment.

FOOTNOTES

Author contributions: MU YZ contributed to the data acquisition and analysis, and writing of the manuscript; Zhang Q contributed to the language editing and writing involving the imaging part of the manuscript; Liu Y and Zhao J contributed to the data collection; Ding ZX and Kong LW contributed to the work concept and language editing and important revisions to the manuscript.

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