

PRIMARY ROLE OF EUS, CT, AND ESOPHAGOSCOPY IN DIAGNOSING MULTIPLE GIANT LEIOMYOMA OF THE ESOPHAGUS: A LITERATURE REVIEW

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ABSTRACT

Multiple leiomyoma is a rare benign esophageal disorder which is capable of producing severe complications. The aim of this study is to review the case reports of multiple leiomyomas reported in the English language literature in order to increase the awareness of this entity in producing dysphagia and respiratory complications. To our knowledge, six cases of patients with multiple leiomyoma have been described. The major complaints were dysphagia, dyspnea, cough and other respiratory symptoms; pseudoachlasia was rarely reported. Chest X rays, computed tomography (CT) scan and endoscopic ultrasonography (EUS) were useful as diagnostic tools. CT scan demonstrated homogenous or is of attenuation on the lesions. EUS was accurate in visualization of the lesions and showing exact locations of the mass in the esophageal wall. All of the patients were diagnosed prior to surgery. In the current study, one case from our department is also presented; thoracic CT scan, upper gastroscopy and EUS findings were in favor of benign multiple leiomyoma. EUS, thoracic CT scan and upper endoscopy should be strongly considered for preoperative workup in those patients due to the high diagnostic accuracy rates.

Keywords: Esophagus, Giant Leiomyoma, Multiple, Benign Tumor.

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INTRODUCTION

Multiple leiomyoma of the esophagus is a rare disease with incidence rate less than 4% of benign esophageal lesions. The first case of leiomyoma of the esophagus was described by Sussius in 1559, and the first case of intrathoracic removed case was reported by Ohsawa in 1933 [1-3] It could be found mainly in the lower and middle thirds of the esophagus. If leiomyoma with smaller sizes are asymptomatic, dysphagia, substernal pain, heartburn, weight loss and respiratory symptoms are reported when sizes are larger. They could be usually diagnosed by computerized tomography, esophagography, upper endoscopy and endoscopic ultrasonography sonography (EUS) [4-6] Once diagnosed it should be removed - even if asymptomatic, the malignancy could not be excluded and may occur [1, 6]

To the best knowledge of authors, there are no review studies interested in multiple leiomyoma of the esophagus in the literature. We present a review of the

English language literature and a case report of symptomatic multiple leiomyoma extended on mid thoracic, lower third of esophagus and the cardia and protruded into the stomach. It was resected by VATS and gastric pull-up (GPU) procedure (known as trans hiatal esophagectomy)

MATERIALS AND METHODS

In the current review study, a literature review on Google Scholar and PubMed databases as well as a case presentation was carried out. The search query included the terms "multiple", "giant", "leiomyoma*", "esophagus" or "esophageal" until August 2018. The diffuse leiomyomatosis of esophagus was excluded. Moreover, the case reports without enough data on the diagnostic tools such as CT, EUS or esophagoscopy were not considered in this study. Solitary giant/non-giant esophageal leiomyomas were not included.

CASE PRESENTATION

An 18-year-old woman was admitted to our hospital's clinics in May 2018 with two years history of severe progressive dysphagia to solid and fluid diet, intermittent nocturnal aspirations, as well as weight loss. She had mild intermittent dysphagia before 2016. On esophagoscopy, a larger mass was seen in the mid-thoracic esophagus with normal mucosa while compressing the carina to the anterior. The esophagogastric junction was severely narrowed. The whole lumen of the esophagus was diffusely dilated. Manometry test examination was normal.

The esophagography showed dilated esophagus with pseudoachlasia appearances. A large soft demarcated mass was present posterior to the carina in the middle third and two other isolated masses which were appeared below it (figure 1 a and 1b)

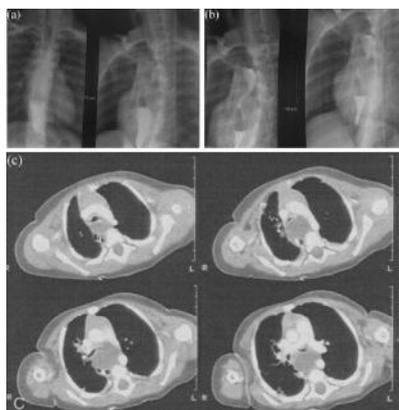


Figure 1: (a,b) Esophagography are showing dilated esophagus and pseudo achlasia appearance with a mass located at the posterior of carina, and stricture of the cardia. (c) CT scan of multiple leiomyoma compressing the carina, left and right bronchi.

CTscan revealed a large size (8×7×7 cm) leiomyoma compressing tracheas left and right bronchi; two other isolated leiomyomas (5×4×4 cm) were found in the lower third of esophagus protruding two centimeters into the stomach (figure 1c) EUS confirmed the findings (Figure 2a and 2b) Trans hiatal esophagectomy was performed while thoracic esophagus was resected thoracoscopically (Figure 2c) The patient tolerated the surgical procedure well and discharged from the hospital on the 14th day on a regular diet. The genes examination of Col 4/A5 and Col4/A6 were negative.

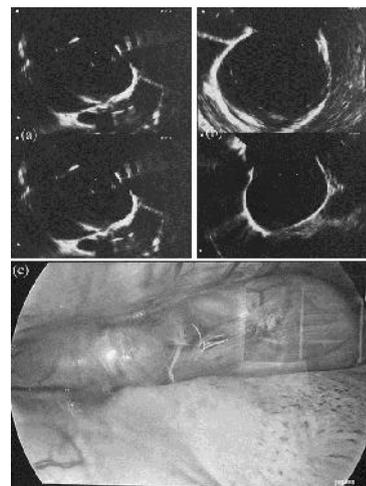


Figure 2: (a,b) EUS are showing dilated esophagus and masses (Multiple leiomyoma). (c) Thoracoscopic appearance of multiple leiomyoma of the esophagus.

The macroscopic appearances (Figure 3a and 3b) and histopathological examinations revealed a giant esophageal leiomyoma at the upper and mid position and two isolated leiomyoma (5×6 cm) were detected at the lower third and cardia with infiltration toward 2-3 cm of the esophagus (figure 3c and 3d) The IHC staining showed strong immunoreactivity for SMA and desmin in all neoplastic cells and negative reactions were seen for CD117, S100, and CD34.

Also, the IHC features were in favor of leiomyoma. Six months of follow up showed the good evolution and gained 9kg. No complication has been reported.

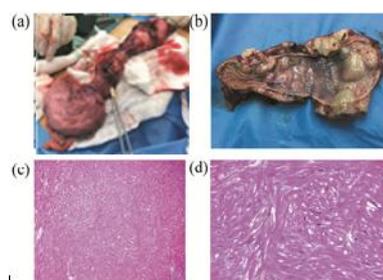


Figure 3: (a,b) Giant esophageal leiomyoma and two isolated discrete leiomyoma of the esophagus at macroscopy (After gastric and esophageal release during THE). (c,d) Histopathology of multiple esophageal leiomyoma with whorled appearance of smooth muscles without atypia, or mitosis (H&E 100, 400).

RESULTS

Considering English literature, six cases with multiple giant esophageal leiomyoma were reported and were all treated by surgery, however, those with small ones or not in multiple giant forms were excluded. Among six cases, one was included manually [7] The demographic features are shown in Table 1. Their ages ranged from 18 to 65 years, with an average of age 37.2 years. All patients were men (Table 1) One patient was asymptomatic [8] and respiratory signs such as acute bronchitis [4] and severe left sided pleuritic chest pain [7] were reported in 2 patients. Mild intermittent dysphagia was reported in 2 cases [9-11] and upper gastrointestinal bleeding with epigastric pain was the circumstance of diagnosis in one patient [12] One patient had recurrent vomiting [6] Four presented patients of Shaffer's study did not have enough data and excluded from this study in terms of results and discussion [13]

In all cases, the esophagoscopy was the reliable detection method describing intact mucosa with presence of a well-defined sub mucosal lesion in two or three parts of the esophagus and extrinsic compression of the esophageal wall. Chest X-ray and CT scan revealed posterior mediastinal masses compressing the

trachea or bronchi, and pulmonary lobes. Marked wall thickening and calcified sub mucosal mass [8], multiple tumor formation of the esophageal wall protruding the cardia and lesser curvature could be the characteristics of CT findings [12]

Esophagography showed lower third stricture, proximal dilated lumen of the esophagus with two large sharply and smooth demarcated mass below the tracheal bifurcation with normal mucosa [7], tumor formation of muscular layer of the esophagus, and rounded crescent filling defects in mid third and lower third of esophagus [8] However, there was no evidence of mucosal infiltration of tumor margins.

Esophagoscopy was negative in one patient [4] Multiple firm sub mucosal and encapsulated mass covered by normal mucosa of the esophagus and cardia were the findings of esophagoscopy in these series. Bleeding ulceration was also seen in one case [12]

EUS was not performed for all cases. Hypo echoic lesions with comet-tail sign was reported due to the presence of sub mucosa calcification [8] Dilated esophagus was reported in only one case [7]

In five cases, diagnosis was retained before surgery (Table 1) Leiomyosarcoma (LMS) was the differential diagnosis of leiomyoma before surgery in only one case [12]

Table I: Demographic characteristics of multiple leiomyoma patients

	Gender & Age	Complaint	Chest X-ray	Esophagoscopy	Esophagography	CT scan	EUS	Bronchoscopy	Diagnosis	Treatment
Aurea 2002	M 42	Acute bronchitis	Post mediastinal mass atelectasis	negative	Structure of Lower esophagus Compressing the left	Post mediastinal mass (15cm)	----	Tracheal compressing	Leiomyoma FNA & biopsy	Right thoracotomy enucleation
Codard JE 1973	M 28	Mild intermittent dysphagia for 3 months duration	-----	Firm submucosal mass in 32 cm from upper incisors	Two large sharply demarcated, crescent filling defect in mid and lower third	-----	-----	-----	Multiple leiomyoma	Thoracotomy 11 & 3.2 cm mass in lower & smaller in middle third (2cm)
Standerfer 1982	M 51	Sever left sided pleuritic chest pain	Large lobulated opacity in left lower hemithorax pushed the left bronchus posteriorly Recurrency	Two esophageal mass in the lower 3 small nodules near inf pulmonary ligament Recurrency	Right deviated distal esophagus & proximal dilation of esophagus Recurrency	Mass Recurrency	-----	Left mainstem bronchus compression	Multiple leiomyoma Recurrence	Left thoracotomy Recurrency: right thoracotomy
Prenzel 2005	M 19	Upper GI bleeding Epigastric pain	normal	Multiple encapsulated tumors in mid/3, cardia, stomach, bleeding ulceration	Tumor formation of muscular layer of the esophagus Narrowing esophagus Extended obstruction of upper 3 of stomach	Multiple tumor formation of esophageal wall Huge mass in lesser curvature	-----	-----	Leiomyoma? Or Leiomyosarcoma? IHC are showing desmin (+) Sm-actin (+) CD34 (-)	esophagogastrectomy
Okugawa 2011	M 65	incidentally	Calcified mass in the posterior mediastinum	-----	Multiple smooth filling defects below the bronchial bifurcation protruding lesions covered by normal mucosa	Marked well thickening & mass calcifications (2.4 cm)	More than 4 hypoecho lesions Comet-tail signs due to submucosal calcifications	-----	- Diagnosis after surgery (multiple leiomyoma)	Esophagectomy (THE)
Rahhal 2009	M 18	Recurrent vomiting	Not stated (NS)	5 polypoid lesions in Mid and upper third	5 polypoid lesions in Mid and upper third	NS	NS	-----	Esophageal leiomyoma	NS

DISCUSSION

In searching of the English studies included in Google Scholar and PubMed databases, six out of ten derived case reports were included for this study. However, four out of ten potential case studies were excluded due to insufficient data considering the diagnostic tools (i.e., CT, EUS or esophagoscopy) and the others that did not

satisfy the criterion for the giant size of esophageal leiomyoma were not of interest.

The incidence of benign tumor of the esophagus is rare and constitutes less than 1% of esophageal tumors. The literature review revealed that lowest incidence of leiomyoma occurred in the esophagus and it was the most common solid benign tumor of the esophagus [1, 10] Multiple leiomyoma occurred in about 0.04% [9] Approximately 90% of esophageal leiomyoma were

seen between 20-60 years old patients. It occurred predominantly in males 2:1. 56%, 33%, 11% of them occurred in the lower, middle, and upper thirds of the esophagus [7] The incidence of recurrence following the surgery was very rare. Only one case of recurrence has been reported [7] The main symptoms were oesophageal including dysphagia, regurgitation, heartburn and rarely vomiting. Respiratory symptoms such as dyspnea, cough, hoarseness, chest pain and substernal pain were reported in patients with large size masses [11, 14] A doubt was generated in one case with large mass that increased the possible malignancy of leiomyosarcoma [12] The tumor may compress the esophageal lumen and cause obstruction with mild to moderate dysphagia. Those are the surgical indications of all patients.

Two theories about the origin of multiple leiomyoma have been proposed. The first one arises from the pre-existing smooth muscles in the muscularis mucosa and vascular muscles or circular muscular layer. In the second theory, tumor is supposed to be resulted from hamartoma arising from hyperplasia of aberrant embryonal muscle tissues.

The second theory could explain multiplicity of esophageal leiomyoma [7] Multiple leiomyomas of the esophagus were also reported in the Multiple Endocrine Neoplasia type I [15]

Although multiple leiomyoma had typical appearances on upper gastrointestinal endoscopy, esophagography, thoracic CT scan and EUS, it may not be diagnosed easily before surgery and esophagoscopy biopsies which are contraindicated in these patients.

Of six presented patients, two were diagnosed after surgery. One patient misdiagnosed with leiomyosarcoma. Two patients were not diagnosed properly before surgery due to the presence of calcification [8] and tumor formation [12] in the mass and this reason was relevant to point out the importance of diagnosis of multiple leiomyoma [8, 12]

In 2006, Pranzel and colleagues reported a case similar to our patient [12]

The patient of this study had an esophagoscopy, esophagography, CT scan of the thorax, EUS study that all of them confirmed multiple leiomyoma. The characteristics of esophagography revealed dilated esophagus with intact mucosa and pseudo achlasia appearances due to severe narrowing of the cardia. Transhiatal esophagectomy was indicated in 4 patients. esophagogastrectomy was performed in one and thoracotomy and enucleation of the leiomyoma was done in the Vth case. The esophagectomy was performed in the VIth patient as in the current. The only difference was in esophageal releasing performance which was performed by video-assisted thoracoscopic surgery (VATS)

Roentgenographic features of multiple leiomyoma on chest X-ray are (i) lobulated projecting masses into the

mediastinum (ii), Obstruction of normal mediastinal shadow (ciii), rarely calcification (i) and (ii) signs were seen in the presented case of this article .

Moreover, esophagography features are (i) smooth rounded or lobulated filling defects without mucosal irregularities (ii), no infiltration at the tumor margins (iii), tumor projection beyond the esophageal wall (iv), The freely mass movement with swallowing and peristaltism (v), multiple narrowing of the esophageal lumen (vi), There is no evidence of obstruction to the barium swallowing (vii) Mucosal fold flattening and stretching over the mass can produce smear defect appearance (viii), Normal mucosa, (ix) Sharp demarcation on tumor edges and normal mucosa, (x) Presence of a shelf in the lumen with abrupt angulations at the both tumor margins, (xi) Splitting of the barium column on either side of tumor can produce a forked-stream appearance (xii) Normal esophageal motility on fluoroscopy, (xiii) Esophageal lumen dilations can produce pseudo-achlasia appearances [9, 13] . (i - xiii) and the radiographic signs were preset in our presented case. Indeed, bronchoscopy may also have a role in diagnosing malignant tumors of the esophagus invading or compressing the tracheo-bronchial tree [4, 7]

The indications for resection are based on symptoms, tumor size > 5 cm, growing tumor and presence of malignancy signs (rare condition) [15] In the cases of benign leiomyoma of the esophagus, biopsy was not recommended and indeed EUS-FNA was only indicated to rule out malignancy (e.g., leiomyosarcoma) [16]

Multiple leiomyoma of the esophagus appear macroscopically as well demarcated nodules with capsules. These nodules are covered with normal mucosa. Microscopically, it has low cellularity, increasing growth from interlaced smooth muscle cells and hypovascularity [17, 18] Today, the possibility of endoscopic resection of esophageal as therapeutic option has been reported for example by Tan et al [19] And, it has been recommended for most of those with small leiomyomas less than or equal to 3.5 cm [20], but the procedure cannot be beneficial due to its difficult nature and high rates of complications [21-24] Similarly, it cannot be applied for giant ones.

Multiple leiomyoma should be differentiated from diffuse leiomyomatosis of the esophagus. Diffuse leiomyomatosis of the esophagus is not encapsulated and presents considerable interstitial hypertrophy with lymphatic and plasma cell infiltration of whole esophageal muscle layer rather than discrete tumor nodules. It commonly occurred in the young woman and occasionally associated with Alport syndrome which is associated with larger deletions and rearrangement of COL4/A5 and COL5/A6 genes [8] Hematuria, hearing loss and ocular abnormalities are the common symptoms of diffuse leiomyomatosis [18, 12] And hence, this review article along with the presented case can be of significance and valuable to be widely known

not only in the gastroenterologist but also in the cardiologists or pulmonologist.

CONCLUSION

EUS, thoracic CT scan, esophagography and upper gastrointestinal endoscopy should be strongly considered for preoperative management of multiple giant leiomyoma.

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