**Complete Title :** Esophageal leiomyomatosis: a case report and review of the literature

**A short title use as a running head :**

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**Abstract: Do not use abbreviations, footnotes, or references. Limit: 200 words. Submit 3 to 5 key words using standard Index Medicus terminology at the bottom of the abstract**

**Introduction ( 200 words )**

Diffuse leiomyomatosis of the esophagus is

**Keywords ( 3-5 words ) :**

**( 1 ) introduction**

Esophageal Leiomyomatosis ( EL ) is **defined as a diffuse form of marked hypertrophy of the muscular layer of the esophagus** and was originally described by Fernandes in 1975★. Herein we present a case of EL in a 11-year-old girl who was successfully treated by a thoracoscopic total esophagectomy in a prone position. The clinical and radiological feature and the optimal treatment strategy of this rare entity is discussed on the basis of a review of the literature.

**( 2 ) Case report**

A 11-year-old girl who is suffering from dysphagia and post-meal vomit since 4 years old admitted in the diagnosis of pneumonia. She had a past history of recurrent pneumonia at the age of 1 and 7 year and pointed out cough during sleep by her parent. She didn’t have difficulty in dietary intake and history of failure to thrive. Her younger sister underwent operation for esophageal atresia in neonatal period, but anyone in her family didn’t have similar medical history. She was transferred to our hospital for the finding of Chest X ray showing widened and distorted shadow in mediastinum suggesting esophageal tumor.

Blood test showed just only mild leukocytosis and other results were within normal limit including tumor markers: carciｎoembryonic antigen, square cell carcinoma related antigen, neuron-specific enolase and soluble interleukin-2 receptor. Contrast enhanced CT showed massive and multiple tumor at lower esophagus and wall thickening from upper esophagus to cardiac part of stomach. Oral side of esophageal tumors is extended and filled with fluid. (Fig. X) Barium contrast radiography showed an irregular esophageal wall and weakened peristalsis of lower-middle esophagus. Holded-up barium indicated stenosis at the lower esophagus and shaped Bird's beak sign like achalasia. (Fig. X) Endoscopically, diffuse elevated lesions covered by normal mucosa suggesting submucosal tumor were identified in whole esophagus including fornix of stomach. (Fig. X) Endoscopic Ultrasonography showed muscle layer of esophagus was significantly thickening from 8mm at midlle esophagus to 23mm at lower esophagus. (Fig. X). She diagnosed clinically as esophageal leiomyomatosis from these specific imaging findings.

We decided to perform subtotal esophagectomy because relapse of symptoms occurred frequently after endoscopical approach and palliative surgery according to previous reports. We started operation in a complete prone position on magic bed® under differential lung ventilation and inserted five trocars: third, fifth, and seventh right intercostal space on posterior axillary line and seventh and ninth on inferior angle of the scapular line. (Fig. X) We could clear view around posterior mediastinum with complete prone position could make lung lean forward to provide a clear view of posterior mediastinum.　 Esophagus was dissected at the point of 6cm from upper edge of thoracic esophagus by Ethelon flex® 45mm.

Subsequently the patient was placed in lithotomy position and five abdominal trocars were inserted. (Fig. X) Mobilization of the stomach, separation of adhesion around cardia and dissection of right crus of diaphragm were performed. Distal esophagus was tugged into abdomen and retrieved through a trans-umbilical mini laparotomy. Esophageal proximal stomach resection was performed extracorporeally and a gastric tube was created, then conducted to cervical wound through mediastinum and anastomosed to proximal esophagus by Delta-shaped gastroduodenal anastomosis. Right crus of diaphlagm was repaired, Other antireflux procedure was not added. Operation time was 7 hours and 39 min and loss of bleeding was 56g.

Macroscopically, the esophagus and stomach thickened by confluent cream-colored nodules and thickness measured up to 40 mm in lower esophagus (Fig. X). Microscopically, mucosal membrane and muscularis mucosae were normal. However, smooth muscle cell was outgrowing diffusely like leiomyomas and thickening partially in making nodular pattern. It was more evident that the inner muscular layer of the muscularis propia were thickening, wheareas the outer layer were only moderately increased. Mitoses and typical cells were absent. Distal margin was negative, but Proximal one was positive. In immunostaining, Vimentin. Alpha-smooth muscle antigen and Caldesmon were positive, on the other hand, Myoglobin, CD34, c-kit, S-100 and HMB45 were negative.

The post operative course was uneventful and the patient was discharged on the 9th post operation day. She sometimes finds some regurgitation during sleep but it is under control. However, constipation because of rectal leiomyomatosis is her main clinical problem and was controllable by laxative agent and enema.

The presented case showed an uneventful recovery after surgery, and was discharged on the ~th postoperation day. She remains uneventful three years after the surgery.

**( 3 ) Discussion**

**Material and Methods**

We searched MEDLINE/PubMed using the keyword “esophageal lyomyomatosis” within the period 1975 to January 2015. Details of the background of the patients, symptoms, treatment strategy and outcome were extracted. The relevance between treatment options and outcome was statistically analyzed using indicated methods.

**Result**

A full review of the literature revealed 60 reports on 140 patients which were diagnosed EL, including our case, in the English literature The age at diagnosis ranged from 1 to 89 years (median age: 24 years) and the ratio of male to female was 0.69. Pediatric patients less than 19 years accounted for 31.1% of the cohort. Dysphagia ( 70.8% ) and regurgitation ( 35.4% ) representing obstruction at the esophagus commonly appeared as the symptoms at diagnosis, followed by respiratory symptoms ( 26.6% ). The interval from the onset of symptoms to the diagnosis of EL was generally long, with a median of 3.5 years (range 0 ~ 50 years) .The delay in diagnosis is presumably caused by the rareness of the entity and the slow progression of the symptoms.

Extra-esophageal leiomyomatosis and Alport’s syndrome are the two major conditions that are known to be associated with EL. Extra-esophageal leiomyomatosis was identified in 36 patients ( 24.5% ), located in female genital lesions including uterus and vulva in 21 patients (14.2% ), rectum in 12 patients (8.2% ) and trachea or bronchi in 5 patients (3.4%). Alport’s syndrome, which is characterized by nephropathy, ocular abnormality and sensorineural deafness resulting from the mutation of gene for encoding typeIV collagen, COL4A5, was genetically proven in twenty nine patients ( 19.7% ) , whereas 37 more patients ( 25.2% ) represented at least one symptom of the triad.

The middle and lower portions of the esophagus were involved in all patients without exception. The lesion extended further within the esophagus variously, in a continuous fashion.. Cervical esophagus was involved in 23.4%, whereas the cardia and the gastric fundus was involved in 59.4%.

10 cases (7.1%) were initially misdiagnosed as esophageal achalasia. Features of barium swallowing test findings in EL, such as proximal dilatation, smooth narrowing at lower part and abnormal peristalsis, mimic those of achalasia, and the endoscopic findings are not specific. Computer tomography test and endoscopic ultrasonography are reliable tools for accurate diagnosis, demonstrating the bulky muscular hypertrophy of the esophageal wall, which is specific for EL.

Initial operative procedure and outcome of 83 patients with clear description were reviewed ( Fig.1 ) . Seventy-seven patients underwent surgery, including 60 esophagectomies, 12 myotomies, 3 leiomyomectomies and 2 fundoplications. The number of relapsed cases after each procedure was 4, 9, 2 and 1, respectively. There were only ~ thoracoscopic esophagectomies, our case being the first to be performed with the patients in a prone position. The relapse rate in the esophagectomy group ( 6.7% ) is significantly lower than in the latter three groups ( 70.6%, p=0.000002, Fisher’s exact test ). The establishment of a correct diagnosis and the choice of esophagectomy are essential for the prompt relief of symptoms.

**( 4 ) Conclusion**

The diagnosis of EL should be carefully made by multimodal imaging approaches with attention to the extent of disease and extra-esophageal leasion. The optimal choice of treatment is radical esophagectomy, and there are limited advantages in palliative procedures. Thoracoscopic esophagectomy in a prone position has been increasingly used in esophageal cancer surgery, owing for its better exposure of the operative field. The procedure may particularly be beneficial for EL, since the tumor tends to be bulky, and thus interferes with the operative view exposure in thoracoscopic surgeries.

( 5 ) Reference