

Case Report

Esophageal tuberculosis presenting as a submucosal tumor

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Abstract: Introduction: Esophageal involvement by tuberculosis is quite rare and the diagnosis can be difficult. In this article, we report a case of esophageal tuberculosis in a patient who at first presented as a submucosal tumor. Methods: The diagnostic process of the patient was described in this article. And an online search was performed in PubMed and Web of Science databases for articles describing the information of esophageal tuberculosis. Results and Conclusions: Most esophageal tuberculosis cases are secondary to the adjacent sites. Endoscopic features mainly include two types, ulcers and extrinsic bulge, which may be two stages of lesion. EUS combine biopsy can help diagnosis. In cases which are difficult to diagnose, the endoscopic mucosal resection combined with PCR test of the tissue can increase the positive rate.

Keywords: Esophageal tuberculosis, endoscopic manifestation, diagnostic process

Introduction

Gastrointestinal tuberculosis is often seen in countries with high prevalence rates of tuberculosis, the most common location being the ileocecal junction. Esophageal involvement is rare, constituting approximately 0.3% of gastrointestinal tuberculosis cases. Most esophageal tuberculosis cases are secondary to pulmonary tuberculosis or mediastinal lymph node tuberculosis. Primary esophageal tuberculosis is rarely reported. Endoscopic characteristics of esophageal tuberculosis can be diverse, which makes the diagnosis difficult. Here we report a case of esophageal tuberculosis in a patient who at first presented as a submucosal tumor.

Clinical summary

A 48-year-old woman presented with a 1-month history of swallowing discomfort and foreign body sensation in the pharyngeal area. She had no other symptoms such as cough, fever, fatigue, weight loss, or night sweating, and also denied any history of tuberculosis. Her medical history was unremarkable, and no positive sign was found on examination. Serum chemistry was within normal limits. Tests for infectious diseases were all negative, including hepatitis B, hepatitis C, HIV, and syphilis.

Chest contrast enhanced computed tomography (CECT) showed calcification spots of both lower lungs and subcarinal lymphadenectasis in the posterior mediastinum, also with calcification (**Figure 1**).

Upper endoscopy showed a protruding lesion covered by normal mucosa at 30 cm from the upper incisor (**Figure 2**). An endoscopic ultrasonography (EUS) scan revealed a heterogeneous hypoechoic lesion in the fourth layer, which we suspected an esophageal stromal tumor or a leiomyoma (**Figure 3**). To relieve the patient's swallowing discomfort, we decided to initiate surgery to remove the "tumor". Since the lesion appeared to be quite large and EUS indicated its origin as the fourth layer, we scheduled submucosal tunnel endoscopic resection (STER) as previously performed [1].

After obtaining the patient's informed consent, we arranged the endoscopic surgery, during which purulent secretion was seen before we incised the mucosa (**Figure 4**); we immediately realized that the lesion was not a tumor but a submucosal abscess, although how it was formed remained unknown. We remembered the calcification spots on the lung and subcarinal lymphadenectasis in the posterior mediastinum. From the two points of view, we made the

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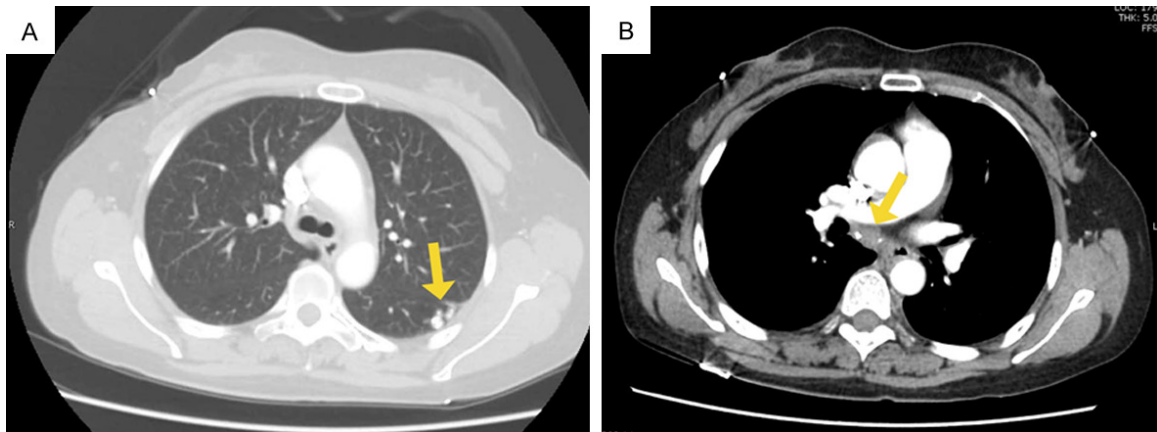


Figure 1. A. Chest CECT showing calcification spots of both lower lungs (arrow showing the calcification of lung). B. Chest CECT showing subcarinal lymphadenectasis in the posterior mediastinum (arrow showing the enlarged lymph node with calcification).

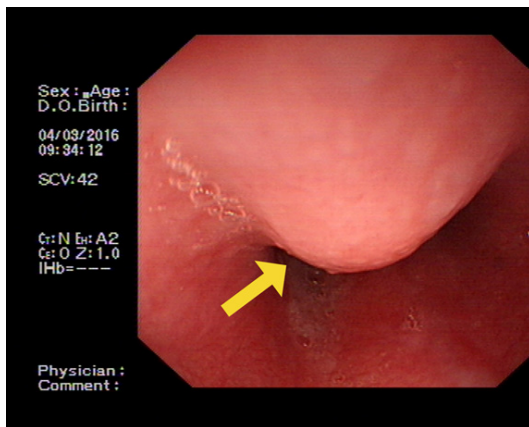


Figure 2. Endoscope showing a protruding lesion covered by normal mucosa at 30 cm from the upper incisor (arrow showing the lesion).

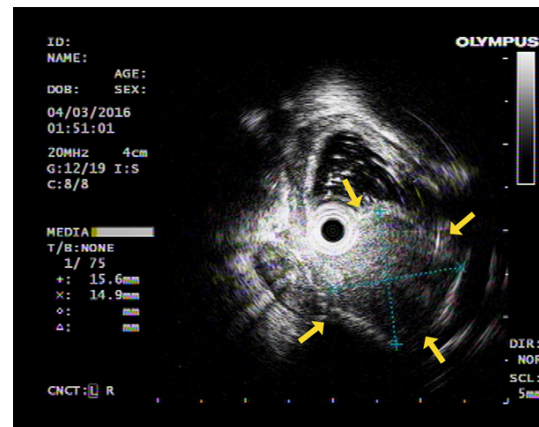


Figure 3. Endoscopic ultrasonography revealing a heterogeneous hypoechoic lesion in the fourth layer of the esophagus (arrow showing the lesion).

speculation on the possibility of tuberculous abscess. To obtain pathogenic evidence and increase the positive rate as much as possible, we performed endoscopic mucosal resection with a hook knife and retrieved a large specimen. H&E staining of the tissue showed chronic inflammatory cell infiltration and proliferation of granulation tissue (**Figure 5**).

After surgery, the patient's swallowing discomfort was markedly relieved. A check for T-SPOT was arranged, which proved positive. A further acid-fast bacilli stain also gave a positive result (**Figure 6**).

Given the results of our investigations, we reached a diagnosis of esophageal tuberculosis. The patient received anti-tuberculosis treatment comprising isoniazid, rifampin, pyra-

zinamide, and ethambutol for a duration of 6 months. The follow-up endoscopy 2 months after the endpoint of treatment showed no abnormality (She did the endoscopy in local hospital, so we did not get a picture).

Discussion

Esophageal involvement by tuberculosis is quite rare, even in countries with high prevalence rates of tuberculosis. Studies indicate that esophageal tuberculosis constitutes about 0.14-0.15% of all tuberculosis-related deaths based on autopsy studies [2] and 0.3% of gastrointestinal tuberculosis cases [3]. Most cases are secondary to tuberculosis of adjacent sites, such as pulmonary tuberculosis or tuberculosis of mediastinal lymph nodes. Primary esopha-

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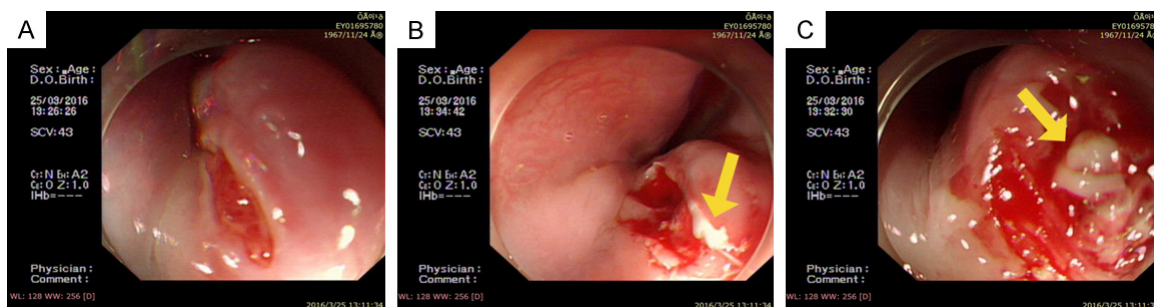


Figure 4. A. During endoscopic surgery, the mucous membrane ruptured and purulent secretion was seen before incision. B. More purulent secretion was seen after the incision (arrow). C. After we did the endoscopic mucosal resection, the purulent secretion was clearer (arrow).

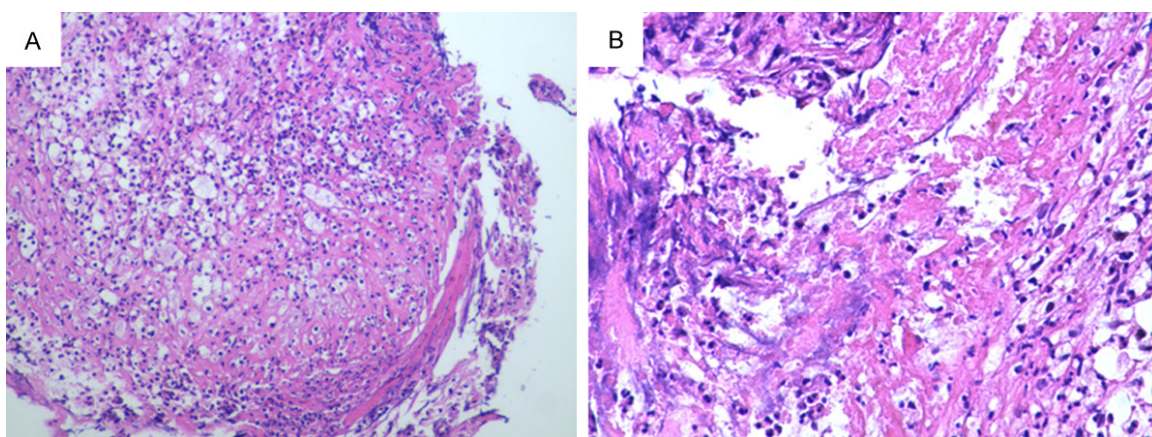


Figure 5. A. H&E staining showing granulation tissue proliferation ($\times 100$). B. Necrosis of tissue and granulation proliferation ($\times 200$).

No.	Item	Result	Normal value
1	T-SPOT	Positive(+)	Negative
2	γ -IFN value	103.38 \uparrow	0--14pg/ml

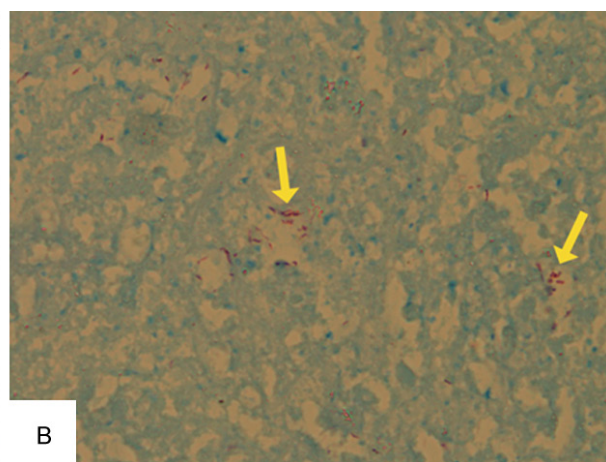


Figure 6. A. T-SPOT result was positive. B. Acid-fast bacilli stain of the tissue was positive (arrow shows *Mycobacterium tuberculosis*).

geal tuberculosis is rarely reported. Studies have shown that the most common location of involvement is the middle one-third of the esophagus [4], which may be associated with

adjacent mediastinal lymph nodes. Tuberculosis can be spread either through direct extension or through hematogenous and lymphatic routes (mostly retrograde). In our case the patient

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Table 1. Clinical and endoscopic manifestations of esophageal tuberculosis cases for the recent five years

Country/ Time	Age/ Gender	Clinical manifestation	General symptoms	Endoscopic manifestation	Location of lesion in the esophagus	EUS manifestation	Initial impression
China 2017	59/M	epigastric pain	negative	bulging lesion	middle	homogenous hypoechoic lesion interrupted structure of esophageal wall	—
India 2017	60/F	dysphagia	loss of weight and appetite	ulcerative lesion	distal	—	—
France 2016	35/M	abdominal pain constipation, dysphagia	weight loss	bulging lesion	middle	enlarged mediastinal lymph nodes infiltrating esophageal wall	—
India 2016	30/F	dysphagia	loss of weight and appetite	polypoidal and ulcerated lesion	middle	asymmetrical thickening of esophageal wall with loss of the wall stratification	esophageal cancer
China 2015	65/F	Dysphagia retrosternal pain	negative	bulging lesion at first, then turned to an ulcer	middle	hypoechoic lumps with heterogeneous internal echo	submucosal tumor
India 2013	24/M	upper abdominal discomfort, odynophagia	negative	longitudinal esophageal friable ulcers	middle	—	—
China 2013	32/M	chest pain dysphagia	mild fever, cough night sweating	protruding lesion with normal mucosa	middle	hypoechoic lesion in the fourth layer	stromal tumor
Malay 2012	73/M	Constipation abdominal pain	weight loss	excavated ulcer	proximal	—	malignant tumor
Malay 2012	45/M	retrosternal discomfort laryngopharyngeal reflux	weight loss	two ulcerated lesions	proximal	—	squamous cell carcinoma
Somalia 2012	36/M	thoracic tightness	negative	ulcerating lesion	—	—	—
India 2012	65/F	dysphagia	loss of weight and appetite	a punched-out ulcer with elevated edges	middle	enlarged lymph nodes with calcification eroding the esophageal wall	—
India 2012	37/M	dysphagia	negative	a bulging lesion	distal	an intramural cystic lesion	malignant tumor

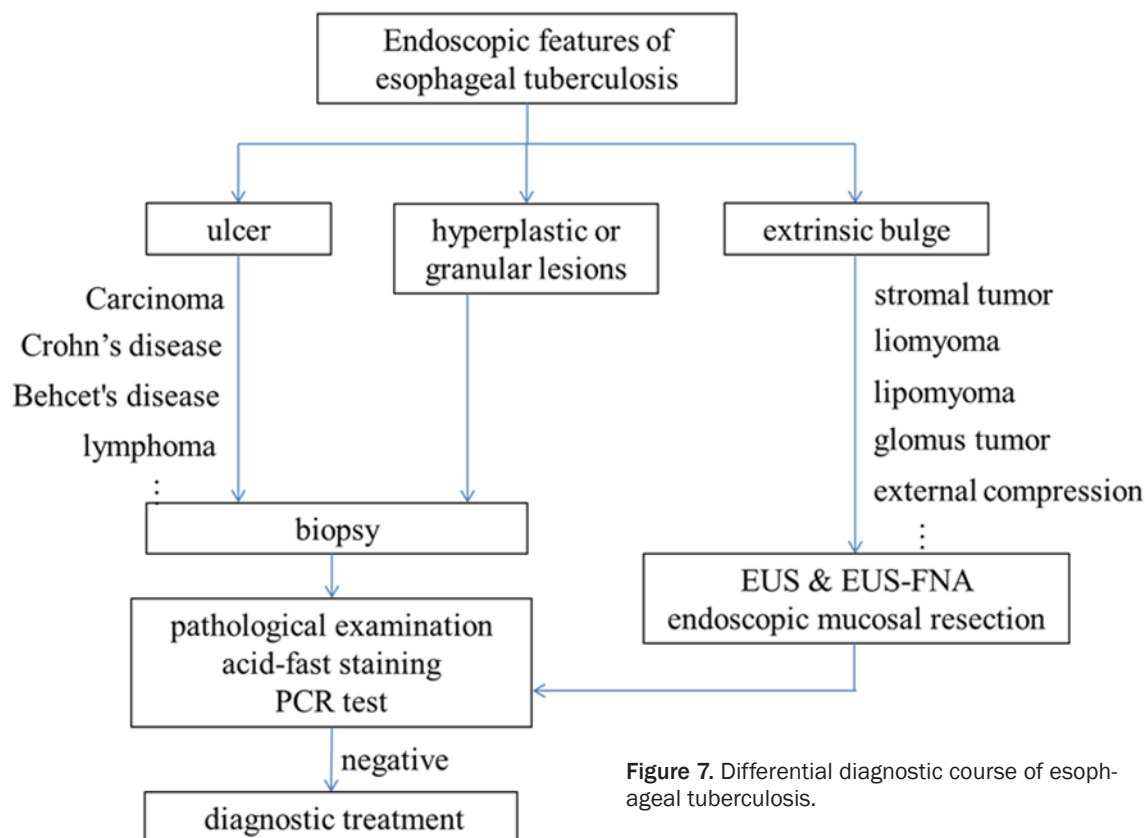


Figure 7. Differential diagnostic course of esophageal tuberculosis.

denied a history of pulmonary tuberculosis, but as a computed tomography scan showed calcification spots of both lower lungs and subcarinal lymphadenectasis in the posterior mediastinum, also with calcification, we suspected that she was once infected with tuberculosis without knowing it, with the esophageal lesion possibly being secondary to mediastinal lymph node tuberculosis.

Clinically esophageal tuberculosis mainly presents with dysphagia, which is the most frequent symptom, occurring in nearly 90% of cases as noted by others [5]. Other symptoms such as upper gastrointestinal bleeding, odynophagia, and retrosternal pain have also been reported. In addition, some patients may also have low-grade fever, weight loss, and poor appetite, common occurrences in both tuberculosis and tumor, making it sometimes difficult for the clinician to differentiate. In some serious cases, esophagus-tracheal fistula can also occur, leading to choking on swallowing and aspiration pneumonia in some patients.

The diagnosis of esophageal tuberculosis is difficult. Endoscopic features can be diverse but mainly include two types, ulcers and extrinsic bulge. According to Puri's report, the ulcers are usually linear, measuring 1.5-3 cm, and non-circumferential, with slightly infiltrated and elevated edges and a base with grayish exudates or granulation tissue [6], which should be differentiated with carcinoma and Crohn's disease of the esophagus. The extrinsic bulge, always with overlying normal mucosa, may be mistaken as submucosal tumor in many cases. Hyperplastic or granular lesions have also been reported [7]. Regarding our case, we speculate that the extrinsic bulge and ulcers may represent two stages. At the first stage the lesion manifested as a submucosal tumor, but before we were able to undertake the endoscopic surgery the lesion ruptured, leading to the purulent secretion visible to us that showed the natural course of the disease. The ulcers then formed secondarily to the lesion rupture, representing the second stage. A bulging lesion with an ulcer atop it, which can also be seen clinically, may

represent an intermediate stage. On the other hand, lesions presenting firstly as ulcers may also develop into hyperplastic or granular lesions because of the chronic persistent inflammation. Therefore, the natural course of esophageal tuberculosis can lead to diverse endoscopic approaches and outcomes.

EUS can be used to identify a submucosal tumor. It can not only evaluate the esophageal wall and define the exact origin of a submucosal lesion but can also help observe the mediastinal lymph nodes, thus significantly improving the accuracy of diagnosis. EUS evokes different echoes from which we can make a preliminary inspection of the lesion. An earlier study described EUS features of lesions of esophageal tuberculosis and found that extrinsic bulge lesions of the esophagus usually present as heterogeneous or homogeneous hypoechoic masses in the esophageal wall, with incrassation, interruption of esophageal adventitia, and mediastinal lymphadenitis [8]. However, unlike submucosal tumors such as stromal tumor or leiomyoma, most tuberculous lesions have hyperechoic spots and strips in the parenchyma, and can involve the whole esophagus wall, which shows different characteristics. EUS is also helpful in observing mediastinal lymph nodes. Rana et al. reported that mediastinal tubercular lymphadenopathy usually appeared as patchy anechoic or hypoechoic areas or hyperechoic foci in the mediastinal lymph nodes [9]. The most common location of the involved lymph nodes was the subcarinal region, which is probably why tuberculosis mainly affects the middle third of the esophagus. EUS is also able in some cases to detect esophageal lesions conglutinated with the mediastinal lymph nodes. Here we summarized the clinical and endoscopic manifestations of esophageal tuberculosis cases for the recent five years (**Table 1**).

Apart from endoscopy, biopsy can help to define the properties of lesions. Ultrasound-guided fine-needle aspiration (EUS-FNA) is widely used to obtain tissue in deep locations. For lesions presenting as ulcers, endoscopic biopsy can usually obtain valuable diagnostic tissue, although for lesions presenting as a submucosal tumor the positive rate of conventional biopsy is low. Under these circumstances, EUS-FNA is a helpful tool because it can get the biopsy from both the lesion itself and the adjacent lymph nodes. A combination of endoscopic

biopsies alongside EUS-FNA of the lymph nodes is better than either procedure alone. However, the acid-fast bacilli stain always provides a low positive rate, in order to increase the positive rate, the endoscopic mucosal resection combined with PCR test of the tissue should be considered when necessary.

The natural course of esophageal tuberculosis makes the endoscopic features diverse, which leads to varied differential diagnoses. When it presents as an ulcer lesion it should generally be distinguished from Crohn's disease, esophageal carcinoma, and Behcet's disease. On such occasions biopsy (or endoscopic mucosal resection) is always worthwhile. When the disease presents as an extrinsic bulge, such as a submucosal tumor, it should be distinguished from other kinds of submucosal tumors (e.g., stromal tumor, leiomyoma, lipomyoma, or glomus tumor). In such cases, EUS and EUS-FNA is the preferred option to help reach a diagnosis. If the lesion was highly suspected of tuberculosis, but acid-fast bacilli stain or PCR test of lesion shows negative, then a diagnostic treatment should be considered (**Figure 7**).

Treatment of esophageal tuberculosis depends on the presentation of the disease. For most patients, the standard chemical therapy including isoniazid, rifampicin, pyrazinamide, and ethambutol usually leads to a complete cure. However, for patients with serious complications such as esophagus-tracheal fistula, severe gastrointestinal bleeding, and high-grade dysphagia, surgery should be considered.

Conclusion

Esophageal involvement by tuberculosis is quite rare; most of them are secondary to the adjacent sites. The natural course of esophageal tuberculosis can lead to diverse endoscopic features, but mainly include two types, ulcers and extrinsic bulge, which may be two stages of lesion. EUS combine biopsy can help diagnosis. In some cases which are difficult to diagnose, the endoscopic mucosal resection combined with PCR test of the tissue can increase the positive rate.

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Disclosure of conflict of interest

None.

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