JOURNAL OF CLINICAL CASE STUDIES, REVIEWS AND REPORTS

Dysphagia as the only Manifestation of Esophageal Tuberculosis: Atypical Presentation and Review of Literature

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Submitted: 29 Aug 2023 Accepted: 04 Sep 2023 Published: 11 Sep 2023

Citation: Mohammad Al Yaseen1, Moamena El Matbouly1,2*, Ehab Massad1, Ahmed Suliman1, Ahmed Al Bahrani1 (2023). Dysphagia as the only Manifestation of Esophageal Tuberculosis: Atypical Presentation and Review of Literature. J of Clin Case Stu, Reviews & Camp; Reports 2(1)., 01-07.

Abstract

Introduction: Tuberculosis is a disease that can affect many organs of the human body. tuberculosis (TB) infection rarely manifests itself solely in the digestive tract; in fact, the gastrointestinal tract ranks as the sixth most common site of extrapulmonary TB. Moreover, the involvement of the esophagus by tuberculosis is extremely uncommon. Our goal is to share our findings and provide an in-depth review of the literature on the pathophysiology to provide a better understanding of diagnostic techniques and guidelines for the evaluation and treatment of Esophageal tuberculosis (ET).

Case summary: We present a case of esophageal TB in a 37-year-old male. He presented with progressive dysphagia with weight loss. His endoscopy showed a large polypoidal mass 30-34 cm from incisors with avid uptake in PET scan in keeping with suspected malignancy. The patient underwent Endoscopic ultrasound that showed a mass arising from 2-3rd layer of the esophagus and the mass was biopsied 5 times prior to confirming the diagnosis of esophageal TB. He received 9 months of quadrable TB treatment and had complete resolution of symptoms and his follow-up endoscopy showed regression of the mass.

Conclusion: Isolated esophageal TB is a rare entity that can mimic esophageal cancer in imaging studies and endoscopy. Anti-TBN medication leads to complete resolution of the infection as well as the associated symptoms of dysphagia with excellent prognosis. If the diagnosis is made correctly, it can save the patient from major surgical resection.

Keywords: Esophageal Tuberculosis, Misdiagnosis, Medically Curable, Endoscopic Ultrasound, Esophageal Cancer

Core Tip

Esophageal and intestinal tuberculosis are very rare forms of tuberculosis. There are only a few cases of ET complicated by intestinal tuberculosis. In our case, the patient had progressive dysphagia but no other major medical history. The esophageal lesions were positive for M. tuberculosis.

The patient responded satisfactorily to antimicrobial therapy. This case highlights the need for ET to be suspected in patients at high risk of tuberculosis when presenting with dysphagia.

Introduction

Tuberculosis (TB) predominantly affects the respiratory tract; it rarely presents in the esophagus alone. TB of the gastrointestinal tract is usually secondary to current or previous TB infection in other sites, mainly respiratory tract infection [1]. Eleven percent of individuals with extrapulmonary TB had gastrointestinal (GI) involvement, with the terminal ileum, cecum, and peritoneum being the most common sites [2].

Other structures/organs such as the mediastinal lymph node, lungs and spine are often involved in these patients. The most common presentations are dysphagia (dysphagia), odynophagia, hematemesis, and constitutional symptoms. Due to the rare nature of the condition and the lack of a specific presentation, it is sometimes misdiagnosed as malignancy and only a small number of patients may need surgery. The disease is medically curable; therefore, it is essential to make all efforts to diagnose the pathology with non-surgical diagnostic modalities in suspected cases to save patients from the trauma of major surgical resection. Surgical intervention is indicated for failed medical therapy and complications [3].

Characteristic histopathology includes caseating granuloma but is infrequent. The presence of acid-fast bacilli (AFB) positivity or positivity of other microbiological tests (culture, polymerase chain reaction, i.e., PCR-based test) may provide specificity but the yield is low [5].

The role of EUS in the diagnosis and monitoring of these pa-

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tients is growing as EUS can characterize the lymph node lesion in these patients as well as providing tissue for cytogenetic and microbiological analysis. Patients respond well to antitubercular drugs and rarely require endoscopic or surgical intervention [6].

Methods and Results

Systematic search of the literature was performed on PubMed and Medline from 1980 to 2022. Electronic searches were undertaken in PUBMED and MEDLINE using the MeSH terms "esophagus" in combination with "tuberculosis", "tuberculous", "tubercular", "miliary tuberculosis", "disseminated tuberculosis", "tuberculosis in immunocompromised patients", "complications", "management". One author independently reviewed the articles. Table 1 summarizes the case studies included in the review of literature.

Case Summary

37-year-old male presented to emergency department with progressive dysphagia with odynophagia and weight loss. The patient reported 10 kg weight loss in the last year. On review of systems, the patient denied chest pain, dyspnea, productive cough, nausea, vomiting, hematemesis, melena, hematochezia, altered bowel habits, fever, night sweats or anorexia.

Routine laboratory work-up was done which turned out to be normal. The chest X-ray was unremarkable. He had an upper endoscopy that showed large polypoid mass at 30-34 cm from incisors, extending for about 4 cm as shown in image 1:







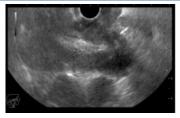
Image 1: Pretreatment Upper Endoscopy: Large Polypoid Mass At 30-34 Cm from Incisors, Extending for About 4 Cm.





Image 2: Post Treatment Upper Endoscpy: Esophagus: The Mass Has Regressed Significantly, Fibrotic Base Noticed

Multiple biopsies were taken at the index endoscopy that failed to reveal any diagnosis, so he underwent endoscopic ultrasound (EUS) that showed a mid-esophageal hypoechoic lesion arising from the 2nd layer of esophageal wall with a lobulated appearance. Although the lesion is well contained in most parts, it is seen to breach the muscularis and invade the serosal plane in one aspect (locally invasive). A 7 mm paraoesophageal lymph node appreciated. The main lesion was hypoechoic and homogenous and originating from layer 2-3 as it is shown in image 3.



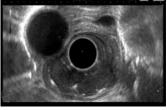


Image 3: Pre -Treatment Endoscopic Ultrasound: A Mid Esophageal Lesion Appreciated on Endoscopy. The Echoendoscope Showed a Hypoechoic Lesion Arising from the 2nd Layer of Esophageal Wall with A Lobulated Appearance. Although The Lesion Is Well Contained in Most Parts, It Is Seen to Breach the Muscularis and Invade the Serosal Plane in One Aspect (locally invasive). A 7 Mm Paraoesophageal Lymph Node Appreciated. The Main Lesion Was Hypoechoic and Homogenous and Originating from Layer 2-3

Multiple biopsies were taken during the EUS that also failed to reveal the pathology and acid- fast bacilli test came negative.

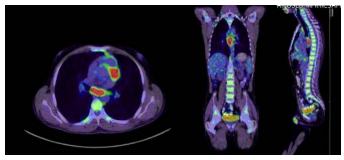


Image 4: pretreatment PET scan: There is intense uptake (SUV max 19.6) projected to a 4 cm long section of the mid esophagus. Intense hypermetabolism in the mid esophagus is highly suspicious for malignancy Small separate uptake is noted with 1 cm size in the right subcarinal region. Minimal focal uptake projects to the right lung hilum.

Image 4 showed an intense uptake (SUV max 19.6) projected to a 4 cm long section of the mid esophagus. Intense hypermetabolism in the mid esophagus is highly suspicious for malignancy. Small separate uptake is noted with 1 cm size in the right subcarinal region. Minimal focal uptake projects to the right lung hilum. After 5 trials of trying to establish a diagnosis with upper endoscopy and EUS, he underwent rigid esophagoscopy and obtained multiple biopsies and the confirmative diagnosis of tuberculosis was defined by isolation of tuberculous mycobacterium and staining of acid-fast bacilli with Ziehl-Neelsen method from the surgical biopsy specimens.

Antituberculous regimens were applied according to the results of drug-sensitive tests. The patient took quadrable antituberculous medications for 9 months. His symptoms subsided, and he was able to eat normally and gain weight. He had a follow up upper endoscopy in image 2 that showed that the mass has regressed significantly, fibrotic base noticed. This was also evident in the PET CT scan in image 5 that showed complete metabolic resolution of the esophageal mass as well as the hilar lymph nodes.

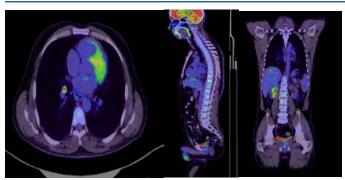


Image 5: Post treatment PET scan: complete metabolic resolution of the esophageal mass as well as the hilar lymph nodes.

Discussion

Tuberculosis of the gastrointestinal tract is the 6th most common site of infection in patients with extrapulmonary tuberculosis (EPTB). The involvement of the esophagus with tuberculosis infection is uncommon. The majority of reported cases of gastrointestinal tuberculosis are in Asia. The incidence of EPTB in the esophagus accounts for less than 2% of total ECT cases, about 2.8% in gastrointestinal EBTB cases, and about 15% of patients who died of EPTB [3,4].

Symptoms of Esophageal TB (ET) include dysphagia, odynophagia, chest pain, low-grade fever, and weight loss. ET usually occurs in the middle third of the esophagus at the level of the carina [4]. Our patient was presented with a mass in the middle third of the esophagus in keeping with the most common location of EPTB.

The diagnostic approach is contingent upon the morphological profile of the lesions. Patients with mucosal lesions, such as ulcers, are treated with endoscopic biopsy. Patients with sub-mucosal, or subcutaneous, lesions should be treated with endoscopic ultrasonography (EUS). EUS not only allows for a clear identification of site of involvement, but also allows for tissue collection for microbiological and/or cytological examination. Thickening of the eosinophilic wall and discontinuation of adventitia may also indicate its diagnostic potential [27]. EUS is a great tool for demonstrating lesions on the esophageal walls, mediastinal nodes, and other anatomical structures of the chest. In one retrospective study of 32 patients with esophageal tuberculosis, EUS demonstrated enlarged lymph nodes in 18 of the 32 cases, and lymphadenopathy was most common in the subcarinal region [10].

Diagnosis is often delayed due to the rarity of the disease, and lack of specific symptoms. Up to 3/4 of patients experience delayed evaluation and management. Up to 20 % of cases are diagnosed after major surgery on histology examination. Clinical presentation, laboratory features, and imaging studies are

nonspecific; definitive diagnosis requires demonstration of microtumor mass biopsy (MTB) on histopathology examination. Therefore, it is essential to take image /endoscopy guided tissue for histological evaluation for early diagnosis. Isolated or primary esophagus TB is even more rare and challenging to diagnose [26]. In endemic countries and especially in patients where an initial endoscopic/endosonographic biopsy is negative, the diagnosis of esophageal TB must be considered [10].

Which is the case with our patient, as he was delayed starting any targeted therapy or to reach a diagnosis for 5 months and underwent endoscopy and EUS five times prior to reaching a final diagnosis.

The most frequent complications observed in patients with ET were Esophago-Tracheal/Esophago-Mediastinal Fistula (36, 20.3% in 13 studies) and Hematemesis (7, 15.6% in 4 studies). Mediastinal Abscess (1) and esophago-cutaneous Fistula (2) were less commonly reported [9,13,22].

Patients with ET can present with esophago-tracheal/mediastinal fistula requiring interventions other than ATT. Short-term placement of naso-gastric tube (n=10, two studies) and percutaneous endoscopic gastrostomy tube (n=3, one study) was reported to bypass diseased esophagus and subsequent healing of fistula [7, 25]. In the study done by Rajasekar et al., all the three placed stents were removed after 6 weeks [9].

Another concern relates to the lack of clarity on the duration of treatment. While the standard anti-tuberculosis therapy (i.e., Isoniazid/Rifampicin/Ethambutol/Pyrazinamide) for abdominal and peritoneal tuberculosis (intestinal and TB) is sufficient, there is little clarity on the appropriate duration of treatment for Esophageal TB. Our review found a large variability in the duration of ATT, but most studies indicated a range between 6 and 12 months. Clinical symptoms typically resolve after 6 to 8 weeks on follow-up. Some studies have reported complete endoscopic healing at 6 months of ATT for intestinal TB, but none of the studies documented the usefulness of an early endoscopy on mucosal healing. Response to ATT is excellent and endoscopic or surgical interventions have been rarely needed specially to manage the associated complications such as stricture, tracheo/ broncho-esophageal fistula, bleeding or when instead of malignancy, a misdiagnosis was made. We suggest endoscopy after 8-12 weeks to document mucosal healing especially if initial diagnosis was not microbiologically confirmed. ATT should be continued for at least 6 months. An alternate diagnosis should be considered in patients without mucosal healing/persistent symptoms or lesions. Unless there is a complication related to ET like fistula or others, the treatment is conservative, and the response is excellent.

Table 1: Result of Review of Literature

Study	Study pe- riod	Number (M/F)	Presentation	Endoscopy findings	EUS findings	Final outcomes
Devarbhavi et al. [7]	1995-2000	10 (4/6)	Dysphagia 9 Cough 3 Constitutional symptoms 2	Ulcer 10 Sinus/fistula 5 Submucosal bulge 3 Diverticulum 4	N/A	Recovery 8 Death 1 F/U NA 1
Jain et al. [8]	1995-1999	12 (1/11)	Dysphagia 12 Chest pain 4 Constitutional symptoms 2	Ulcer 7 Stricture 3 Pseudotumor 4 Diverticulum 1 Submucosal bulge 1	N/A	Recovery 9 Death 3 (SCC) Surgery 2 (SCC)
Rajasekar et al. [9]	1996-2013	21 (21 males)	Dysphagia 18 Cough 7	Ulcer 21 Sinus/Fistula 8	N/A	Recovery 12 Surgery 6 Stenting 3 Death 0
Puri et al. [10]	2003-2009	32 (18/14)	Dysphagia 32 Odynophagia 8 Constitutional symptoms 20	Ulcer 24 Extrinsic compression 26	Hypoechoic 27 Heteroechoic 27 Oesophageal Wall Involvement 14 Hyperechoic strands + Subcarinal LN 30 Paraoesophageal LN 2 Matted LN 32	Recovery 32 Death 0 Surgery 0
Park et al. [11]	1997-2006	6 (3/3)	Dysphagia 3 Odynophagia 1 Cough 1 Hematemesis 1 Constitutional symptoms 1	Ulcer 4 Pseudotumor 2	N/A	Recovery 6 Death 0 Surgery 0 Intervention 0
Ni et al. [12]	2006-2011	6 (2/4)	Dysphagia 6 Cough 1 Chest pain 1 Constitutional symptoms 4	Ulcer 1 Pseudotumor 1 Diverticulum 1 Extrinsic Compression 4 TEF 1	LN with Hypoechoic center, interruption of esophageal adven- titia	Recovery 6 Death 0 Iatrogenic TEF 1
Mokoena et al. [13]	1972-1990	11 (6/5)	Dysphagia 9 Hematemesis 2 Hoarseness of Voice 2	Ulcer 2 Sinus/fistula 2 Pseudotumor 2 Diverticulum 1	N/A	Recovery 9 Death 2
Zhu et al. [14]	2011-2018	9 (3/6)	Dysphagia 5 Chest pain 6	Ulcer 7 Sinus/fistula 1 Pseudotumor 5 Diverticulum 1 Submucosal bulge 2	Hypoechoic 4 Esophageal wall involvement 9 Paraoesophageal LN 8	Recovery 9 Death 0
Dahale et al. [15]	2014-2016	19 (9/10)	Dysphagia 16 Odynophagia 8 Cough 4 Hematemesis 2 Constitutional Symptoms 17	Ulcer 17 Sinus/fistula 4 Diverticulum 1 Extrinsic compression 8	EUS in 8 patients, all had subcarinal and paraoesophageal LAP, matted LN in 5	Recovery 18 Clipping 1 Surgery 0
Bhatia et al. [16]	2007-2012	9 (6/3)	Dysphagia 5 Hematemesis 2 Constitutional symptoms 5	Sinus/fistula 1	N/A	Recovery 9 Death 0 Surgery 0

Rathinam et al [17]	1996-2003	14 (9/5)	Dysphagia 14 Cough 4 Constitutional Symptoms 14	Ulcer 2 Extrinsic Compression 10 TEF 4	N/A	Recovery 14 Surgery 7 Stenting 1 Iatrogenic TEF 1
Nagi et al. [18]	1985-2001	23 (15/8)	Dysphagia/ Odynophagia 19 Chest pain 7 Cough 6	Done in 23, details not mentioned	N/A	Recovery 22 Death 1 Surgery 1
Rana et al. [19]	2009-2013	14 (10/4)	Dysphagia 14 Constitutional Symptoms 11	Ulcer 5 Submucosal bulge 12 Extrinsic Compression 7	All had Echogenic strands. Focal anechoic/ Hypoechoic areas in 3, Calcification in 1	Recovery 14 Death 0 Surgery 0
Seo et al. [20]	2007-2014	6 (3/3)	Dysphagia 2 Chest pain 1	Submucosal bulge 6	Hypoechoic 6 Heteroechoic 4 Esophageal Wall involvement 6 Hyperechoic strands 4	Recovery 6 Death 0 Surgery 0
Tang et al. [21]	2006-2015	34 (15/9)	Dysphagia 32 Odynophagia 8 Chest pain 5 Constitutional symptoms 5	Ulcer 27 Submucosal bulge 27	Esophageal Wall Full thickness Involvement = 30, Intact mucosa = 5, Adventitia disruption In all 35 patients Homogeneous/ heterogeneous hypoechoic LN in all 35 patients	Recovery 35 Death 0 Surgery 0
Xiong et al. [22]	1999-2019	14 (7/7)	Dysphagia 7 Odynophagia 1 Chest pain, cough 5	Ulcer 6 Sinus/fistula 1 Submucosal bulge 10	Done in 11 patients. Hypo/heteroechoic LN 8 Interrupted Esophageal wall 3 Paraoesophageal LN 7 Matted LN 7	Recovery 11 Death 0 Surgery 3
Wang et al. [23]	2008-1012	11 (6/5)	Dysphagia 4 Odynophagia 4 Chest pain 3 Constitutional symptoms 1	Ulcer 4 Submucosal bulge 7	Hypoechoic 9 Hyperechoic strands 3 Mediastinal LN 6 Esophageal wall thickening 3 Adventitia disruption 3	Recovery 10 Surgery 1 Death 0
Youngguang et al. [24]	1980-2004	9 (7/2)	Dysphagia 8 Chest pain 5 Cough 3 Constitutional symptoms 4	Ulcer 1 Stricture 3 Pseudotumor 2 Extrinsic compression 5	N/A	Recovery 2 Surgery 7
Yang et al. [25]	2008-2012	30 (13/17)	Dysphagia 11 Odynophagia 7 Chest pain 10 Constitutional symptoms	Miliary TB 2 Mediastinal LN 4 Ulcer 23 Stricture 4 Sinus/fistula 2 Submucosal bulge 14	Done in 28 patients. Thickened esophageal wall, adventitia. dis- ruption, hypoechoic lesions, punctate hyperechoic shadows, thickening of serosa, LN next to esophagus, calcification	Recovery 30 Death 0 Surgery 0
Chaudhary et al. [26]	2011-2019	4 (2/2)	Dysphagia 3 Constitutional symptoms 2 Fever of unknown origin 1	Esophageal mass 4	Mediastinal LN 4	Recovery 3 Death 1

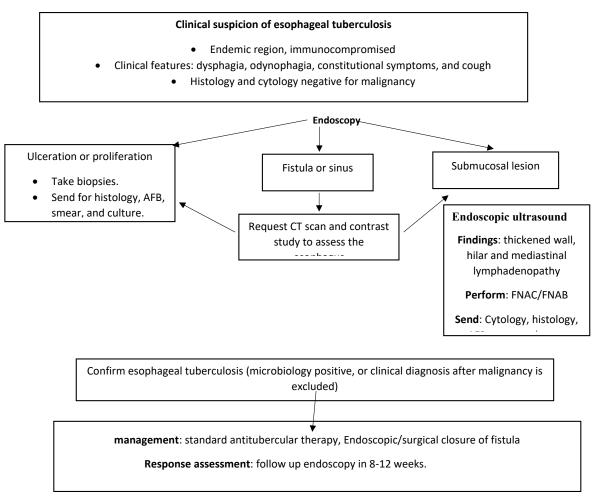


Figure 1: Suggested Management Algorithm for Esophageal Tuberculosis

Conclusion

There is a scarcity of information in the literature on the cases of isolated esophageal tuberculosis. Epigastric pain is rarely associated with esophageal tuberculosis and a refractory case should be tested by upper gastrointestinal endoscopy with biopsies followed by a mandatory AFB test. Anti-tubercular medication leads to complete resolution of the infection as well as the associated symptoms of dysphagia with excellent prognosis [14-21-23,24].

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