

Esophageal Tuberculosis as a Rare Cause of Dysphagia: Case Report

Billy Zhao¹, Hyun Jae Kim¹, Jessica Farrell², Wei Xiong¹, Jennifer Telford¹, and Sarvee Moosavi¹

¹The University of British Columbia Faculty of Medicine

²Mount Saint Joseph Hospital

October 19, 2023

Introduction:

Gastrointestinal tuberculosis (TB) is a rare extrapulmonary manifestation of TB.¹ Involvement of terminal ileum, cecum, and peritoneum are more commonly documented while esophageal involvement accounts for less than 0.2% of all TB patients.²⁻⁴ Despite the lower incidence of TB in Western countries, given the vague clinical manifestations of gastrointestinal TB, clinicians are required to keep TB on their differentials in work-up of various gastrointestinal symptoms, even if the patient has been previously vaccinated. We present a unique case of esophageal and duodenal TB in a patient who was vaccinated with BCG, with a prior negative Mantoux tuberculin skin test (TST).

Case report:

A 37-year-old Filipino female presented to the emergency department with a four-month history of progressive dysphagia to solids and then liquids. She was otherwise healthy and did not take any prescribed medication. She denied odynophagia, food bolus obstruction, chest pain, regurgitation, heartburn, and respiratory symptoms. She had unintentional weight loss of 3kg over 4 months with no other constitutional symptoms.

The patient had received BCG vaccination in the Philippines as a child. Her chest x-ray on Canadian immigration screening in 2009 was negative for latent or active TB. Her only known TB exposure occurred 14 months ago when her mother visited Canada and was diagnosed with active pulmonary TB after returning to the Philippines. Interestingly, she had a negative TST as a part of her care aide employment screening five months before her emergency department presentation.

Cardiac, respiratory, and abdominal examinations revealed no abnormalities with no palpable lymphadenopathy. Complete blood count with differential showed mild normocytic anemia with hemoglobin of 108 g/L (115-155). WBC was normal at $5.3 \times 10^9/L$ (4.0-11.0). She had a normal neutrophil count of $3.6 \times 10^9/L$ (2.0-8.0), mildly decreased lymphocyte at $1.1 \times 10^9/L$ (1.2-3.5), and normal monocyte, eosinophil, and basophil counts. Electrolytes and hepatic panels were normal. Her chest x-ray in the emergency department showed no signs of lung scarring.

Esophagogastroduodenoscopy (EGD) revealed a 2 cm ulcerated mass, abutting the gastroesophageal junction (GEJ) inferiorly on retroflexion (Figure 1) and a subepithelial lesion in the duodenal bulb with normal overlying mucosa. The exam was otherwise normal. Mucosal biopsies were taken from both lesions and histopathology revealed ulcerated mucosa with acute and chronic inflammatory infiltrates composed of histiocytes, granulocytes, and lymphocytes (Figure 2). No granulomas were identified. Ziehl-Neelsen stain was negative for acid-fast bacilli. Although a lymphoproliferative disorder was not identified, it could not be

excluded in the limited tissue sample.

Additionally, computed tomography (CT) scan of her chest, abdomen, and pelvis was performed for staging due to suspicion of lymphoma or other malignancy. This demonstrated infiltrative soft tissue masses at the GEJ and duodenal bulb, each measuring up to 4.5 cm in size (Figure 3). There was linear scarring and several discrete nodules at the left lung apex, the largest 12 mm (Figure 4). No pathologically enlarged lymph nodes were noted.

Endoscopic ultrasound (EUS) demonstrated an ill-defined, hypoechoic lesion, involving the GEJ, extending into the region of the celiac axis. A second lesion, involving the proximal duodenum, was round with well-defined margins and measured 20 mm x 14 mm (Figure 5). No enlarged lymph node was seen. EUS-guided fine-needle biopsy of both lesions was performed, which revealed fragments of necrotizing granulomatous inflammation (Figure 6). No mycobacteria were seen on Ziehl-Neelsen stain (Figure 6). Concurrent flow cytometry was completed with a 10-color lymphoma screening panel. The CD45 gated lymphocyte population accounted for 4% of all events. T-cells were 66% of the lymphocyte gate and showed normal antigen expression. The CD4/CD8 ratio is 1.7. Overall, the flow cytometry analysis was not consistent with lymphoproliferative disorders. Given this finding along with the fact that previous infectious investigations are not highly sensitive, infectious etiologies cannot be ruled out and the patient was referred to the infectious disease team and underwent an IGRA/QuantIFERON assay, which came back positive. Diagnosis of TB was further confirmed by a positive TB PCR testing on paraffin block on esophageal biopsies from index EGD. The patient was subsequently referred to a TB-specialized clinic and was started on Rifampin, isoniazid, vitamin B6, and pyrazinamide for 6 months. Given the lack of respiratory symptoms or active findings on chest imaging, isolation was not required, and her immediate family members were all screened for TB.

Discussion:

Dysphagia is the most common presenting symptom of esophageal TB; however, this is a common presenting symptom of a rare disease.⁵⁻⁷ Other symptoms of esophageal TB include chest pain, fever, odynophagia, and weight loss.

Endoscopic findings of esophageal TB can vary, but typically present as either ulcerated, bulging mucosal or submucosal mass and rarely as a stricture or fistula.^{5,8-10} Given its appearance, upper gastrointestinal TB is often mistaken for malignancy in reported cases, as it was in our case.^{11,12}

Adding to the diagnostic dilemma was the fact that our patient was both previously vaccinated with BCG and had a prior negative TST five months before presentation. BCG has an effectiveness of 46-50% regardless of the time of vaccination.^{13,14} TST has a sensitivity of 60-98% but is prone to false-negative results from technical errors or decreased skin reactivity.¹⁵ Acid-fast bacilli staining on biopsied tissue has high specificity but low sensitivity for TB.¹⁶ Instead, tissue PCR should be used, given the higher sensitivity estimated to be between 74% to 100% with most false-negatives as a result of insufficient tissue sampling.¹⁶⁻¹⁸

The most common etiology of esophageal TB is local spread from adjacent respiratory tract or mediastinal lymph nodes.^{5,19} While our patient had no respiratory symptoms, normal chest x-ray, and negative TST, lung scarring seen on her CT chest may indicate latent pulmonary TB. Lymphadenopathy was absent on both EUS and cross-sectional imaging, making spread from lymph nodes less likely.

Other than enlarged lymph nodes, other EUS features of esophageal TB include thickened esophageal wall and hypoechoic lesions that may contain hyperechoic calcifications, which we did not see in our patient.¹⁹ However, none of these features is sensitive nor specific to esophageal TB.

Primary esophageal TB is also unlikely as it is rare and occurs when mycobacterium tuberculosis adheres to the esophageal wall after direct ingestion and needs to bypass protective mechanisms such as the mucus barrier and stratified squamous epithelium of the esophagus.^{9,19}

Despite previous vaccination, a negative skin test, and the absence of other features of TB other than generalized weight loss, our patient was found to have esophageal and duodenal TB. Although rare in a

Western setting, an index of suspicion is needed to keep gastrointestinal TB as part of the differential for workup of dysphagia for patients from endemic areas, even with prior BCG vaccination and negative screening TST.

References

1. Evans RP, Mourad MM, Dvorkin L, Bramhall SR. Hepatic and intra-abdominal tuberculosis: 2016 update. *Current Infectious Disease Reports*. 2016;18(12). doi:10.1007/s11908-016-0546-5
2. Sheer TA, Coyle WJ. Gastrointestinal tuberculosis. *Curr Gastroenterol Rep*. 2003;5(4):273-278. doi:10.1007/s11894-003-0063-1
3. Carr DT, Spain DM. Tuberculosis in a Carcinoma of the Oesophagus. *American Review of Tuberculosis*. 1942;46(3):346-349.
4. Xiong J, Guo W, Guo Y, Gong L, Liu S. Clinical and endoscopic features of esophageal tuberculosis: a 20-year retrospective study. *Scand J Gastroenterol*. 2020;55(10):1200-1204. doi:10.1080/00365521.2020.1813799
5. Puri R, Khaliq A, Kumar M, Sud R, Vasdev N. Esophageal tuberculosis: role of endoscopic ultrasound in diagnosis. *Dis Esophagus*. 2012;25(2):102-106. doi:10.1111/j.1442-2050.2011.01223.x
6. Vahid B, Huda N, Esmaili A. An unusual case of dysphagia and chest pain in a non-HIV patient: esophageal tuberculosis. *Am J Med*. 2007;120(4):e1-e2. doi:10.1016/j.amjmed.2005.12.026
7. Park JH, Kim SU, Sohn JW, et al. Endoscopic findings and clinical features of esophageal tuberculosis. *Scand J Gastroenterol*. 2010;45(11):1269-1272. doi:10.3109/00365521.2010.501524
8. Birda CL, Kumar A, Gupta P, Singh H, Sharma V. Oesophageal Tuberculosis: A Systematic Review Focusing on Clinical Management [published online ahead of print, 2021 Sep 4]. *Dysphagia*. 2021;10.1007/s00455-021-10360-x. doi:10.1007/s00455-021-10360-x
9. Jain SK, Jain S, Jain M, Yaduvanshi A. Esophageal tuberculosis: is it so rare? Report of 12 cases and review of the literature. *Am J Gastroenterol*. 2002;97(2):287-291. doi:10.1111/j.1572-0241.2002.05456.x
10. Nie D, Li J, Liu W, et al. Esophagomediastinal fistula due to secondary esophageal tuberculosis: report of two cases. *J Int Med Res*. 2021;49(7):3000605211023696. doi:10.1177/03000605211023696
11. Fujiwara Y, Osugi H, Takada N, et al. Esophageal tuberculosis presenting with an appearance similar to that of carcinoma of the esophagus. *J Gastroenterol*. 2003;38(5):477-481. doi:10.1007/s00535-002-1088-1
12. Zhu R, Zhou Y, Wang H, et al. Gastric tuberculosis mimicking submucosal tumor: a case series. *BMC Gastroenterol*. 2020;20(1):23. Published 2020 Jan 30. doi:10.1186/s12876-020-1175-x
13. Michelsen SW, Soborg B, Koch A, Carstensen L, Hoff ST, Agger EM, et al. The effectiveness of BCG vaccination in preventing *mycobacterium tuberculosis* infection and disease in Greenland. *Thorax*. 2014;69(9):851-6.
14. Colditz GA, Brewer TF, Berkey CS, Wilson ME, Burdick E, Fineberg HV, et al. Efficacy of BCG vaccine in the prevention of tuberculosis. meta-analysis of the published literature. *JAMA: The Journal of the American Medical Association*. 1994;271(9):698-702.
15. WHO Tuberculosis Research Office. FURTHER studies of geographic variation in naturally acquired tuberculin sensitivity. *Bull World Health Organ*. 1955;12(1-2):63-83.
16. Ma J, Yin H, Xie H. Critical role of molecular test in early diagnosis of gastric tuberculosis: a rare case report and review of literature. *BMC Infect Dis*. 2019;19(1):589. Published 2019 Jul 5. doi:10.1186/s12879-019-4225-7
17. Baylan O, Kilciler G, Albay A, Tuzun A, Kisa O, Dagalp K. Polymerase chain reaction based diagnosis of primary gastric tuberculosis in an 80-year-old woman: a case report and review of the literature. *New Microbiol*. 2009;32(2):217-221.
18. Kaul KL. Molecular detection of *Mycobacterium tuberculosis*: impact on patient care. *Clin Chem*. 2001;47(8):1553-8.
19. Zhu R, Bai Y, Zhou Y, et al. EUS in the diagnosis of pathologically undiagnosed esophageal tuberculosis. *BMC Gastroenterol*. 2020;20(1):291. Published 2020 Aug 28. doi:10.1186/s12876-020-01432-7



