

# Primary Esophageal Tuberculosis Without Dysphagia or Odynophagia in a Patient Without HIV

Henry Ogbomo, PhD<sup>1,2</sup>, Aducio Thiesen, MD<sup>3</sup>, Sergio Zepeda-Gomez, MD<sup>4</sup>, and Ali Kohansal-Vajargah, MD<sup>4</sup>

<sup>1</sup>Undergraduate Medical Education, University of Calgary, Calgary, Canada

<sup>2</sup>Department of Microbiology, Immunology and Infectious Diseases, University of Calgary, Calgary, Canada

<sup>3</sup>Department of Laboratory Medicine and Pathology, University of Alberta, Alberta, Canada

<sup>4</sup>Division of Gastroenterology, University of Alberta, Alberta, Canada

## ABSTRACT

We report a case of primary esophageal tuberculosis in a 35-year-old woman without HIV who presented with a month's history of epigastric and chest pain without dysphagia or odynophagia and was found to have histologic evidence of multiple caseating granulomata on esophageal biopsy, which was confirmed positive for *Mycobacterium tuberculosis* complex DNA and cultures.

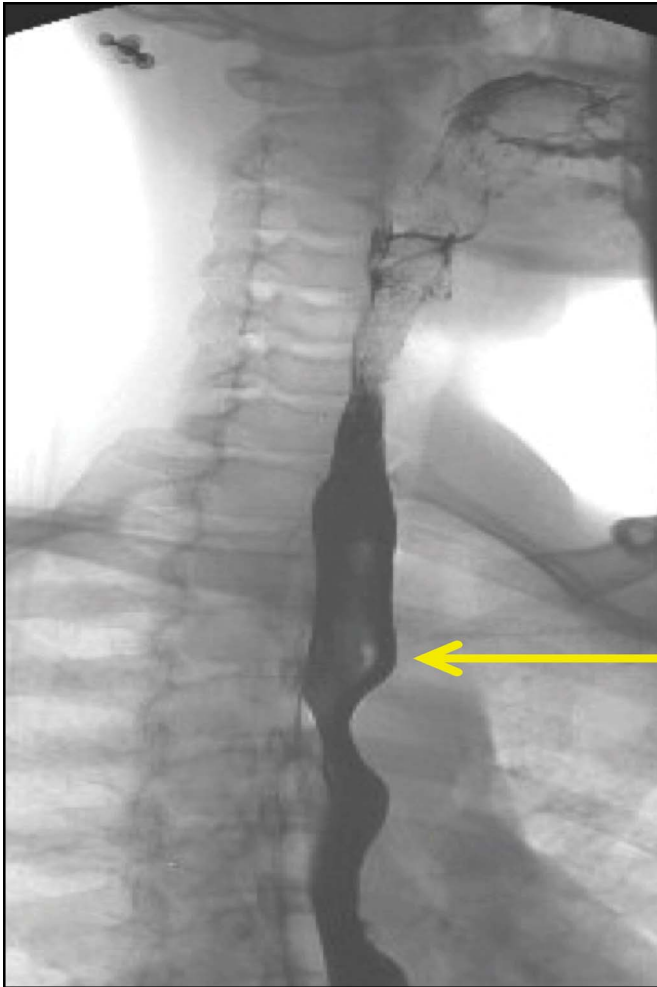
## INTRODUCTION

Recent reports described tuberculosis (TB) as the leading cause of death from a single infectious disease agent globally.<sup>1</sup> In the Philippines, it is the 6th leading cause of morbidity and mortality.<sup>2</sup> Esophageal tuberculosis (ET) is believed to be a rare disease in both immunocompetent and immunocompromised individuals, and only 0.15% of patients who died of TB had esophageal involvement.<sup>3</sup> However, in the past 2 decades, reports of ET have increased. Patients generally present with dysphagia and/or odynophagia, and sometimes with epigastric pain, chest pain, or hematemesis.<sup>4-13</sup> There are 2 categories of ET: primary ET, which only involves the esophagus and is a less common finding, and secondary ET, which is an extrinsic manifestation of pulmonary TB.<sup>14</sup> Of the several mechanisms proposed to explain secondary ET, direct extension of mediastinal and pulmonary TB or spinal TB is the most common.<sup>13-15</sup> The other mechanisms for secondary ET, although uncommon, include contiguous seeding from lesions within the larynx or pharynx, spreading via the lymphatics, and hematogenous spread.<sup>13</sup> One mechanism that suggests a primary ET transmission is swallowing of tuberculous saliva.<sup>13,14</sup>

## CASE REPORT

We present a case of primary ET in an otherwise healthy, 35-year-old woman without human immunodeficiency virus (HIV) from the Philippines who immigrated to Canada in 2007. Since immigrating to Canada, she has traveled back to the Philippines on a yearly basis. The patient presented with a 1-month medical history of epigastric and chest pain, which was worsened by food ingestion. She denied symptoms of dysphagia or odynophagia and constitutional symptoms. She did not have any known TB contacts. On physical examination, there was no cervical lymphadenopathy noted. The abdomen was soft without any palpable masses.

Initial investigations with an upper gastrointestinal contrast study revealed a well-circumscribed mass in the midesophagus along the left anterolateral wall with linear ulceration, which was concerning for malignancy. There was also spontaneous gastroesophageal reflux identified with features consistent with reflux esophagitis (Figure 1). Subsequently, an esophagogastroduodenoscopy was performed, which revealed a raised lesion that appeared to arise from the submucosal layer (Figure 2). It also revealed an area of central ulceration concerning for a dysplastic process (Figure 3). The lesion started at approximately 25 cm from the incisors and is estimated to be approximately 3 cm in length (25–28 cm). Multiple biopsies were taken from the lesion. Gastric biopsies were taken for the diagnosis of *Helicobacter pylori*.



**Figure 1.** Fluoroscopic image of the esophagus showing a well-circumscribed mass in the midesophagus (yellow arrow).

Histopathologic report of the esophageal biopsies showed multiple caseating granulomata with a dense mixed inflammatory infiltrate rich in eosinophils (Figure 4). The gastric biopsies were negative for *H. pylori*. Fungal stains (Grocott methenamine silver and periodic acid Schiff) and culture of esophageal biopsy, as well as Ziehl-Neelsen and Warthin Starry stains and immunohistochemistry for herpes simplex virus and cytomegalovirus, were negative. There was no evidence of dysplastic changes. Overall,

the histological features were highly suspicious for an infection, including TB, especially because the granulomata were caseating.

The definitive diagnosis of TB was confirmed with a nucleic acid test using the Xpert *Mycobacterium tuberculosis* complex (MTB)/resistance to rifampin polymerase chain reaction kit from Cepheid (Sunnyvale, CA). The DNA samples were positive for MTB. In addition, MTB was isolated using the automated system BACTEC (BD, Berkshire, United Kingdom) Mycobacteria Growth Indicator Tube and growth was detected after 12 days of incubation.

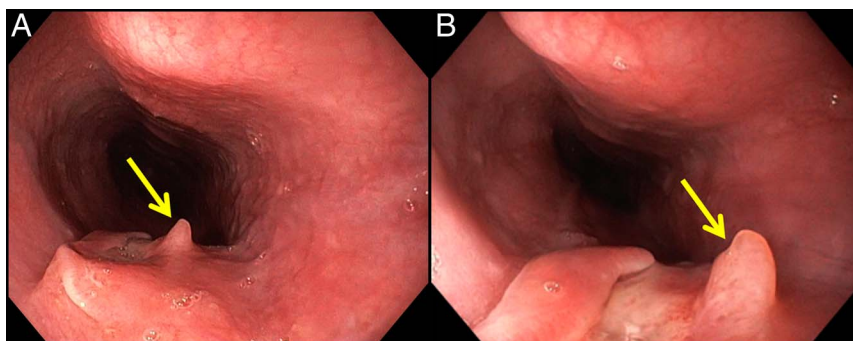
A thoracic x-ray was performed, which was reported as normal. This was followed by a thoracic computed tomography which did not show any evidence of mediastinum lymphadenopathy. HIV test was negative. She was started on a 6-month treatment regimen of quadruple therapy with isoniazid, rifampin, pyrazinamide, and ethambutol. The patient was clinically asymptomatic after 1 week of therapy.

## DISCUSSION

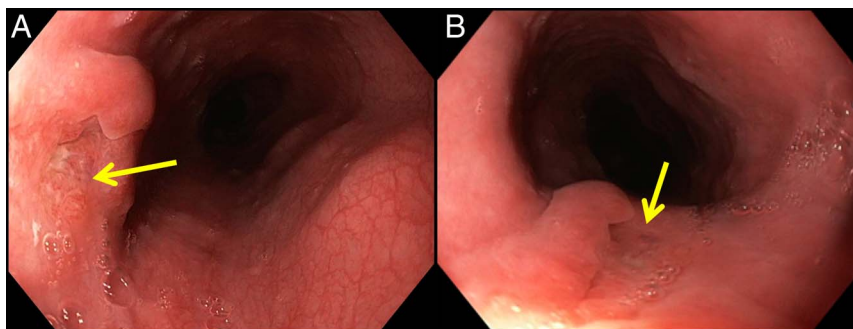
The differential diagnoses for granulomata include infection, autoimmune (vasculitis, Crohn's disease, and sarcoidosis), and drugs (Bacillus Calmette-Guerin vaccine and methotrexate).<sup>16</sup> Some infectious causes of granulomata include *M. tuberculosis*, nontuberculous mycobacteria, and fungi (*Histoplasma*, *Cryptococcus*, *Coccidioides*, *Aspergillus*, and *Blastomyces*).<sup>16</sup>

Unlike Crohn's disease and sarcoidosis (2 most frequent causes of granulomatous esophagitis), which are noncaseating, TB is a caseating granulomata.<sup>16-18</sup> The patient had multiple caseating granulomata, which were confirmed to be MTB and diagnosed as TB.

A retrospective study of 24 patients with suspected ET revealed that 19 patients had definite ET and presented mostly with dysphagia (84%) and odynophagia (42%).<sup>19</sup> Most recently, a case of primary ET was reported in a 25-year-old man who presented with progressive dysphagia, epigastric pain, and 10 kg weight loss over 8 months.<sup>20</sup> Presentation of ET without dysphagia and/or odynophagia is a rare finding.



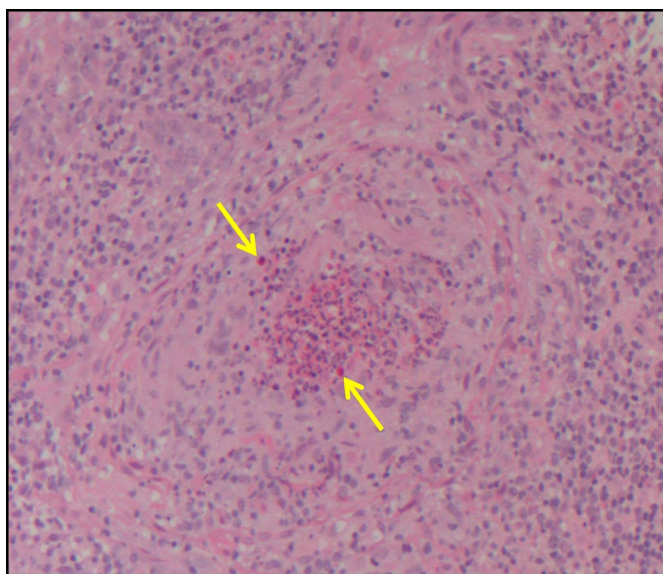
**Figure 2.** Esophagogastroduodenal images showing raised lesions (yellow arrows).



**Figure 3.** Esophagogastrroduodenal images showing areas of central ulceration (yellow arrows).

Among HIV-associated diseases, TB is the most common, causing the highest number of deaths worldwide.<sup>21</sup> The classic symptoms of TB include productive cough, chest pain, shortness of breath, hemoptysis, fever, night sweats, and/or weight loss. These symptoms occur in patients with TB with or without HIV.<sup>21</sup> In addition, many patients infected with HIV with TB are less likely to have pulmonary cavitation than patients with only TB, whereas some patients infected with HIV with pulmonary TB have normal chest radiograph.<sup>22–24</sup> Others have indicated that patients with HIV are more likely than patients without HIV to have extrapulmonary TB, with or without concomitant pulmonary disease.<sup>21,25</sup> Extrapulmonary TB commonly occurs in the pleura, abdomen, central nervous system, lymphatic system, and skeletal system.<sup>26,27</sup> Our patient was HIV negative and presented with no classic symptoms of TB except for chest pain. She had no radiographic findings of pulmonary TB but had an extrapulmonary TB finding in a rare site, the esophagus.

Because our patient did not have detectable evidence of pulmonary TB, it is reasonable to conclude that ET did not seed from other sites but was rather swallowed, suggesting



**Figure 4.** Hematoxylin and eosin stain (100×) showing the necrotizing granuloma with few eosinophils (yellow arrows).

a diagnosis of primary ET. It is unclear how this would occur considering the fact that the esophageal transit time is likely inadequate for the infectious agent to attach to the squamous epithelial mucosa of the esophagus unless there was a disruption of the esophageal mucosal or delayed esophageal clearance.<sup>14</sup> This case study adds to the bulk of evidence supporting unusual presentations of primary ET and warrants the need to include ET as one of the differential diagnoses for epigastric and chest pain, especially in patients with risk factors for TB. Although reflux esophagitis could account for the epigastric pain experienced by our patient, it is reasonable to have a broad differential that includes ET in patients presenting with epigastric and chest pain so as to not miss a possible case of ET.

## DISCLOSURES

Author contributions: H. Ogbomo wrote the manuscript. A. Thiesen provided pathology slides and reviewed the manuscript. S. Zepeda-Gomez reviewed and edited the manuscript. A. Kohansal-Vajargah provided esophagogastrroduodenal images, reviewed and edited the manuscript, and is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received July 4, 2019; Accepted December 19, 2019

## REFERENCES

1. MacNeil A, Glaziou P, Sismanidis C, Maloney S, Floyd K. Global epidemiology of tuberculosis and progress toward achieving global Targets—2017. *MMWR Morb Mortal Wkly Rep*. 2019;68:263–6.
2. Kim S, de Los Reyes AA V, Jung E. Mathematical model and intervention strategies for mitigating tuberculosis in the Philippines. *J Theor Biol*. 2018; 443:100–12.
3. Devarbhavi HC, Alvares JF, Radhikadevi M. Esophageal tuberculosis associated with esophagotracheal or esophagomediastinal fistula: Report of 10 cases. *Gastrointest Endosc*. 2003;57:588–92.
4. Jain SK, Jain S, Jain M, et al. Esophageal tuberculosis: Is it so rare? Report of 12 cases and review of the literature. *Am J Gastroenterol*. 2002;97:287–91.
5. Kotanidou A, Andrianakis I, Mavrommatis A, Politis P, Roussos C, Bellenis I. Mediastinal mass with Dysphagia in an elderly patient. *Infection*. 2003;31: 178–80.
6. Welzel TM, Kawan T, Bohle W, et al. An unusual cause of dysphagia: Esophageal tuberculosis. *J Gastrointest Liver Dis*. 2010;19:321–4.

7. Garg R, Carter S, Barawi M. Dysphagia from esophageal tuberculosis in a patient with undiagnosed HIV infection. *Endoscopy*. 2017;49:E195–6.
8. Fujiwara T, Yoshida Y, Yamada S, Kawamata H, Fujimori T, Imawari M. A case of primary esophageal tuberculosis diagnosed by identification of Mycobacteria in paraffin-embedded esophageal biopsy specimens by polymerase chain reaction. *J Gastroenterol*. 2003;38:74–8.
9. Gordon AH, Marshall JB. Esophageal tuberculosis: Definitive diagnosis by endoscopy. *Am J Gastroenterol*. 1990;85:174–7.
10. Wu C, Xu M, Hu B. A large changing mass in the esophagus. *Gastroenterology*. 2017;153:901–2.
11. 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:e1–2.
12. Mokoena T, Shama DM, Ngakane H, Bryer JV. Oesophageal tuberculosis: A review of eleven cases. *Postgrad Med J*. 1992;68:110–5.
13. Jain SS, Somani PO, Mahey RC, Shah DK, Contractor QQ, Rathi PM. Esophageal tuberculosis presenting with hematemesis. *World J Gastrointest Endosc*. 2013;5:581–3.
14. Momin RN, Chong VH. Oesophageal tuberculosis: Rare but not to be forgotten. *Singapore Med J*. 2012;53:e192–4.
15. Nagi B, Lal A, Kochhar R, et al. Imaging of esophageal tuberculosis: A review of 23 cases. *Acta Radiol*. 2003;44:329–33.
16. Mukhopadhyay S, Gal AA. Granulomatous lung disease: An approach to the differential diagnosis. *Arch Pathol Lab Med*. 2010;134:667–90.
17. LiVolsi VA, Jaretzki A III. Granulomatous esophagitis. A case of Crohn's disease limited to the esophagus. *Gastroenterology*. 1973;64:313–9.
18. Abraham A, Hajar R, Viridi R, Singh J, Mustacchia P. Esophageal sarcoidosis: A review of cases and an update. *ISRN Gastroenterol*. 2013;2013:836203.
19. Dahale AS, Kumar A, Srivastava S, Varakanahalli S, Sachdeva S, Puri AS. Esophageal tuberculosis: Uncommon of common. *JGH Open*. 2018;2:34–8.
20. Khan MS, Maan MHA, Sohail AH, Memon WA. Primary esophageal tuberculosis mimicking esophageal carcinoma on computed tomography: A case report. *World J Gastrointest Surg*. 2019;11:373–80.
21. Sterling TR, Pham PA, Chaisson RE. HIV infection-related tuberculosis: Clinical manifestations and treatment. *Clin Infect Dis*. 2010;50(Suppl 3):S223–30.
22. Greenberg SD, Frager D, Suster B, Walker S, Stavropoulos C, Rothpearl A. Active pulmonary tuberculosis in patients with AIDS: Spectrum of radiographic findings (including a normal appearance). *Radiology*. 1994;193:115–9.
23. Perlman DC, el-Sadr WM, Nelson ET, et al. Variation of chest radiographic patterns in pulmonary tuberculosis by degree of human immunodeficiency virus-related immunosuppression. The Terry Bein Community Programs for Clinical Research on AIDS (CPCRA). The AIDS Clinical Trials Group (ACTG). *Clin Infect Dis*. 1997;25:242–6.
24. Pepper T, Joseph P, Mwenya C, et al. Normal chest radiography in pulmonary tuberculosis: Implications for obtaining respiratory specimen cultures. *Int J Tuberc Lung Dis*. 2008;12:397–403.
25. Chaisson RE, Schechter GF, Theuer CP, Rutherford GW, Echenberg DF, Hopewell PC. Tuberculosis in patients with the acquired immunodeficiency syndrome. Clinical features, response to therapy, and survival. *Am Rev Respir Dis*. 1987;136:570–4.
26. Golden MP, Vikram HR. Extrapulmonary tuberculosis: An overview. *Am Fam Physician*. 2005;72:1761–8.
27. Sunnetcioglu A, Sunnetcioglu M, Binici I, Baran AI, Karahocagil MK, Saydan MR. Comparative analysis of pulmonary and extrapulmonary tuberculosis of 411 cases. *Ann Clin Microbiol Antimicrob*. 2015;14:34.

---

**Copyright:** © 2020 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of The American College of Gastroenterology. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.