

# Esophageal tuberculosis as an uncommon cause of dysphagia

Tuberculose esofágica como causa infrequente de disfagia



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## ABSTRACT

Although rare, gastrointestinal tuberculosis can affect the esophagus and cause dysphagia through primary or secondary mechanisms of disease spread. We report here on two immunocompetent patients whose chief complaint of dysphagia was the main symptom that motivated seeking health services. Upper digestive endoscopy identified nonspecific lesions that initially led to the formulation of other diagnostic hypotheses; however, respective biopsies allowed the diagnosis of tuberculosis — one primary and the other secondary. There was complete resolution of symptoms with specific treatment.

**Headings:** Tuberculosis, Gastrointestinal; Esophageal Diseases; Deglutition Disorders; Endoscopy, Gastrointestinal; Case Report.

## RESUMO

Apesar de rara, a tuberculose gastrointestinal pode afetar o esôfago e provocar disfagia tanto por mecanismos primários como secundários de disseminação da doença. Relatamos aqui dois casos de pacientes imunocompetentes cuja queixa de disfagia foi o principal sintoma que motivou a procura por um serviço de saúde. A endoscopia digestiva alta identificou lesões inespecíficas que inicialmente levaram à formulação de outras hipóteses diagnósticas, todavia, as respectivas biópsias permitiram o diagnóstico de tuberculose - uma primária e outra secundária. Houve resolução completa dos sintomas com o tratamento específico.

**Descritores:** Tuberculose Gastrointestinal; Doenças do Esôfago; Transtornos de Deglutição; Endoscopia Gastrointestinal; Relato de Caso.

## INTRODUCTION

Dysphagia is defined as difficulty in swallowing and is a fairly common symptom, reported by one in every six patients<sup>1</sup>. More frequent among men and the elderly, there are several possible etiologies, including infectious causes<sup>1,2</sup>.

We present here two clinical cases in which the cause of dysphagia was the surprising diagnosis of esophageal tuberculosis (TB), an eventuality to be especially remembered in countries where TB is endemic, such as Brazil.

## CASE REPORTS

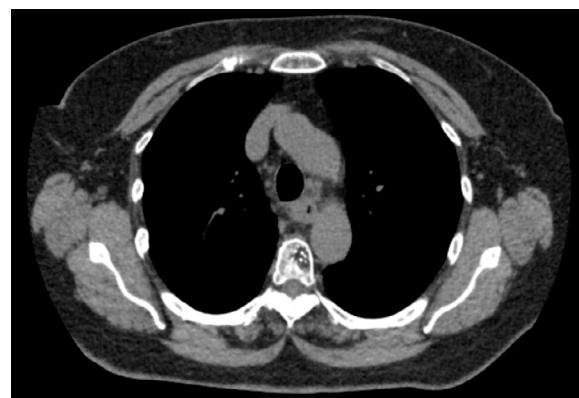
Patient #1: 73-year-old woman with complaints of heartburn and dysphagia for solids for one month, accompanied by non-productive cough and occasional episodes of bronchospasm. She also reported unintentional and unquantified weight loss. She denied smoking, alcoholism, and other

comorbidities. Upper digestive endoscopy (EGD) identified a single elevated lesion measuring approximately 15mm in diameter in the proximal esophagus (Figure 1), with a shallow linear ulceration in the center. There was also mild erythematous gastritis of the antrum, and esophageal carcinoma was initially suspected. Given this hypothesis, a chest computed tomography (CT) scan was performed, which demonstrated only the presence of small and non-confluent mediastinal lymph nodes increased in number (Figure 2), in addition to heterogeneous attenuation of the lung parenchyma at the bases with a discrete mosaic pattern. Histopathological analysis of esophageal biopsies showed exulceration with intense inflammatory infiltrate of histiocytic predominance and aggregates of epithelioid histiocytes in granulomatous arrangement, with foci of necrosis and no signs of malignancy. Research for acid-fast bacilli (AFB) by specific staining was positive. Samples were not sent for culture or rapid molecular test (RMT) to search for *Mycobacterium tuberculosis* DNA. Serology for HIV was negative, and the tuberculin test (TT) yielded a result of 2mm. After questioning, the patient recalled the epidemiological history of an aunt who had TB more than 60 years ago. There was symptomatic improvement soon after starting specific treatment with rifampicin, isoniazid, pyrazinamide, and ethambutol (RHZE), and the control EGD at the end of treatment (after six months) confirmed remission and complete healing of the lesion.



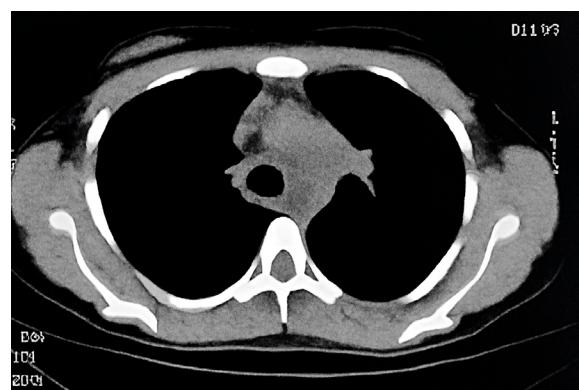
**Figure 1.** Single elevated lesion with shallow linear ulceration in the center visualized in Upper Digestive Endoscopy performed on Patient #1 (pre-biopsy on the left and post-biopsy on the right).

Patient #2: 36-year-old woman with persistent and progressive dysphagia and epigastralgia for about a year, associated with a slightly productive cough, sporadic evening fever, night sweats, asthenia, and weight loss of 10kg during the period. She denied smoking, alcoholism, and other comorbidities. Chest CT identified mediastinal lymphadenomegaly (Figure 3), without infiltrates or pulmonary condensations. An initial sputum smear was negative. Then, EGD was performed, which identified a fistulous orifice in the proximal esophagus with an



**Figure 2.** Tomographic section showing a certain thickening of the esophageal wall and increased mediastinal lymph nodes, although small and non-confluent (Patient #1).

approximate diameter of 0.5cm, without secretion or air output. A second fistulous lesion was found on the posterior wall of the stomach body, which drained a small amount of serous secretion; a third lesion was still visualized in the duodenum, this being a deep ulcer with regular borders and a granulomatous bottom (Figure 4). The histological study of the various biopsies performed on these lesions identified chronic granulomatous inflammatory process with areas of necrosis, suggestive of TB. Samples were not sent for smear, culture, or RMT. It was also decided to biopsy a palpable supraclavicular lymph node where granulomas and multinucleated giant cells with caseous necrosis were also identified (sample also not sent for microbiological tests). Serology for HIV was negative. The TT measurement was 12mm. The patient received treatment with RHZE (standard sequence maintained for nine months) and evolved with rapid symptomatic improvement. A barium esophagogram and a new control EGD performed in the 8th month of treatment showed complete resolution of the lesions, without sequelae.



**Figure 3.** Non-contrast tomographic section showing para-aortic mediastinal lymph node enlargement (Patient #2).



**Figure 4.** Endoscopic images visualized in Patient #2: A. esophageal fistula; B. gastric fistula; C. duodenal ulcer.

## DISCUSSION

Esophageal TB corresponds to a prevalence of only 2.8% of cases of gastrointestinal TB<sup>3</sup>, however dysphagia is its most common symptom, present in about 90% of patients<sup>2</sup>. Esophageal involvement by TB can occur in primary or secondary form<sup>2,3</sup>. The primary form corresponds to exclusive infection of the esophagus, without evidence of any other focus of infection, as exemplified in our Patient #1. This is an even rarer manifestation due to the esophagus' own defense mechanisms, such as the presence of saliva and mucus, the squamous epithelium, and peristaltic movements<sup>3,4</sup>. Secondary esophageal TB, in turn, is related to concomitant lesions in the larynx, lungs, and especially in the mediastinal lymph nodes<sup>2</sup>, both by contiguous dissemination and by swallowing bacilliferous sputum, in addition to a relatively frequent multifocal involvement of the gastrointestinal tract<sup>3</sup> such as that of Patient #2.

EGD is usually the first and main diagnostic method used to investigate dysphagic complaints, but the findings of esophageal TB can be varied and nonspecific. The most common endoscopic finding is that of superficial ulcers, generally unique, of varying size, with regular or infiltrative borders, very similar to neoplasms<sup>4</sup>. Other types of lesions such as submucosal nodules, polyps, and aphthous and deep (usually blind) ulcers are also possible and equally nonspecific, while localized areas of stenosis may even occur<sup>3</sup>. Esophageal fistulas attributed to TB generally manifest through more than one orifice, whose path can cross the mediastinum and, more frequently, the trachea and/or left main bronchus<sup>2</sup> - here, once again, esophageal carcinoma stands out as the main differential diagnosis<sup>4</sup>. Most lesions associated with TB predominate in the middle third of the esophagus<sup>2,5</sup>, probably due to their proximity to the mediastinal lymph nodes located next to the bifurcation of the trachea. Both of our patients, however, had lesions in the upper third, which can be explained by the primary form of esophageal TB in Patient #1 and the multifocal involvement in Patient #2.

More than the visualization of the lesions, EGD also allows multiple biopsies to be performed, which must

be deep and representative to increase the sensitivity of the definitive diagnosis<sup>3</sup>, which depends mainly on the histopathological analysis of these samples. The identification of granulomas is the classic tissue manifestation of tuberculous infection, but also occurs in other pathologies such as Crohn's disease, non-infectious granulomatosis or even endemic fungal infections such as histoplasmosis and paracoccidioidomycosis<sup>4,6,7</sup>. The presence of caseous necrosis and multinucleated giant cells may strengthen the suspicion of esophageal TB<sup>3</sup>, but the identification of AFB and/or genetic components of the mycobacteria are ideally necessary. It is worth mentioning that in the two cases reported here, there was no forwarding of "fresh" endoscopic samples to the microbiology laboratory; this is common practice in most endoscopy services which, in addition to being justified by its low sensitivity<sup>8</sup>, reflects the undervaluation of specific infections as possible etiologies in this context. Specific stains (as happened with Patient #1 samples) and polymerase chain reaction (PCR) techniques, however, can (or rather, should) be performed on paraffin-fixed samples<sup>3</sup>, giving these last sensitivity of 80 and specificity of 98%<sup>4</sup>.

An even more challenging situation is caused by esophageal involvement in Crohn's disease: although also infrequent, it mainly manifests in an equally multifocal way<sup>6,7</sup>, while EGD is an examination usually requested for patients who already have a previous diagnosis of Crohn's and evolve with dysphagia. The identification of granulomas in those biopsies, moreover, presupposes the confirmation of the underlying disease and the consequent introduction or intensification of immunosuppressive therapies, so the exclusion of TB requires even greater care due to its risk of dissemination and death if this supposed diagnosis is wrong<sup>9</sup>. The fact is that both the symptoms (starting with dysphagia) and the common endoscopic lesions to all these diseases (including esophageal carcinoma) imply the necessary remembrance of TB as a suspected diagnosis, even if this is not the first hypothesis<sup>3,9</sup>. In our reports, the younger age of Patient #2 and the concomitant lymph node TB certainly facilitated this reasoning, but the same can't be said in relation to Patient #1, whose neoplasia hypothesis could only have been ruled out with the final result of the biopsies.

In addition to EGD, the chest CT scan is the most useful complementary exam in the investigation of possible esophageal TB by allowing the evaluation of the thickness of the esophageal wall, the mediastinum, and pulmonary involvement<sup>3</sup>. A chest CT scan also

helps, among other things, the medical team to define the differentiation between primary and secondary TB. Another potentially useful imaging examination is the contrasted esophagogram (usually with barium) to assess extrinsic compression and/or fistulous paths<sup>5</sup>, since fistulas are the main complications associated with esophageal TB. Tracheoesophageal fistulas cause choking and episodes of aspiration pneumonia<sup>10,11</sup>, while other types of fistulas such as esophagoarterial and esophagomediastinal can generate more disastrous complications such as massive hematemesis<sup>8</sup> and mediastinitis<sup>12</sup> - however, there are few reports in the literature. The TT, despite having been performed in both cases, has little diagnostic significance in endemic areas and does not allow the diagnosis of active TB<sup>3,13</sup>.

The standard treatment with RHZE for six months is the recommended regimen<sup>13</sup> for esophageal TB, including cases involving the formation of fistulas<sup>11,14</sup>, provided that a possible resistance to these drugs is not proven. In clinical practice and in the literature, however, there are several reports in which the treatment was prolonged for 9 or 12 months<sup>5,10,11</sup>, as was the case of our Patient #2. In case of fistulas, fasting associated with enteral or parenteral nutrition is debatable<sup>15</sup> and reinforces the importance of a multidisciplinary approach. Symptomatic improvement in these cases usually occurs only in the second month of treatment and endoscopic evolution must be monitored. In situations of therapeutic failure - fortunately rare - surgical correction may be indicated<sup>2,3</sup>.

## CONCLUSION

The two cases reported here exemplify the possibility of esophageal TB being one of the differential diagnoses of patients with dysphagia and weight loss, even in the absence of classic pulmonary symptoms. Biopsies performed by EGD are the main tool available to define this diagnosis, but the finding of granulomas in histological sections requires, whenever possible, deepening the investigation through specific stains and molecular biology tests.

*"This case report deserved an official declaration of acknowledgement and ethical approval by its institution of origin and was peer-reviewed before publication, whilst the authors declare no fundings nor any conflicts of interest concerning this paper. It is noteworthy that case reports provide a valuable learning resource for the scientific community but should not be used in isolation to guide diagnostic or treatment choices in practical care or health policies. This Open Access article is distributed under the terms of the Creative Commons Attribution License (CC-BY), which allows immediate and free access to the work and permits users to read, download, copy, distribute, print, search, link and crawl it for indexing, or use it for any other lawful purpose without asking prior permission from the publisher or the author, provided the original work and authorship are properly cited."*

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