An Unusual Cause of Dysphagia: Esophageal Tuberculosis

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Abstract

A 25-year old Indian exchange-student presented to our department with a three week history of dysphagia. Diagnostic evaluation by upper gastrointestinal endoscopy, endosonography and chest-CT revealed a tumor-suspect ulcerative lesion at the middle esophagus, and a mediastinal lymph node enlargement. Initial histopathological evaluation of multiple esophageal tissue biopsies showed an unspecific esophagitis without signs for malignancy. A positive T-spot® TB assay result, together with the bronchoscopic detection of a small exophytic lesion at the right main bronchus depicting caseating epitheloid cell granulomas, provided evidence for a tuberculous etiology of the esophageal tumor. Multiple further deep submucosal biopsies were needed to finally detect epitheloid cell granulomas in the esophageal lesion. Microbacteriological or molecular tests were negative for M. tuberculosis. Tuberculostatic treatment resulted in a good response with complete remission of the esophageal lesion and the mediastinal lymph node enlargement. Esophageal tuberculosis is rare in developed countries, and its possible presence deserves consideration particularly in patients at risk.

Keywords

Dysphagia – ulcerating esophageal lesion – M. tuberculosis – esophageal tuberculosis

Introduction

Tuberculosis is a common and often deadly infectious disease caused by Mycobacterium tuberculosis. According to WHO estimates, approximately one third of the World population has been exposed to M. tuberculosis [1], and high annual incidence rates are reported from Asia and Africa contributing ~85% of the incident cases. In Germany, the annual tuberculosis incidence is low (6/100,000). At risk populations particularly include immunocompromised or homeless persons, and immigrants from endemic areas. Although tuberculosis primarily affects the lungs, extraintestinal tuberculosis can occur at any organ site. Among those, gastrointestinal tuberculosis is the sixth most common extrapulmonary location, representing ~1.2% of the tuberculosis cases reported in Germany [2]. Infection of the gastrointestinal tract with M. tuberculosis or other pathogens (M.tuberculosis complex) may affect solid or hollow organs, abdominal lymph nodes and/or the peritoneal cavity. In the following, we present a patient with esophageal tuberculosis, accounting for approximately 0.2% of the reported gastrointestinal tuberculosis cases.

Case report

The 25-year old Indian exchange student presented to our department with a three week history of dysphagia. She did not report weight loss or fever. She negated intake of regular medications, alcohol consumption, and smoking. The past medical history was unremarkable. The vital signs and physical examination were normal. Laboratory tests showed a mild hypochromic anemia (Hb 11.4 g/dL, MCV 73.9 fl), a C-reactive protein of 0.6 mg/dL (normal 0.5 mg/dL). All other routine lab parameters were within normal limits. Upper gastrointestinal endoscopy showed an ulcerating, tumor-suspect lesion at the middle esophagus (Fig. 1). Endosonographically, this lesion penetrated the esophageal wall, adjoining an enlarged mediastinal lymph node (Fig. 2). Histological examination of the collected esophageal biopsies revealed a severe ulcerating esophagitis without signs of malignancy. Extensive biopsy sampling was repeated twice, again demonstrating unspecific inflammatory changes. Further evaluation by chest-CT depicted the mediastinal lymph node enlargement with no evidence for other focal lesions (Fig. 3). Abdominal ultrasound was normal.
Ten days after the initial admission, the patient developed strong lower back pain and fever (38.2°C). Clinical examination revealed lumbar muscular tenderness and pain on percussion, without visible signs of inflammation. Further diagnostics by magnetic resonance imaging (MRI)-imaging showed a retroperitoneal abscess (Fig. 4), that was revised surgically. Microbiological and histopathological workup of the abscess fluid collection revealed granulocyte rich abscess material, however, no specific pathogen was detected in direct smear and culture. Further microbiological diagnostics showed a positive T-spot®.TB (Oxford Immunotec) assay result. Subsequent diagnostic bronchoscopy found a very small, exophytic lesion at the right main bronchus (Fig. 5), histopathologically depicting caseating epitheloid cell granulomas. Extensive tissue sampling that included deep submucosal biopsies of the esophageal lesion was repeated, finally revealing epitheloid cell granulomas in only one of the multiple collected esophageal biopsies (Fig. 6).

The microbiological examination of body fluids such as sputum, bronchoalveolar lavage, blood, abscess collection, urine, stool was tested negative for M. tuberculosis by direct microscopy smear, specimen culture and polymerase chain reaction (PCR). Also, tissue samples were tested negative for specific DNA by PCR and tissue microarray. A HIV-
test was negative. We initiated a standard tuberculostatic treatment with isoniazid, rifampicin, pyrazinamide, and ethambutol for two months, then isoniazid and rifampicin alone were continued for further six months. Follow-up endoscopy and endoscopic ultrasound six weeks and three months after the initial presentation showed a regression of the esophageal lesion, indicating a good treatment response. Six months after the therapy initiation, the esophageal lesion and mediastinal lymph node enlargement had completely resolved (Fig. 7), and further follow-up examinations (1 year p.i.) were normal.

Discussion

Gastrointestinal tuberculosis is rare in developed countries and has mainly been reported in immunocompromised (e.g. HIV-infected) persons and immigrants from high risk areas. Involvement of the gastrointestinal tract occurs through ingestion of infected sputum or hematogenous spread from primary pulmonary tuberculosis or minimal lesions that are however apparent in less than half of the patients [3]. Gastrointestinal tuberculosis can involve any site of the GI-tract and peritoneum, and clinical symptoms may be vague (e.g. fever, night sweats) and site specific.

Esophageal manifestation of the disease, as reported herein, is extremely rare and has been reported to only account for approximately 0.2-1% of the reported gastrointestinal tuberculosis cases [2]. In the esophagus, tuberculosis infection most commonly occurs in the middle part as ulcerative, tumor-like lesions. Related site-specific symptoms include retrosternal pain, dysphagia and odynophagia. Mediastinal lymphadenopathy, as reported in our patient may be present. Whether the esophageal tuberculosis is primarily attributable to ingestion of infected sputum or occurred via direct extension from the adjacent mediastinal lymph node (or vice versa) or hematogenous spread from the small endobronchial lesion remains unclear, as all routes of dissemination are generally possible.

The development of a “cold” abscess, defined as an abscess without the usual clinical signs of inflammatory tissue reaction, has been reported in patients with disseminated tuberculosis. Predilection sites include – as in our patient - the lumbar spine or the ileopsoas muscle- where tuberculous abscesses present with strong back pain and possibly fever, but may lack redness and swelling.

In the present case, the diagnosis of the esophageal tuberculosis was hampered and delayed by the low sensitivity of the available histological or microbiological methods. The diagnostic difficulties as reported herein are in line with previous case reports or case series of patients with gastrointestinal tuberculosis [4-6].

In our patient, multiple esophageal tissue biopsies were necessary to finally detect tuberculous granulomas in only one of 35 esophageal tissue biopsies. This is related to the fact that the density of tuberculous granulomas in the infected organ tissue may be low. Furthermore, tuberculous granulomas are located in the submucosal layer that frequently is not adequately represented in endoscopic tissue biopsies, highlighting the need of multiple and deep tissue samples in patients with suspected esophageal or intestinal tuberculosis. Accordingly, sensitivity as reported in the literature for histopathological detection of typical caseation granulomas in endoscopy samples ranged from 25% to 60.8%, and a higher sensitivity was achieved only when the tissue specimens were obtained surgically or through laparotomy [4-6].

Among microbiological methods, the reported clinical sensitivity of tests such as direct acid-fast bacilli (AFB) smear, culture or PCR is quite variable in different clinical settings. More specifically, the diagnostic sensitivity depends on the density of Mycobacterium tuberculosis in the collected sample, the sample volume, the sample handling, and usually the investigation of several samples, including early morning collections, are recommended [7]. In our patient, all microbiological investigations that included direct smear, culture, PCR, and tissue microarray were negative. However, a low diagnostic yield to microbiologically confirm the diagnosis was also reported in case series on patients with abdominal or intestinal tuberculosis [4-6].
Interferon-gamma release assays such as T-spot®.TB (Oxford Immunotec), which tested positive in our patient, indicate infection with *M. tuberculosis* by detection of specific antigens (ESAT-6 and CFP10), that are, for example, not represented in BCG strains [8]. However, although well suited to delineate prior vaccination from infection with *M. tuberculosis*, this assay does not allow to distinguish latent tuberculosis from active disease [9]. Although the test may support a diagnosis of tuberculosis in low-risk patients, the diagnostic information is lower in patients from high prevalence areas such as India, where two out of every five persons - or more than 400 million people - have latent tuberculosis infection [10]. In this setting, a positive test result does not necessarily indicate an active tuberculosis, and a negative result does not necessarily rule out active disease in an individual strongly suspected to have tuberculosis, particularly when anergy due to advanced disease, malnutrition or immunosuppression is present [9].

We initiated a standard tuberculostatic treatment in our patient, and continued the treatment over a period of eight months. Follow-up endoscopy and endoscopic ultrasound six weeks and three months after the initial presentation showed a regression of the esophageal lesion. Six months after therapy initiation, there was a complete remission of the tuberculous esophageal lesion and the enlarged mediastinal lymph node, and further follow-up examinations (1 year p.i.) were normal.

**Conclusion**

The prevalence of gastrointestinal tuberculosis is low. However, its possible presence deserves consideration, particularly in at risk populations such as immunocompromised, homeless or immigrants from high-risk areas, as was the Indian exchange student reported. The diagnostic confirmation of the disease may be hampered and delayed by the low sensitivity of the available diagnostic methods. As an early diagnosis and therapy is critical for the disease outcome, the initiation of a specific chemotherapy is essential when the disease is strongly suspected, possibly even in the absence of a diagnostic confirmation.

**References**