Case report

Oesophageal tuberculosis with concomitant candidiasis: a rare cause of dysphagia

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SUMMARY

We present a case of a 23-year-old woman with dysphagia. She was reportedly newly diagnosed with HIV and had been initiated on antiretroviral treatment and tuberculosis (TB) prophylaxis. Oesophagogastroduodenoscopy revealed an irregular, ulcerative oesophageal lesion. Subsequent histopathology revealed *Mycobacterium tuberculosis* as well as *Candida albicans*. A CT scan demonstrated widespread disease with miliary TB. She was subsequently initiated on antituberculous and antifungal medications. TB is one of the most common and deadly infectious diseases in the world, with the highest rates seen in the developing countries. It commonly occurs as an opportunistic infection of HIV. Despite its potential for systemic infection, infection of the oesophagus is incredibly rare, more so as a co-infection with candida. This case highlights the need to have a high index of suspicion in high risk groups, as early treatment is crucial in addressing this global health crisis.

BACKGROUND

South Africa is one of the countries with highest rates of tuberculosis (TB). In 2017, the WHO estimated the incidence to be 322 000 with a rate of 567/100 000 people, 60% of which are coinfecting with the HIV.¹ TB may affect any organ in the body but a widespread disseminated form, known as miliary TB, occurs in 1–3% of cases.^{1,2} Despite this high prevalence and possible systemic involvement, TB of the oesophagus is rare. It has been reported to occur in 0.3% of cases of TB involving the gastrointestinal tract, as well as 0.3–0.5% of patients presenting with dysphagia.^{3,4} It usually occurs as a secondary infection from TB elsewhere in the body, such as by contiguous spread from compressive mediastinal nodes, haematogenous spread from the lungs or from swallowing infected sputum.⁴ Symptoms vary and may include those secondary to the lesions such as dysphagia, odynophagia or haematemesis; a productive cough associated with fistula or constitutional TB symptoms such as fever, weight loss and night sweats.^{4,5} Endoscopic findings usually vary and are non-specific which can make diagnosis difficult. The following case documents the presentation and clinical course of a patient who presented with dysphagia, which was subsequently diagnosed as TB. This case is also unique in that the patient had co-infection with candidiasis of the oesophagus.

CASE PRESENTATION

A 23-year-old woman, presented to the emergency department with a 1-day history of haematemesis. On further enquiry, she reported a 1-month history of progressive dysphagia to solids with associated hoarseness and weight loss. These symptoms were accompanied by palpitations, fatigue, loss of appetite and night sweats. She had no problems initiating swallowing, neurological dysfunction or reflux symptoms. She had no halitosis, retrosternal chest pain or coughing/gagging while swallowing. She did not report any cough, fever or have any known TB contacts.

Her medical history included HIV infection which she reported to have been initiated on treatment for past 1 month. However, further investigation revealed laboratory testing in keeping with HIV infection 4 years earlier. Her antiretroviral treatment (ART) comprised of a fixed-dose combination of tenofovir, lamivudine and efavirenz. She was reportedly receiving isoniazid preventative therapy (IPT) for TB prophylaxis. She reported her last CD4 count at 608 cells/unit (332–1642 cells/ μ L) at diagnosis (investigation revealed initial CD4 of 564 cells/ μ L (332–1642 cells/ μ L) in 2015). She had no other significant allergies, medical or surgical history. She reported a history of non-steroidal anti-inflammatory use but denied any ethanol ingestion or smoking.

On examination, she had a blood pressure of 102/71 mm Hg with a heart rate of 137 beats/min. She had a respiratory rate of 18 breaths/min, a saturation of 98% on room air and a temperature of 37.1°C. She had no significant conjunctival pallor but was noted to be chronically wasted. The respiratory, cardiovascular and abdominal examinations were unremarkable. She was given intravenous fluid, electrolyte replacement and was sent for an oesophagogastroduodenoscopy (OGD).

INVESTIGATIONS

An arterial blood gas was done which showed a mild respiratory alkalosis and some electrolyte abnormalities (sodium 134 mmol/L (136–145 mmol/L), potassium 2.9 (3.5–5.1 mmol/L)), but was otherwise unremarkable. Her formal bloods showed a normal white cell count of 6.11×10^9 /L (3.90 – 12.60×10^9 /L) and her haemoglobin level was 116 g/L (116–164 g/L). She had a CD4 count of 115 cells/units (322–1642 cells/ μ L) and a viral load of 38 copies/mL (no baseline for comparison). Her chest X-ray was unremarkable. The findings on

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Figure 1 Image from initial oesophagogastrroduodenoscopy showing irregular ulceration of the oesophageal mucosa at 25 cm from the teeth.

OGD revealed an irregular, ulcerative area in the oesophageal mucosa at 25 cm from the teeth with no fistula visible ([figure 1](#)). Biopsies of the lesion were taken.

She was discharged while awaiting results but returned with worsening symptoms 2 months later, citing transport problems as the reason for her delay. Blood test showed normal electrolytes and renal function but her haemoglobin had dropped to 97 g/L (116–164 g/L). Her X-ray appeared to have miliary infiltrates ([figure 2](#)). The OGD was repeated, which showed worsening of the ulceration but still no visible fistula ([figure 3](#)) as well as gastritis. A repeat biopsy of the lesion was taken.

The initial histology revealed ‘suppurative inflammation with a focal histiocytic reaction and focal giant cells. Vague granulomata were identified in some of the fields but caseative necrosis was not visible ([figures 4 and 5](#)). Myriads of acid-fast bacilli were identified on Ziehl-Neelsen stain ([figure 6](#)). The superficial exudate contained candidal pseudohyphal forms. In conclusion, the histopathological features were in keeping with superficial candida and TB’. The second biopsy confirmed these results showing ‘granulomatous inflammation with epithelioid histiocytes with occasional giant cells and positive stains for acid-fast bacilli’.

A CT scan of the chest and abdomen showed innumerable randomly distributed miliary pulmonary nodules ([figure 7](#)). It also showed mediastinal adenopathy with central necrosis which was abutting the oesophagus with mass effect. The size (largest diameter) and site of the adenopathy was as follows: 26 mm upper tracheal, 9.6 mm lower paratracheal, 12 mm subcarinal and 7 mm prevascular ([figure 8](#)). The spleen was enlarged to 12.5 cm with multiple hypodensities in keeping with splenic microabscesses ([figure 9](#)). There was also thickening of the

Figure 2 Erect posteroanterior chest X-ray showing diffuse uniform ‘millet’ infiltrates in bilateral lung fields.

terminal ileum and caecum with associated mesenteric adenopathy. These features were suggestive of disseminated TB.

Sputum collection for microscopy, culture and sensitivity was attempted; however the patient had a non-productive cough. Hypertonic saline nebulisation was unsuccessful in producing any sputum. A blood culture for *Mycobacterium tuberculosis* came back negative after 42 days.

DIFFERENTIAL DIAGNOSIS

1. Non-benign oesophageal lesion: due to the progressive onset of her symptoms, her nutritional status and the irregular lesion noted on OGD. This was excluded on both biopsies and CT scan.
2. Viral oesophagitis: for example, cytomegalovirus (CMV), herpes simplex virus (HSV), Epstein-Barr virus (EBV) oesophagitis. These organisms are known to cause ulceration and can affect any part of the gastrointestinal tract, particularly as opportunistic infections of HIV. This was excluded on biopsy which showed no viral inclusions and a blood tests which showed a negative CMV viral load. Treatment for these would have targetted the specific organism, for example, Ganciclovir.
3. Reflux oesophagitis: no convincing history or visualised reflux/hiatal hernia on OGD.

Differentiating these conditions was of utmost importance as treatment varies based on these important distinctions.

TREATMENT

The patient was initiated on fluconazole antifungal therapy and was initiated on antituberculous therapy according to the South African National Tuberculosis Management Guidelines which recommend treatment with a fixed drug combination of rifampicin (R) 150mg, isoniazid (H) 75mg, pyrazinamide (Z) 400mg and ethambutol (E) 275mg according to her weight category.⁶

Figure 3 Image taken from second oesophagoscopy showing irregular oesophageal ulceration and inflammation.

Due to confirmed extra-pulmonary tuberculosis (EPTB), the duration of treatment would be a total of 9 months: 2 months intensive phase (RHZE) followed by 7 months of the continuation phase of treatment (RH).⁶ Pyridoxine 25mg orally daily was initiated at the same time as prophylaxis against peripheral neuropathy due to isoniazid therapy.⁶

OUTCOME AND FOLLOW-UP

She was discharged from the hospital after a week of hospital therapy. She was tolerating her treatment and oral feeds with progressive relief of her dysphagia. She was referred to a TB centre for continuation of her treatment. On her 1-month

Figure 4 Histopathological slide of H&E stain of oesophageal mucosa demonstrating a central caseating granuloma with surrounding epithelioid histiocytes palisading the granuloma.

Figure 5 Close up of caseating granuloma with surrounding epithelioid histiocytes palisading the granuloma on H&E stain of oesophageal mucosa.

follow-up, she reported improvement in her symptoms. She had gained weight and was feeling more energetic. Psychosocially, she was determined to see her therapy to completion.

DISCUSSION

Dysphagia refers to disruption or discomfort in the migration of a food bolus from the mouth to the stomach. Its severity ranges from mild to serious, with complications such as aspiration pneumonia, malnutrition, dehydration and airway obstruction.^{4,5} Causes may be (1) functional, for example, neurological or co-ordination disorders or (2) mechanical, including but not limited to malignancy, cervical webs, strictures or infections (eg, candidiasis).^{4,5} Although candidiasis (as seen in this case) is common, infection of the oesophagus with TB is unusual.

TB is a communicable disease caused by the bacillus *M. tuberculosis*. Worldwide, TB is listed as one of the top 10 causes of death and accounts for the leading cause of death from a single infectious agent.⁷ In 2017, the estimated global incidence of TB was 10million new cases equivalent to 133 per 100 000 population.⁷ South Africa is listed among the top 30 high TB burden countries in the world according to the WHO, with a best estimated incidence of TB (across HIV positive and negative patients) of 322 000 in the year 2017.^{7,8} At-risk populations particularly include immunocompromised patients, for example, HIV infected. It typically affects the pulmonary system, however EPTB infection can occur involving pleura, lymph nodes and abdominal organs.⁷ A widespread disseminated form, known as miliary TB, occurs in 1%–3% of cases.^{1,2} The prevalence of

Figure 6 Ziehl-Neelsen staining of oesophageal granuloma demonstrating an acid-fast bacillus (AFB) suggestive of *Mycobacterium tuberculosis*.

Figure 7 Axial view of CT chest demonstrating diffuse pulmonary nodules in bilateral lung fields, in keeping with military tuberculosis.

EPTB among notified TB cases globally in 2017 was 15% and 16% in Africa.⁹

Gastrointestinal TB occurs through ingestion of infected sputum or haematogenous spread from pulmonary lesions, and can involve any site of the GIT and peritoneum.^{7 10} TB may cause dysphagia through several mechanisms: (1) primary (isolated) intrinsic oesophageal ulcers or (2) secondary such as trachea-oesophageal fistulae and infiltration from mediastinal or cervical lymph nodes.^{4 5 11} Despite the close proximity of the oesophagus and the pulmonary system, oesophageal involvement is the rarest form of gastrointestinal TB, accounting for 0.2%–0.3% of all reported cases.^{3 7 10–12} Oesophageal TB typically affects the middle third of the oesophagus at the level of the carina due to its proximity to the hilar and mediastinal lymph nodes, appearing as an ulcerative, tumour-like lesion as seen in this case.^{3 7 10}

In this case, we reported the occurrence of oesophageal TB in an immunocompromised patient with questionable adherence to prescribed treatment (low CD4 count, previous diagnosis

Figure 8 Axial view of contrasted CT scan of the chest and mediastinum demonstrating multiple large mediastinal necrotic nodes abutting the oesophagus with mass effect.

Figure 9 Axial view of CT scan of the abdomen demonstrating splenic enlargement with multiple hypodensities in keeping with splenic microabscesses.

in 2015). Her development of disseminated TB as well as the fungaemia may have been associated with the immune reconstitution inflammatory syndrome due to recent re-initiation of ARVs possibly without excluding underlying TB. This syndrome describes the paradoxical flaring up of symptoms associated with opportunistic HIV infections, shortly after initiating ART.¹³ It is believed to occur as a result of the strengthening of the immune system and its subsequent response to subclinical, dying or previous infections.^{13 14} This may have occurred in the case described above as her symptoms started shortly after being re-initiated on ARV's, and would explain her atypical presentation. However, the clinical criteria needed to make this diagnosis usually includes evidence of immune reconstitution either by an improvement in the CD4 count or reduction in the viral load which we were unable to demonstrate in this case due to an absence of a laboratory confirmed baseline.^{13 14}

The work up of a patient with oesophageal TB includes radiographic investigations such as chest radiographs (although these are sometime normal in patients with extra-pulmonary TB); contrast swallows demonstrating luminal narrowing or fistula; or CT scan demonstrating the adenopathy or lung changes, as were evident in the case above.⁴ Other possible investigations include the tuberculin skin test, blood or sputum microscopy, culture, sensitivity and gene-testing.⁴ Definitive diagnosis is in the form of a biopsy with suggestive features, that is, granuloma's with/without caseous necrosis; acid-fast bacilli on microscopy, positive PCR or culture.⁴ Although histological confirmation was achieved in our case, this is often negative even in the presence of TB and in the correct clinical scenario, treatment is initiated empirically.⁴

Treatment involves an initial four-drug combination of rifampicin, isoniazid, ethambutol and pyrazinamide in the intensive/initiation phase, which is reduced to a two-drug combination (rifampicin and isoniazid) for the continuation phase.^{3 6} The entire course of treatment is usually 9 months in the case of drug-sensitive EPTB. Surgery may be indicated for severe complications such as perforation and fistula formation.^{3 4 6} Other non-therapeutic steps were taken in the management of this case as per national guidelines: (1) isolation: in order to protect other patients and staff, the patient was placed in a well ventilated side cubicle and staff/visitors were encouraged to wear protective equipment such as N95 masks, (2) notification, where the details

Patient's perspective

I came to the hospital because I was having trouble swallowing and had vomitted blood. I had noticed that I was losing weight and was feeling unwell. I agreed to have the scope because I wanted to know what was wrong with me but when they told me that they had seen something I became scared that maybe it was cancer. I was very surprised when they told me that my symptoms were caused by tuberculosis (TB) because I had been taking treatment to prevent TB. I am not sure if it is because I was not eating properly and was struggling to take my medication. I am glad that it is not cancer and that there is treatment for TB but I wish that they could just cure this HIV, it is killing us.

Learning points

- This is a classic case of a common condition occurring in an unusual manner/location: tuberculosis is a highly infective and deadly disease which can affect any organ in the body including, although uncommonly, the oesophagus.
- There should always be a high index of suspicion in immunocompromised patients, who should receive full screening for extrapulmonary manifestations of opportunistic infections prior to initiation of ARV's and isoniazid preventative therapy in an attempt to prevent immune reconstitution inflammatory syndrome and drug resistance.
- Biopsies of suspicious lesions seen on oesophagogastroduodenoscopy may provide crucial information, even in the absence of malignancy and should always be done and followed up timeously.

of diagnosis are entered into a national database for surveillance purposes, (3) contact-tracing, where close contacts are screened for TB and at risk, uninfected groups (children or immunocompromised) are offered IPT prophylaxis and (4) adherence counselling for both her ARV's and TB treatment.⁶ Management of TB remains a global health priority requiring a multidisciplinary, biopsychosocial approach.

Contributors NM (corresponding author) is responsible for patient management, conception of study, interpretation of results and treatment, planning and final design of write up; involved in literature review and discussion; final approval of the

case for publication; agrees to be accountable for all aspect of the work. DMR is involved in interpretation of patient investigations and imaging; involved in literature review and write up; final approval of the case write up for publication; agrees to be accountable for all aspects of the work. OA is involved in acquisition of patient blood work and investigations; involved in write up of patients history and presentation; final approval of the case write up for publication; agrees to be accountable for all aspects of the work. All of the authors were involved in the management of the patient. They also contributed to the design and compilation of the report: patient history, literature review and so on. The authors have read and approved the final draft of this report and take full responsibility for the contents contained in it. All authors agree to be held accountable for all decisions relating to this report.

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