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TUBERCULOUS LYMPHADENOPATHY CAUSING DYSPHAGIA: REPORT OF TWO CASES

Omer S Alamoudi, MRCP, Julio S Montaner, MD,
Kenneth Evans, MD, J Mark FitzGerald, MD
Vancouver General Hospital, University of British Columbia,
St. Paul's Hospital AIDS Research Group
Vancouver, Canada

ABSTRACT

We report two cases of tuberculous lymphadenopathy causing dysphagia. The first patient was HIV positive and the second patient had immigrated recently from India. Culture in both patients grew Mycobacterium tuberculosis that was fully sensitive to first line drugs. Dysphagia may result from intrinsic or extrinsic involvement of the esophagus. Extrinsic involvement is more common and results from cervical and mediastinal lymph node enlargement (as in these 2 cases) that causes external compression on the wall of the esophagus. The dysphagia subsided completely after 4 weeks of antituberculous therapy in both cases.

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INTRODUCTION

Tuberculosis (TB) associated with human immune deficiency virus (HIV) infection is often extrapulmonary.[1] This form has also been reported in immigrants from Asia.[2] Because of the infrequent occurrence of extrapulmonary TB causing dysphagia, clinicians may not suspect a diagnosis of TB and treatment may be delayed. We present two illustrative case reports and a review of the literature concerning dysphagia as a presenting symptom of TB.

CASE 1

A 20-year-old female prostitute known to be HIV positive, presented with significant right-sided cervical lymphadenopathy and a 3-week history of dysphagia to both solids and liquids. She had received amoxicillin for a sore throat with no response. On examination she was febrile and had hairy leukoplakia. She had prominent lymphadenopathy particularly on the right side of the neck, measuring up to 5 cm in diameter with widespread involvement of cervical, submandibular, supraclavicular, lateral, and posterior lymph nodes bilaterally. She also had enlarged bilateral axillary and inguinal lymph nodes. Her spleen was palpable 4 cm below the costal margin. Investigations showed a white cell count of 5.7×10^3 per mm^3, hemoglobin 99 g·L, mean corpuscular volume 84 μm^3, her platelet count was normal, granulocytes 3.6×10^3 per mm^3, lymphocytes 1.7×10^3 per mm^3, helper T cells 0.44×10^3 per mm^3, suppresser T cells 1.26×10^3 per mm^3, helper/suppressor cell ratio 0.35, CD4 cells 440×10^3 per mm^3, hepatitis B surface antigen was negative. A skin test to tuberculin purified protein derivative was negative. Cervical lymph node biopsies showed extensive caseating granulomas, Ziehl-Neelsen staining was positive for acid-fast bacilli, and culture was positive for Mycobacterium tuberculosis that was fully sensitive to first line drugs. Chest radiograph showed mediastinal lymphadenopathy (Figure 1) and abdominal ultrasound showed extensive enlargement of the abdominal lymph nodes. There was no hepatomegaly. She was treated with rifampicin, pyrazinamide, isoniazid, ethambutol, and pyridoxine. Within two weeks, her symptoms improved with resolution of her dysphagia and gradual resolution of her adenopathy both on clinical examination and on chest radiography. She completed a full 9 months of therapy.

CASE 2

A 34-year-old Indian male who had emigrated to Canada in 1989, presented with a 3-week history of dysphagia. Two months earlier, he had noticed general malaise,

For reprint information contact:
Omer S Alamoudi, MRCP
King Abdulaziz University Hospital
Department of Medicine
P.O. Box 6615
Jeddah 21452, Saudi Arabia
Tel: 966 2 687 1195
Fax: 966 2 695 2538

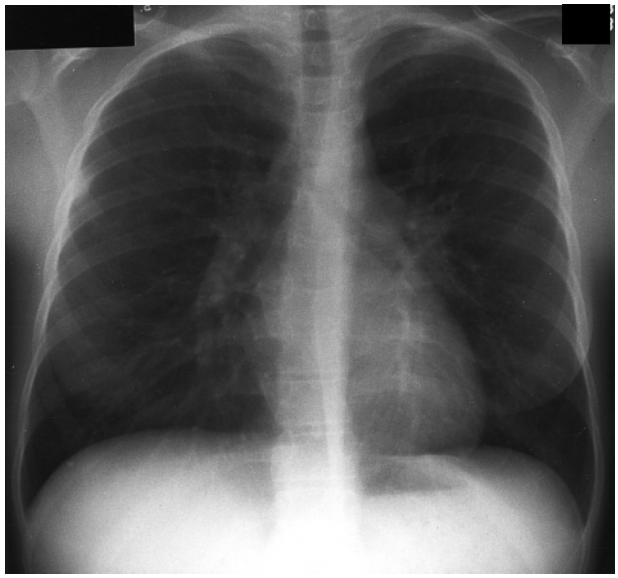

Figure 1. Chest radiograph showing mediastinal lymphadenopathy causing displacement of the trachea to the right side in case no. 1.

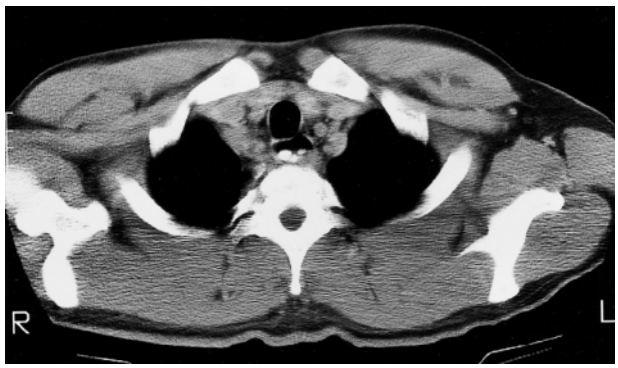

Figure 2. Computed tomography scan of the chest showing extensive mediastinal lymphadenopathy with some calcification causing compression of the esophagus in case no. 2.

fatigue, low-grade intermittent fever, night sweats, loss of appetite, and a weight loss of 7 kg. He denied having cough, dyspnea, hemoptysis, or chest pain. He had no history of TB contact or treatment and no risk factors for HIV infection. On examination, his temperature was 37.7°C. There were no palpable lymph nodes. Routine hematological and biochemical investigations were normal. He was initially evaluated with upper gastrointestinal endoscopy that showed extrinsic compression in the mid-esophagus. Because of uncertainty regarding the diagnosis of lymphoma or tuberculosis, further investigations were arranged. A chest radiograph was normal but a computed tomography (CT) scan of the chest showed extensive mediastinal lymphadenopathy causing esophageal compression (Figure 2). Sputum was negative on smear and culture for Mycobacterium tuberculosis. His Mantoux skin test to tuberculin purified protein derivative was positive (more than 10 mm in diameter). His HIV serology was not evaluated because the subject declined. Mediastinoscopy was difficult because of extensive fibrotic changes in the mediastinum and biopsies showed only fatty infiltration. Bronchoscopy demonstrated a submucosal nodule just to the left of the trachea on the medial wall of the left main bronchus and this area was biopsied. These biopsies showed granulomatous infiltration.

A bronchial aspirate grew a fully-sensitive Mycobacterium tuberculosis organism and treatment with rifampicin, isoniazid, pyrazinamide, ethambutol, and pyridoxine was commenced. Four weeks after starting treatment, the dysphagia had resolved. Five weeks later, he developed a left-sided fluctuating mass in his neck, which ruptured draining clear material from the site of his mediastinoscopy wound and the neck incision had opened up slightly. Material sent for routine as well as TB cultures was negative. Three weeks later, the drainage had subsided and the wound gradually healed.

DISCUSSION

There is concern regarding the resurgence of TB, much of it thought to be related to HIV infection.[1] Extrapulmonary tuberculosis accounted for 3898 (17.4%) cases of tuberculosis in the United States in 1988; lymphatic and pleural diseases were the most common forms of extrapulmonary tuberculosis and accounted for 27% and 26.6% respectively. Cervical lymphadenopathy was the predominant type of lymphatic tuberculosis and accounted for 754 (72%) cases, while mediastinal lymphadenopathy was less common and accounted for 151 (15%) of the total cases.[3] Tuberculous lymphadenopathy is common in patients with acquired immune deficiency syndrome (AIDS) but pleural and gastrointestinal TB are rare.[4] Chaisson and colleagues[4] in their study on 35 tuberculosis patients with AIDS showed that the incidence of TB lymphadenopathy in those patients was 31%, while gastrointestinal and pleural TB were 3% and nil respectively. In 1980, Enarson and colleagues[5] showed in an epidemiological study that extrapulmonary tuberculosis accounted for one-sixth (3671 cases) of all cases of tuberculosis reported in Canada during 1970 to 1974. Tuberculous lymphadenopathy was also the most common form and accounted for 7.1% of all cases. Gastrointestinal tuberculosis was less common and accounted for 0.7% of the total.

Involvement of the esophagus by TB is rare but well recognized.[6–9] Dysphagia is the most common presenting symptom and it is usually painful.[6,10–12] Hematemesis, hoarseness, and constitutional symptoms including fever and weight loss occur rarely.[6,9–12] Dysphagia may result from intrinsic or extrinsic involvement of the esophagus. Intrinsic involvement of the esophagus is infrequent but may result from primary esophageal tuberculosis in which no other systemic manifestation of the disease is present.[12,13] It may present as an irregular filling defect in the lumen of the esophagus and may mimic esophageal

carcinoma.The differential diagnosis also includes metastatic lung carcinoma, candidiasis, actinomycosis, ingestion of caustic material and subsequent scarring, and mediastinal lymphadenopathy due to malignancy.[6] However the diagnosis can be obtained by endoscopy with histological and bacteriological proof from biopsy specimens in patients with primary esophageal TB.

Extrinsic involvement of the esophagus is more common and related to the increased incidence of tuberculous mediastinal lymphadenopathy, especially in Asian immigrants and patients with AIDS.[2,6,7,14] It is caused by lymph node enlargement producing external compression of the esophagus. This usually results from direct extension of caseating subcarinal lymph nodes that may erode the esophageal mucosa and form a sinus tract.[7,9] Tracheoesophageal and brachyesophageal fistulae, especially those involving the right main bronchus, may occur due to mediastinal lymphadenopathy caused by TB.[6,7,9] Interestingly, in some of these cases, the fistulae healed with medical treatment but they usually required 1 to 2 months to heal completely.

Disease of the esophagus may be caused by direct spread from the lungs, hilar, mediastinal lymphadenopathy, or tuberculous spondylitis, or by retrograde lymphatic spread, and dysphagia may also result from mediastinal fibrosis in patients with advanced pulmonary tuberculosis.[6,8,9,12,15] Ramakantan and Shah[15] reported 9 patients with advanced pulmonary TB who presented with dysphagia. In each case, dysphagia was due to compression of the esophagus by fibrosing mediastinitis due to TB and interestingly, dysphagia developed in all of these patients while they were being treated with anti-TB drugs for 2 to 6 months. The mean duration of dysphagia was 2.1 months.

Damtew and colleagues[16] in an analysis of 19 cases of esophageal TB, found that the majority of patients had direct extension from an adjacent caseous mediastinal or hilar lymph node. Most of these cases were diagnosed late and showed predominant involvement of the upper or middle third of the esophagus. Tuberculin purified protein derivative skin testing was positive in the majority of the patients. Barium studies may show intrinsic esophageal involvement including mucosal irregularities or ulceration or extrinsic esophageal compression due to extrinsic TB lymphadenopathy and inflammatory adhesions. Computed axial tomography is a more reliable noninvasive diagnostic tool, especially in the case of mediastinal involvement.[16] Patients with HIV-associated TB tend to have impaired granuloma formation, depressed cell-mediated immunity, less tendency to pulmonary cavitation, negative tuberculin tests, and a decrease in CD4 cell counts.[17–19] Although drug-resistant disease is a problem in some locations, most HIV-related TB is drug sensitive and responds well to therapy.[20]

In our patients, dysphagia was the main presenting symptom and was related to extrinsic compression of the esophagus by tuberculous lymphadenopathy. The diagnosis was obtained in the first patient by culture of the cervical lymph node biopsy specimens, while in the second patient a bronchial aspirate revealed the diagnosis. Histology and microbiology are essential to confirm the diagnosis and to differentiate typical and atypical mycobacterium, especially in patients with AIDS. Cultures of biopsy specimens usually give better results than histological examinations of the same tissue in the majority of the cases.[21] In the first patient, the Mantoux skin test was negative despite her CD4 cell count being more than 400×10^3 per mm^3. CD4 cell counts above 400×10^3 per mm^3 are usually associated with positive tuberculin skin tests.[19] However, our first patient's negative response could be attributed to her positive HIV status despite a normal CD4 count and to her nutritional state.

Dysphagia subsided in both patients at 4 to 8 weeks after TB therapy was initiated. In the second patient, the mediastinal lymph nodes enlarged while the patient was on antituberculous therapy and caused a fluctuating mass in the neck that ruptured and caused a discharging sinus in the neck through the mediastinoscopy wound. Enlargement of mediastinal lymph nodes while the patient is on antituberculous therapy has been reported recently by Kaur and colleagues[22] who described a case of cervical TB lymphadenopathy complicated by extrinsic esophageal compression and esophageal ulceration secondary to mediastinal lymph node enlargement that occurred while the patient was on antituberculous therapy. In addition, enlargement of superficial tuberculous lymph nodes has been well documented.[2,22,23] Iles and Emerson[23] reported that 2 of 43 patients developed TB lymphadenopathy while they were on antituberculous therapy. This may have been due to hypersensitivity to tuberculin protein and to bacterial load.[2]

CT was more sensitive than chest radiography in evaluating mediastinal lymphadenopathy, especially in the second patient who had a normal chest radiograph but extensive mediastinal lymphadenopathy was seen on his CT scan. Neither of our patients had a barium swallow although the second patient had upper gastrointestinal endoscopy because of his dysphagia. This showed extrinsic compression. We did not consider that a barium study was necessary when the CT scan showed mediastinal or hilar lymphadenopathy causing esophageal compression. The clinical presentation, positive Mantoux skin test, and CT scan suggested the diagnosis but bacteriologic proof is important in the differential diagnosis of lymphoma.

Dysphagia is an unusual symptom of esophageal TB and especially of mediastinal TB. The diagnosis should be considered in subjects with HIV infection or patients from Asia. Once the correct diagnosis is made and therapy

initiated, the response to therapy is good although an initial rebound increase in lymphadenopathy may cause some early increase in symptoms.

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