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Case Study

DISSEMINATED TUBERCULOSIS IN IMMUNOCOMPETANT INDIVIDUAL- A CASE REPORT

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ABSTRACT

Tuberculosis, a chronic infectious disease caused by *Mycobacterium tuberculosis*, may invade all organs but mainly affect the lungs. We report a case of disseminated tuberculosis with pulmonary, hepatic, pleural, skeletal muscle, spleen, intestines, cervical and mediastinal lymph node involvement and a review of the relevant literature. A 25year-old male was admitted with cervical swelling and pain abdomen near umbilicus associated with low grade fever, fatigue, nausea, anorexia, weight loss. A chest X-ray showed right upper zone infiltrates and a computed tomographic scan of the thorax and abdomen revealed a consolidation in right upper lobe with necrotic mediastinal lymphadenopathy with mild pleural effusion, focal abscess in right sternocleidomastoid muscle, focal liver lesion and micro abscess in spleen. Liver and cervical lymph node biopsy revealed granulomatous lesions with central caseating necrosis. Tuberculosis is usually associated with atypical clinical manifestations. Imaging examination combined with histopathological features, a high index of clinical suspicion and improvement with antitubercular therapy are necessary to confirm a diagnosis, especially in the cases of extrapulmonary tuberculosis.

Keywords: Immunocompetence, Liver, Spleen, Sternocleidomastoid, Tuberculosis

1. INTRODUCTION

Tuberculosis (TB) is the most common cause of chronic infectious diseases, afflicting up to one-third of the world's population and most commonly impacting the pulmonary system. Extrapulmonary TB is defined as the occurrence of TB at sites other than the lungs, such as the lymph nodes (19%), pleura (7%), gastrointestinal tract (4%), bone and joints (6%), meninges and central nervous system (3%), genitourinary system (1%), cutaneous (1%), and endocrine glands (<1%) [1]. Disseminated TB is defined as a TB infection involving the bloodstream, bone marrow, liver, or two or more noncontiguous sites or systems and includes miliary TB involving the lungs. Disseminated TB has been observed for centuries, but its exact incidence is not known. Moreover, the symptoms and signs are nonspecific and mimic a variety of diseases, requiring a high index of suspicion for early diagnosis. Disseminated TB is often missed antemortem and has been confirmed in 33 to 80 percent of autopsies [2]. The disseminated forms of TB can arise in contiguous, lymphogenous, or hematogenous conditions, which can manifest as a single or multiorgan form of TB [3]. The risk factors include the following: high bacillary-load immunosuppressive condition (*e.g.,* human immunodeficiency virus [HIV]), diabetes, smoking, alcohol abuse, young age, malnutrition, exposure to indoor air pollution, connective tissue disorders, pregnancy (peri- or postpartum), underlying malignancy, use of immunosuppressive drugs like corticosteroids and biologicals, [4] or exposure to an infectious person. In an immunocompetent adult, miliary TB constitutes less than two percent of all TB cases and up to 20 percent of all extrapulmonary TB cases [5]. We present a case of an apparently immunocompetent adult man with disseminated TB with multisystem involvement. Treatment and etiological factors are described and discussed.

2. CASE PRESENTATION

A 25-year-old North Indian man who was referred to our tertiary care centre in MMIMSR (MM deemed to be university) Mullana Ambala, India, presented with cervical lymphadenopathy and pain abdomen from last 3 months. He had an evening rise of fever along with occasional chills, sweats, fatigue, and not significant weight loss. There was no history of hemoptysis, dyspnea, urinary or sensory or motor weakness but there was occasional cough in morning. He was alert but appeared uncomfortable, moderate tenderness in the right upper abdomen with palpable Hepatomegaly. He

had received multiple courses of antibiotics. He had received a bacillus Calmette-Guerin vaccination in childhood. There was no past or family history of TB at the time of presentation.

On physical examination at admission, he had a temperature of 37.2°C, a heart rate of 102/min, a blood pressure of 110/79mmHg and a respiratory rate of 22 breaths per minute with oxygen saturation of 98% on ambient air. Cardiovascular examination revealed sinus rhythm; jugular veins were normal.

Examination revealed (Fig. 1) there is swelling over right neck which is warm and lymph nodes left cervical region also which are not painful, Multiple enlarged, non-tender, firm, matted cervical.

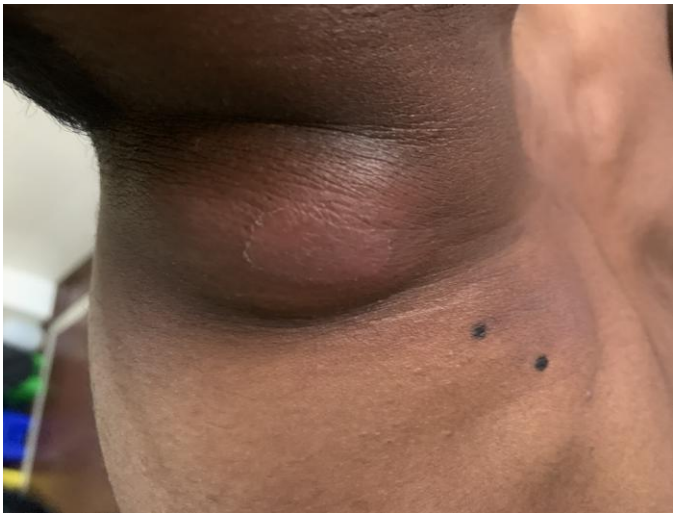

Fig.1: Swelling over right side of the neck

Pus smears were positive for acid-fast bacilli and negative for gram-stain. However, aerobic, anaerobic, mycobacterial, and fungal cultures were negative. Mantoux test was positive (12mm×15mm). Repeated sputum examination for acid-fast bacilli was negative on three consecutive days. Enzyme-linked immunosorbent assay for HIV and venereal disease research laboratory (VDRL) test was nonreactive. HbsAg and HCV are negative. Blood investigation revealed hemoglobin of 12.5gm%, a leukocyte count $7.5\times10^3/\mu L$, a platelet count of 250×103/μL, an erythrocyte sedimentation rate of 30mm/hr, and a C-reactive protein of 7mg/dL. Sputum for gram stain/culture and fungal culture were negative. RBS -65, RFT and LFT are within normal limit. Urine routine microscopy and culture are negative. Even CBNAAT is also negative. FNAC right cervical lymph node and liver granuloma suggestive of necrotizing granulomatous lymphadenitis correlate with tuberculosis.

A chest x-ray (Fig. 2) suggestive of infiltrate over right upper zone.

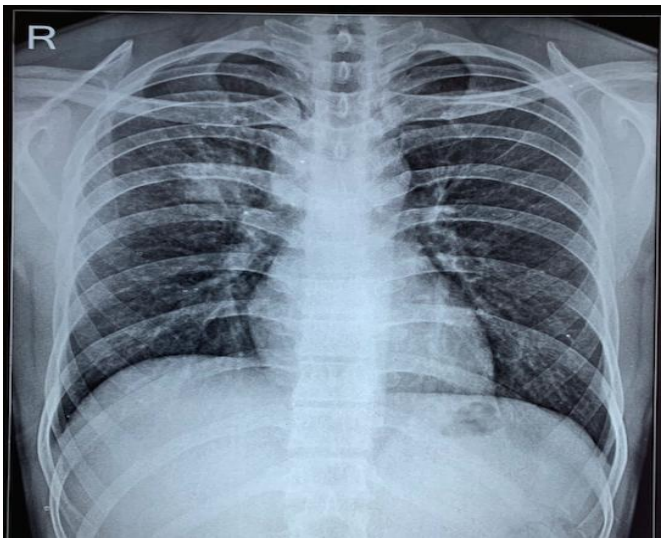

Fig 2: Chest x-ray suggestive of infiltrates in right zone

A computed tomographic (CT) scan of the thorax and abdomen revealed area of consolidation in right upper lobe with necrotic mediastinal lymphadenopathy and pleural tag with mild left side pleural effusion, focal abscess in right sternocleidomastoid muscle, splenic micro-abscesses with focal liver lesion (Figure 3a and 3b).

Usg abdomen suggestive of ileocoecal inflammatory thickening with splenic lesions and peritoneal thickening in perihepatic lesion, multiple nodular lesions within omentum and associated omental thickening. Minimal ascites and loculated pleural effusion. Hepatic granuloma was also present.

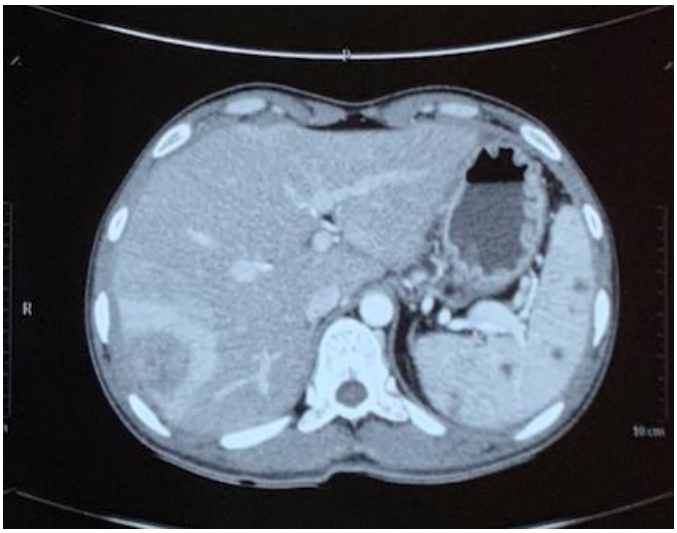

Fig. 3a: CT Chest showing area of consolidation right upper lobe

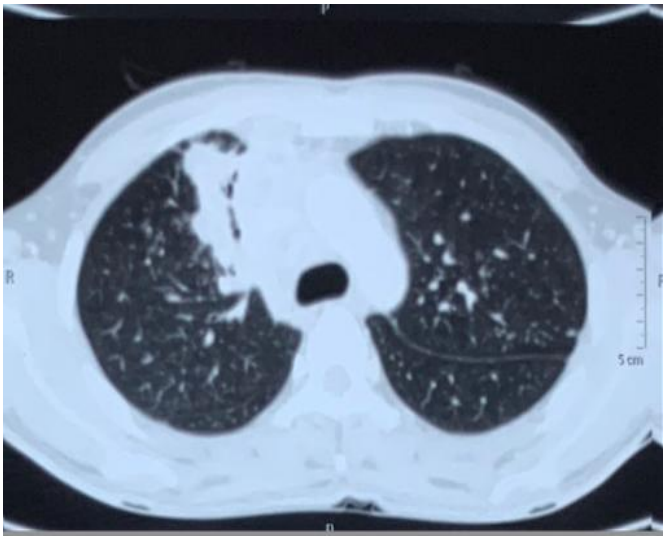

Fig. 3b: CT Abdomen showing focal area of granuloma in liver and micro abscess in spleen

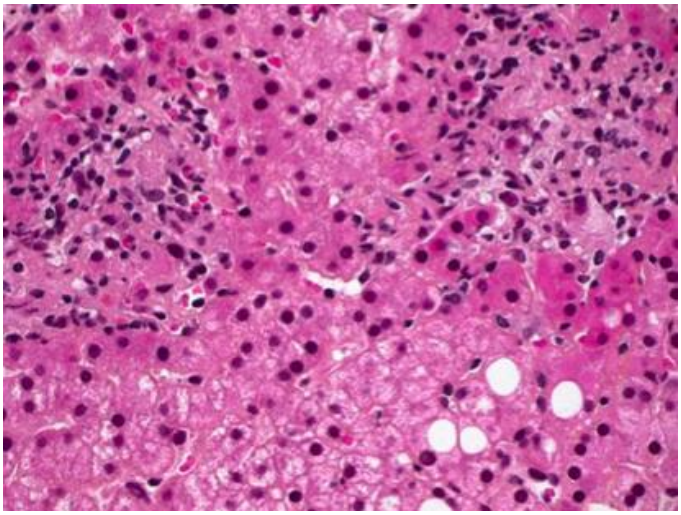

Fig. 4: Histology suggestive of epitheliod granuloma in liver

Histopathology from the liver lesion and neck showed a focally multiple epitheloid cell granulomas. Ziehl-Neelsen stain and Periodic acid-Schiff stain were negative

In light of the aforementioned findings, a diagnosis of disseminated TB was made, with involvement of the lungs, pleura, sternocleidomastoid muscle, liver and spleen. Antitubercular treatment consisting of isoniazid, rifampin, pyrazinamide, and ethambutol was initiated and the abscesses were aspirated.

After three months of antitubercular treatment, the fever resolved, swelling decrease and symptomatically better. Treatment continues till 12 months and HIV repeated again still negative.

3. DISCUSSION

Metastatic TB abscesses might also occur with progressive organ TB or in miliary TB; however, there are reports showing that it can occur without any underlying focus. Hepatic tuberculosis is rare and constitutes less than 1% of all cases of this infection [4]. Hence the clinical misdiagnosis rate is high because of lack of specific clinical manifestations and imaging features [6]. The presenting symptoms are usually nonspecific and are mainly constitutional in nature, including fever, night sweats, malaise, anorexia, weight loss, and abdominal pain, all those were present in our case.

In a recent retrospective study, only 20 cases of muscular tuberculosis were reported during 2000-2010 [7]. The rare occurrence of skeletal muscle tuberculosis has been associated with several characteristics of this highly differentiated tissue, such as high lactic acid content, high vascularity and blood flow, and the absence of reticuloendothelial and lymphatic tissue inhibiting mycobacterial growth. The pathogenesis is still uncertain. It may result from the hematogenous dissemination of pulmonary tubercular lesions, contiguous infection from an underlying structure or, in the absence of active foci of tuberculosis elsewhere, direct traumatic inoculation.

Hepatomegaly is the main sign, present in more than half of patients [6] and is usually found with an increase in liver tests. These findings however are not specific and may occur in other conditions, such as metastatic carcinoma, liver abscess, echinococcosis, amyloidosis and granulomatous diseases of varying etiologies.

Diagnosis of disseminated tuberculosis can be confirmed by histopathology of a tissue sample as in our case; although there was involvement of three organs, liver biopsy and lymphnode biopsy through needle aspiration was considered most feasible. It is of great importance in finding pathological lesions timely to make the diagnosis, in order to give effective treatment as early as possible to improve the cure rate of TB and to reduce the germination of drug-resistant tuberculosis [6]. Liver is a common site for granuloma formation owing to its rich blood supply, lying at the distal end of portal circulation and large number of reticuloendothelial cells. In histopathology, finding hepatic granuloma with central caseating necrosis is characteristic and should be considered diagnostic of tuberculosis until proven otherwise [8].

Extrapulmonary TB is more common in children, women and minorities [9]. Lymphadenitis is the most

common extrapulmonary presentation of TB. It occurs most commonly in the cervical region, representing 63% of all tuberculous lymphadenitis in one study of 1161 patients. In the same study, the incidence of lymph node swelling detected in more than one site was 35.0%, whereas the incidence of inguinal lymph nodes was only 1.7%. Although previously considered a childhood disease, lymphadenitis has a peak age of onset of 20 to 40 years [9, 10].

Pleural tuberculosis is the second more frequent site of extrapulmonary TB after lymph node involvement [11]. Although pleural TB infection is thought to result from the rupture of a subpleuralcaseous focus within the lung into the pleural space, it may occasionally be a result of hematogenous dissemination or contamination from adjacent infected lymph nodes.

Splenic TB is most commonly a part of miliary or disseminated TB and rarely an isolated phenomenon [12]. Spleen may be involved via the bloodstream, usually following reactivation of foci from a primary lung focus, although hematogenous spread may complicate active pulmonary TB or miliary TB. Contiguous spread from mesenteric lymph nodes, intestine, or fallopian tubes may also occur. Most of the reported cases of splenic TB were associated with immune-compromised conditions. However, there were also few cases where splenic TB was associated in immunocompetent patients [13, 14].

The patient described here had involvement of the skeletal muscle, lungs, liver, spleen, lymphnode which led to extensive multisystem disseminated disease. The obvious cause of dissemination could not be elucidated in this apparently immune-competent patient; however, the role of transient immune-suppression due to intercurrent viral, bacterial, or parasitic infection altering immunity to tubercular bacilli could have led to the dissemination of the infection in our patient. Cytomegalovirus, hepatitis C virus, and human herpes virus 2 have been associated with increased rates of atypical TB, as well as the reactivation of latent TB. Deficiency in natural killer cell cytotoxic activity induced by such chronic viral infections might play an important role in the development of the transient suppression of the immune responses to TB [15].

A 6 to 9 month regimen (2 months of isoniazid, rifampin, pyrazinamide, and ethambutol, followed by 4-7 months of isoniazid and rifampin) is recommended as initial therapy for all forms of extrapulmonary tuberculosis unless the organisms are known or strongly suspected to be resistant to the first-line drugs [16].

4. CONCLUSION

Extrapulmonary TB lacks typical clinical symptoms and imaging diagnosis, so can easily be misdiagnosed and treatment delayed. The hallmark of disseminated and extrapulmonary TB histopathology is the epithelioid granuloma with central caseating necrosis and the diagnosis is based on finding acid- fast bacilli in a smear or culture and/or the presence of caseous granulomas in a tissue specimen. However, rarely, if ever, are any TB bacilli seen. A high degree of clinical suspicion is required to diagnose this entity which can be medically managed easily but if not treated can lead to death.

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