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Case Report

Disseminated tuberculosis with tuberculous meningitis in an immunocompetent host

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Disseminated tuberculosis (TB) results from the lymphohematogenous spread of *Mycobacterium tuberculosis*. Despite the availability of effective therapy, diagnosis is usually late and mortality remains high. We report a case of a 29-year-old male with a history of alcohol abuse that presented with altered mental status and was found to have a 'tree-in-bud' sign on chest radiography. Chest computed tomography revealed innumerable pulmonary nodules in a miliary pattern. Examination of sputum and cerebrospinal fluid was positive for *M. tuberculosis* on nucleic acid amplification testing. The case emphasizes the importance of considering disseminated TB in patients with risk factors and typical radiographic patterns even in geographic areas with low disease prevalence.

INTRODUCTION

Disseminated tuberculosis (TB) is rare in the immunocompetent host. It results from lymphohematogenous spread of *Mycobacterium tuberculosis* during both primary and post-primary TB. The presentation is variable and early signs of infection seen on chest radiography are non-specific. In patients with risk factors, however, a strong clinical suspicion is the key to diagnosing the disease. Early initiation of therapy in cases of disseminated TB is associated with a significant improvement in outcomes. We report a case of a young male with known risk factors discussed below who was found to have a miliary pattern on chest radiography, and emphasize the importance of recognizing radiographic patterns suggestive of disseminated TB in patients with risk factors, regardless of geographic prevalence.

CASE REPORT

A 29-year-old Hispanic male was found on the street unconscious by the police and was brought to the emergency department (ED). The patient had a medical history that included alcohol abuse with multiple ED visits for alcohol intoxication and physical trauma over a 7-year period. His social history is remarkable for recent immigration to the USA 8 years ago from Mexico, and he currently resides in a dorm with eight roommates. Further history was not obtainable from the patient due to altered mental status and there were no family members or roommates present at the time of admission.

Initial physical exam revealed vital signs that were within normal limits aside from mild tachycardia and tachypnea with a temperature of 36.7°C, heart rate of 112/min, blood pressure of 110/79 mmHg and respiratory rate of 22 breaths per minute with oxygen saturation of 98% on ambient air. The patient was a thin appearing, disheveled male in mild distress. There was no evidence of trauma to the patient's head or body. He was alert but disoriented, and was unable to follow simple commands. Lung auscultation revealed normal vesicular breath sounds bilaterally with no wheezes or crepitations. Heart and abdominal examinations were unremarkable. Laboratory tests revealed a white blood cell count of 6000/μl, hemoglobin of 12 g/dl, platelet count of 88/μl, sodium of 117 mg/dl, alkaline phosphatase of 269 U/l and total bilirubin of 1.2 mg/dl. Urine drug screen obtained upon admission was negative, and blood alcohol and ammonia levels were normal. A computed tomography (CT) of the head without contrast was negative for a subdural bleed or other intracranial abnormality.

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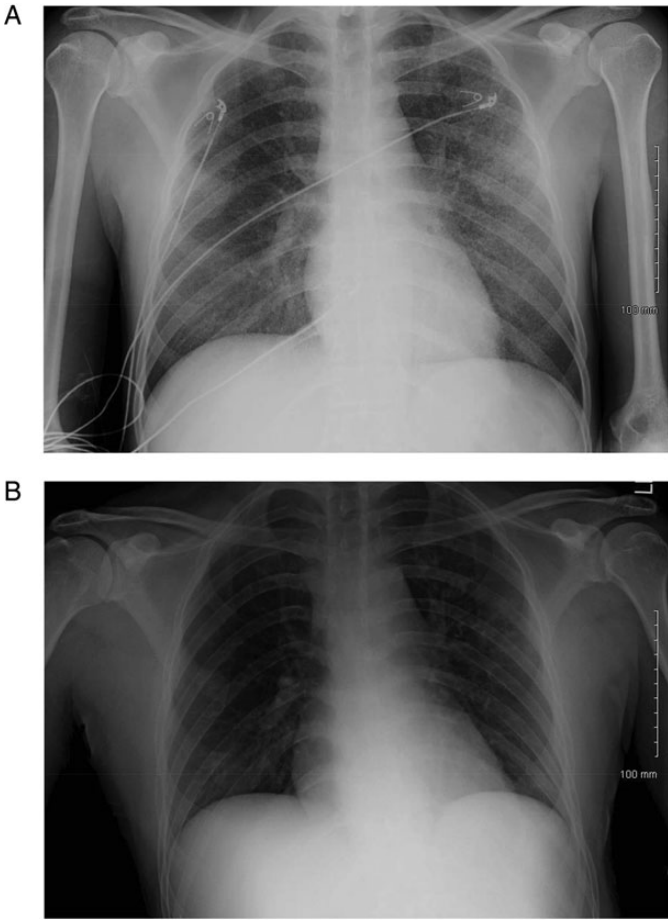

Figure 1: (**A**) Chest X-ray with a miliary pattern and a 'tree-in-bud' sign across right and left lung fields. (**B**) Normal chest X-ray 3 months prior to presentation.

A chest radiograph revealed diffuse ground-glass nodular opacities with a 'tree-in-bud' sign greatest in the left mid-lung (Fig. 1A). These abnormalities were not present on chest radiographs taken 3 months earlier when he presented to the ED with chest pain (Fig. 1B). CT of the chest with intravenous contrast revealed innumerable tiny pulmonary nodules in a random, miliary pattern (Fig. 2). In addition, there were multiple enlarged mediastinal and hilar lymph nodes, the largest of which measured 12 mm in diameter. A calcified granuloma was also noted in the left upper lobe. The differential diagnosis of a relatively new-onset miliary pattern on imaging included disseminated viral, bacterial, fungal and mycobacterial infections, hypersensitivity pneumonitis or metastatic disease with either hematogenous or lymphangitic spread. In the present patient, the findings on chest radiography coupled with risk factors of travel from an endemic area, malnutrition, overcrowding and alcohol abuse made the diagnosis of post-primary miliary TB very likely.

The patient was admitted and placed in a negative pressure room with droplet and respiratory isolation precautions. Sputum samples were obtained and microscopy revealed 3+ acid-fast bacilli (AFB). Concern for tuberculous meningitis was high given the initial presentation of altered mental status. A lumbar puncture was therefore performed and examination of cerebrospinal fluid (CSF) showed 13 nucleated cells (9 lymphocytes, 3 neutrophils and 1 monocyte), protein of 85 mg/dl and glucose of 94 mg/dl. A nucleic acid amplification test (NAAT) on sputum and CSF was positive for *M. tuberculosis*. Additionally, microscopy of a urine sample revealed AFB. The diagnosis of disseminated TB was made, with pulmonary, renal, central nervous system (CNS) and probable hepatobiliary involvement in light of elevated alkaline phosphatase and total bilirubin.

During the first 24 h of admission the patient's respiratory status deteriorated, requiring intubation and mechanical ventilation. His respiratory failure was believed to be due to acute respiratory distress syndrome from overwhelming infection. The patient was started on parenteral isoniazid (INH) and rifampin, due to concern for poor enteral absorption, and oral ethambutol and pyrazinamide as soon as the sputum samples returned positive for AFB. He was also started on dexamethasone as adjunctive anti-inflammatory therapy for tuberculous meningitis. The patient's clinical status improved and repeat chest CT showed significant improvement in miliary nodularity within 2 weeks (Fig. 3).

The patient required quadruple anti-TB therapy for 2 months followed by 7 months of INH and rifampin due to CNS disease. He suffered neurologic sequelae in the form of cognitive impairment, but made a fairly decent recovery.

DISCUSSION

Robert Koch, a German scientist, first identified *M. tuberculosis* in 24 March 1882. The epidemic had already claimed millions of lives, and the discovery of the responsible pathogen was the first step in the development of anti-TB drugs over 60 years ago. Unfortunately, the disease still kills an estimated 1.7 million people each year and the worldwide incidence from the latest World Health Organization (WHO) figures indicates 8.8 million cases reported in 2010 [1]. It is estimated that disseminated TB with a miliary shadow on radiographs account for about less than 2% of all cases of TB in immunocompetent persons [2].

TB remains a disease of poverty that is associated with overcrowding and malnutrition. Other risk factors are related to a host's compromised immune system and include; HIV infection, diabetes mellitus, smoking and alcohol abuse (Table 1). Our patient had multiple of these major risk factors, including immigration from an endemic area, malnutrition, overcrowding and alcohol abuse. The use of immunosuppressive medications including tumor necrosis factor (TNF) alpha antagonists and glucocorticoids must also be considered [3].

The clinical presentation of TB is variable with symptoms reflecting the underlying organ involved. The diagnosis of TB requires a high index of suspicion and can be difficult. Patients may have non-specific constitutional symptoms such as fever, weight loss and night sweats. However, in the early

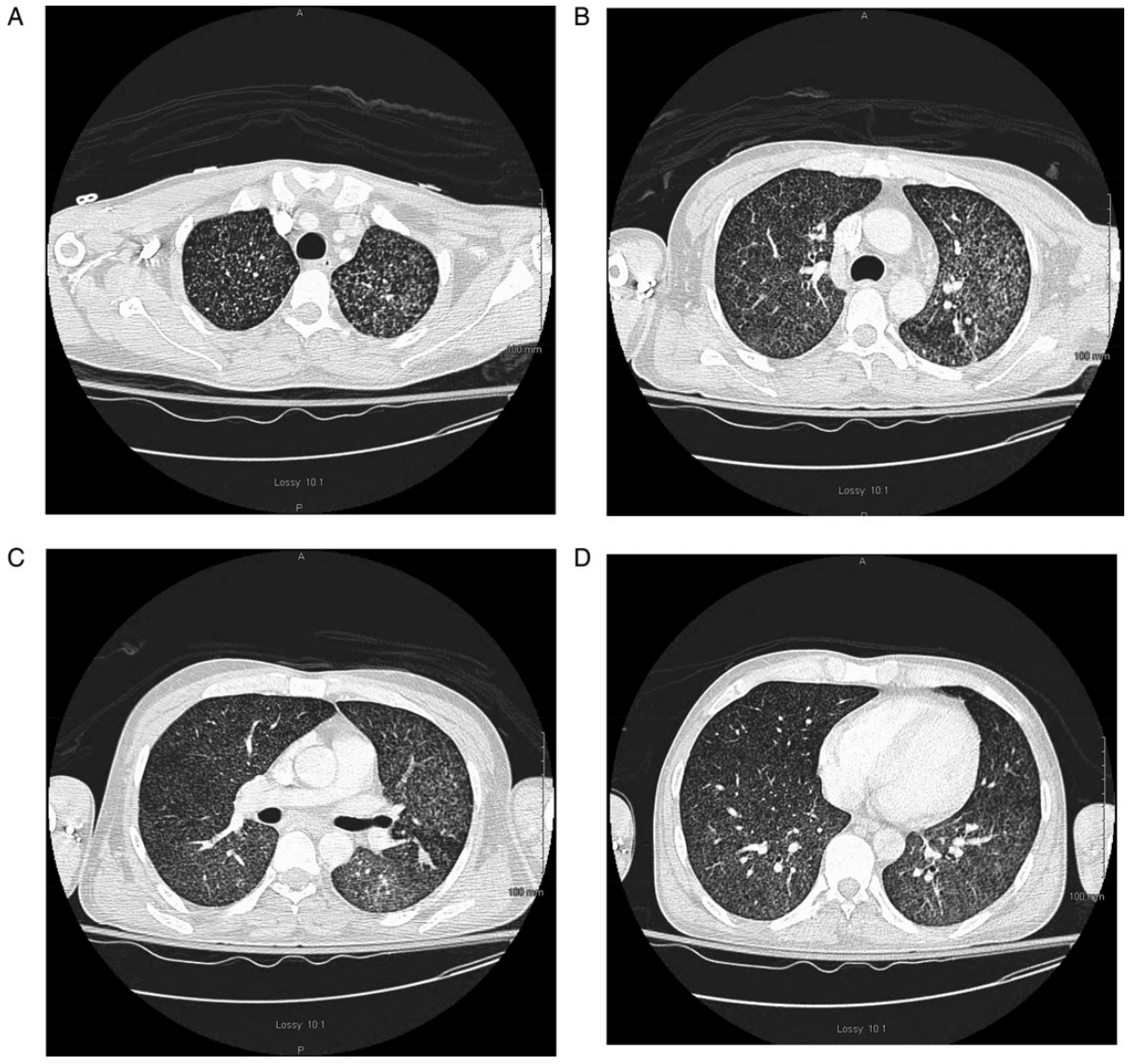

Figure 2: CT with intravenous contrast of the chest at multiple levels showing diffuse micronodular lung disease in random distribution, suggesting hematogenous spread of disease, most commonly seen with miliary TB.

stages of disease, symptoms might be absent [3]. In patients with suspected disseminated TB with pulmonary involvement, in addition to sputum analysis with microscopy and culture, the use of NAATs—specifically GeneXpert MTB/RIF assay—has revolutionized the diagnosis with its ability to detect MTB while simultaneously assessing rifampin resistance within 2 h. The sensitivity of this test is 98–100% in patients with sputum smear-positive disease and 57–83% in sputum smear-negative disease. Testing CSF with polymerase chain reaction is less sensitive with values ranging between 50 and 90%, but highly specific at 100% [2, 3].

Tuberculous meningitis is a rare complication of disseminated TB and is typically a subacute disease with a prodromal phase of low-grade fever, malaise and headache that may persist for a few weeks. Patients then tend to develop altered mental status and focal neurologic deficits [4]. The addition of adjunctive steroids is recommended when suspecting tuberculous meningitis since it has been shown to reduce death and disability by 30%.

The mortality rate of disseminated TB with tuberculous meningitis remains high upwards of 65% with neurologic sequelae present in up to 50% of survivors [5].

CONCLUSION

This case demonstrates the importance of considering disseminated TB in the differential diagnosis of a patient with a miliary pattern on chest radiography, especially with underlying risk factors, regardless of geographic prevalence. A strong clinical suspicion is essential for prompt diagnosis and rapid initiation of appropriate therapy for improved long-term outcomes.

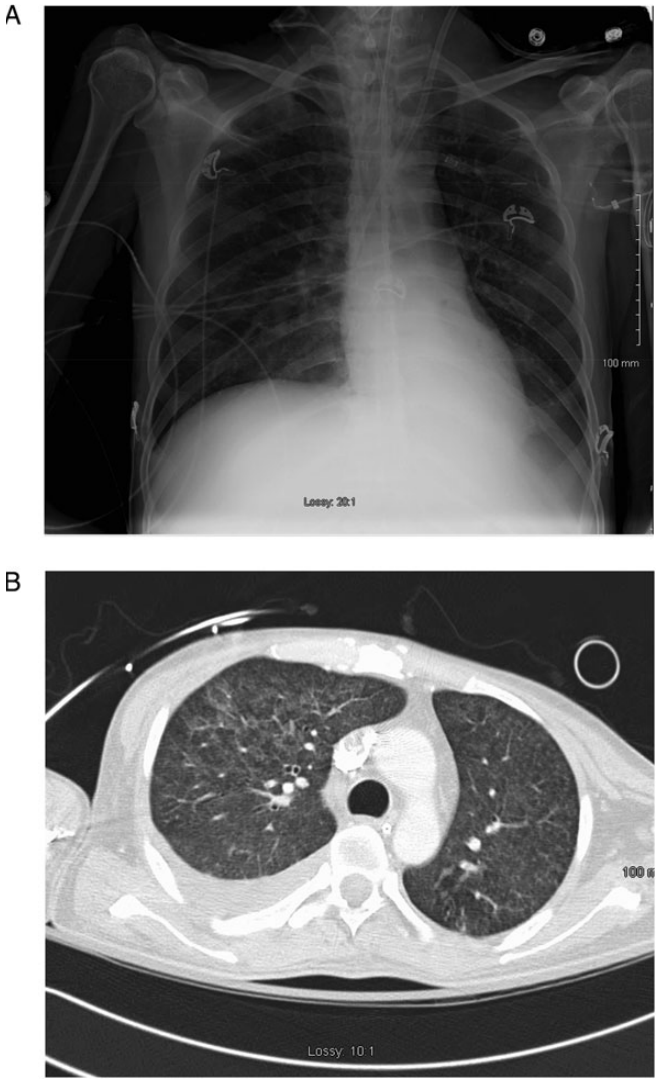

Figure 3: Chest X-ray and CT of the chest without contrast 2 weeks after initiating anti-tuberculous therapy demonstrating significant improvement in micronodular disease.

Table 1: Risk factors for progression to active TB in exposed populations

Social and demographic factors	Associated conditions	Drugs
Overcrowding	Malignancy	TNF antagonist therapy
Injection drug use		
Smoking	End-stage renal disease	
Sex (M : F = 2 : 1)		
Age (children and elderly)	HIV	Corticosteroid therapy
Alcohol		
Malnutrition	Diabetes mellitus	
Genetic susceptibility		

AUTHORS' CONTRIBUTIONS

All authors had access to the data and a role in writing the manuscript.

CONFLICT OF INTEREST STATEMENT

None declared.

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