TREATMENT OF MILIARY TUBERCULOSIS: CASE REPORT

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ABSTRACT

Miliary tuberculosis is a form of tuberculosis that is characterized by a wide diffusion of TB bacilli in human body and causing lesions (1–5 mm). Its name comes from a peculiar pattern seen on a chest radiograph of many tiny spots distributed throughout the pulmonary fields with the appearance identical to millet seeds—thus the term "miliary" tuberculosis. Miliary TB may infect almost every organ or individual organs like the lungs, liver, spleen and brain. The infection is characterized by an enormous amount of TB bacilli, although it may easily be missed and is fatal if left untreated. Miliary disease is more difficult to identify in patients who are very young or very old. Patients with miliary tuberculosis may experience symptoms for days to weeks or occasionally over several months, symptoms include Weakness, Headache, fatigue, Weight loss, Fever, Cough, Generalized Hepatomegaly, lymphadenopathy, Splenomegaly. The diagnosis of miliary tuberculosis is based on the finding of chest x-ray, sputum culture, bronchoscopy, open lung biopsy, head CT/MRI, blood cultures. The standard “short course” treatment for TB includes isoniazid, rifampicin, ethambutol and pyrazinamide for two months, then rifampicin and isoniazid alone for more four months. There have been cases where the delay in diagnosing and starting of appropriate treatment regimen has worsened the overall patient's health and lead to further complications and death. It is important that a protocol is being developed to identify the patients and start appropriate treatment regimen to prevent a fatal outcome.

KEYWORDS: Tuberculosis (TB), Miliary Tuberculosis, Computerized Tomography (CT), Magnetic Resonance Imaging (MRI),
1. INTRODUCTION
Tuberculosis (TB) disease is caused by the Mycobacterium tuberculosis (Mtb) which causes a granulomatous immune reaction and a quintessential tissue necrosis called “caseous necrosis”. In primary infection, the bacillus causes an inflammatory reaction at the site of entry which can cure with formation of sclerosis. The bacteria can also spread locally or throughout the body through the lymphatic system, blood, air, canaliculi and contiguity. \[^1\]

Miliary tuberculosis (TB) is a rare form of TB infection that results from large amount of lympho-hematogenous dissemination of Mycobacterium tuberculosis bacilli. It involves mostly the lungs but may also affect many other organs in the body. It is more likely to occur in immunocompromised patients due to their impaired cellular immunity and is rarely reported in immunocompetent hosts.\[^2\]

Following exposure and reception of TB bacilli in the lung, a primary pulmonary complex is established, followed by development of hilar lymphadenopathy and pulmonary lymphangitis. Mycobacteremia and hematogenous seeding occur after the primary infection. After early inhalation of TB bacilli, miliary tuberculosis may occur as primary TB or may develop years after the initial infection. Up to 25% of patients with miliary TB may have meningeal involvement. In addition, miliary TB may mimic many diseases. In some cases, up to 50% of cases are undiagnosed ante mortem. Therefore, a high index of clinical speculation is important to obtain prior diagnosis and to ensure improved clinical outcome. Different drugs are available for the management of tuberculosis, including isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin. Their combined administration for suitable periods allows not only to cure the disease, but also to avoid relapses. It was mentioned previously that conditions causing a decreased efficiency of the immune system render the human body prone to TB. It is worth to mention as the immunedeficiency is held responsible for the reappearance of serious cases of TB that almost completely disappeared in developing countries. The present study is the clinical case of a 40 years old female patient with Weightloss, fatigue, dyspnoea and lymphadenopathy who is diagnosed with military TB.

1. CASE PRESENTATION
A 40-year-old Asian female with a history of rheumatoid arthritis, for 7 months, with no systemic disorders came to the emergency department for persistent non-productive cough for 2–3 weeks and watery diarrhea with abdominal pain for about 10 days for which she was prescribed antibiotics and antitussives by her primary medical care provider with no relief. She also complained of fatigue, malaise, poor appetite, and significant weight loss (about
9.07 kg in 2–3 months). She complained of fever, chills, night sweats, dyspnea, chest pain, nausea or vomiting. She denied any history of smoking, or illicit drug use, recent travel, sick contacts or exposure to industrial dusts. She worked at social service organization aiming to provide food to the unfortunate people dwelling in the slums. Her current medications were Paracetamol 650mg and Sulfasalazine 500mg which she admits consuming for 5 months.

On physical examination, the patient was alert and in pain or distress. Vital signs were normal. Laboratory evaluation, (normal range is given in brackets) revealed mild leucocytosis with WBC count of 14,300/µL (4,500–11,000/µL), mild anemia with hemoglobin levels 11.5 g/dL (12.0–15.0 g/dL) and mean corpuscular volume (MCV) of 88.3 (80–100), Erythrocyte sedimentation rate (ESR) 29 (0–15), abnormal LFT's (total bilirubin 0.9 mg/dL (0.3–1.2 mg/dL), aspartate aminotransferase (AST) 74 IU/L (15–41 IU/L), alanine aminotransferase (ALT) 89 IU/L (17–63 IU/L), mild elevations of serum amylase 150 U/L (28–100), alkaline phosphatase 98 IU/L (32–91 IU/L), and lipase levels 59 U/L (22–51 U/L). Electrocardiography (EKG) showed no abnormality. Chest X-Ray showed bilateral extensive minute nodular infiltrates. Computed tomography (CT) scan of the abdomen, pelvis, and chest showed many very small nodules (2–3 mm) seen throughout both lungs. There was no retroperitoneal lymphadenopathy or adrenal or pancreatic lesions. Abdominal sonogram was unremarkable.

Acid-fast bacilli were detected in sputum culture and were identified by DNA probe as *Mycobacterium tuberculosis* (Mt). The patient was admitted and repeated serial induced sputum acid-fast bacilli smears showed 1+ AFB. Her anti Rheumatoid arthritis drugs were stopped. She was started on anti-tuberculous therapy with isoniazid (INH), ethambutol, pyrazinamide, pyridoxine and rifampicin. No immediate side effects were observed and she was discharged after 5 days of treatment and negative serial sputum AFB smears. Susceptibility testing disclosed pan sensitivity with isoniazid(INH), ethambutol, pyrazinamide, pyridoxine and rifampicin. The patient completed the therapy with four months of INH, rifampicin, pyrazinamide, ethambutol and five more months of INH and rifampicin. At follow-up, the patient was asymptomatic, chest X-rays were normal and repeated liver function tests were normal.

2. DISCUSSION

Miliary tuberculosis is defined as widespread millet-like (1–5 mm) seeding of *Mycobacterium bacilli* in the lung and possibly in other organs of the body like, liver, spleen, lymph nodes,
It is a very rare form of TB and in literature reviews its frequency is estimated at 2.8% of all TB infections. In the United States 11,192 incident cases of tuberculosis were reported in 2010. Of these, extra pulmonary TB accounts for approximately 23% of cases while miliary TB was reported in only 2.7%.

Miliary TB usually occurs in the presence of immunocompromising conditions such as advanced age, organ transplantation, immunosuppressive and cytotoxic therapy (including antitumor necrosis factor) malnutrition, poorly controlled diabetes alcoholism, cancer, end-stage renal disease, corticosteroids, silicosis and most importantly HIV/AIDS.

Among immunocompetent adults, miliary TB accounts for 2% of all TB cases and 20% of all extra-pulmonary TB cases in clinical studies. In contrast, in patients with AIDS, miliary TB accounts for about 10% of all TB cases and more than 50% of all extra-pulmonary TB cases. Although miliary tuberculosis is uncommon in the immunocompetent population, it is important to recognize that certain genetic defects may make immunocompetent individuals get disseminated tuberculosis, genetic defects like abnormalities in the production of interferon-gamma and interleukin-12, which are important for granuloma formation and provide immunity against M. tuberculosis. Unfortunately, qualitative or quantitative tests for these cytokines are not widely available in clinical practice.

The clinical presentation of miliary tuberculosis can be chronic, subacute or acute. Acute disease is rare and mostly seen in advanced HIV/AIDS or other immunocompromised states. It is usually sudden and includes multi-organ system failure and acute respiratory distress syndrome. Therefore, miliary TB should always be considered in patients with acute respiratory distress syndrome of unknown etiology especially if risk factors are present. The subacute or chronic demonstration of miliary TB are more common than acute disease and it may be difficult for patients with failure to thrive, fever of unknown origin, night chills or dysfunction of one or more organ systems.

The most common laboratory aberration includes anemia, thrombocytopenia, leukopenia, and lymphopenia. Other lab abnormalities may include severe hypercalcemia and C-reactive protein, hyponatremia, elevated ESR and sterile pyuria. Advanced age (> 60 years), lymphopenia, thrombocytopenia, elevated transaminase levels, pancytopenia, hypoalbuminemia and delayed treatment have been recognized as independent predictors of mortality.
The classic chest radiograph appearance are faint, reticulo-nodular intrudes which are distributed uniformly throughout the lungs. This pattern of infiltrates is seen in about 84% of cases.[17] Other chest radiograph abnormalities include hilar/mediastinal adenopathy, pleural effusion, and alveolar or interstitial infiltrates. Chest CT scan is a more sensitive test for investigating miliary TB.

Acid-fast microscopy and culture of body fluids or tissue from an infected focus begin the diagnosis especially if organisms or granulomas are seen. The cumulative diagnostic outcome of different body fluids and tissues in the investigating of miliary TB has been reported as follows urine (33%), cerebrospinal fluid (21%), sputum (41%), lymph node biopsy (91%), liver biopsy (89%), Fibre optic bronchoscopy (47%) and bone marrow aspirate/biopsy (67%). [8] Fibre optic bronchoscopy is usually required if acid-fast bacilli are not detected at multiple sites (ascites, urine, sputum, gastric aspirate, pleural fluid etc.) and there is evidence of pulmonary involvement on chest radiography.[11]

The tuberculin skin test can be a good diagnostic tool if positive, but anergy is seen more common among patients with miliary TB than those with pulmonary or isolated extra pulmonary involvement. PPD conversion may often occur following treatment.[17]

The approach to antimicrobial remedy for curing of miliary TB is the same as for pulmonary TB. Early empirical treatment is possible but not yet definitive. It increases the likelihood of survival and should never be withheld while test results are pending.

3. CONCLUSION

Miliary tuberculosis is a dangerous and very lethal form of tuberculosis. It arises from hematogenous dissemination of *Mycobacterium tuberculosis* bacilli. *Mycobacterium tuberculosis bacilli* are mostly present in immunosuppressed patients but can also affect immunocompetent adults. Due to variable clinical presentations, poorly sensitive smears and diverse radiologic findings diagnosing miliary tuberculosis is difficult. Positive chest radiographic findings or a positive tuberculin skin test support the diagnosis. Extrapulmonary tuberculosis should not be excluded. A high index of clinical suspicion is required and anti *tuberculosis* therapy should be administered instantly to prevent a fatal outcome.
5. REFERENCES


