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**Chidozie Charles Agu, Patolia Setu, Hiba Basheer**

### ABSTRACT

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**Case Report:** We present a case of a 67-year-old African-American male who presented with persistent non-productive cough for three weeks, diarrhea, fatigue and weight loss. There was no history of active TB contacts, HIV infection, or other predisposing factor for immunosuppression. Physical examination was also unremarkable. Chest X-ray and computed tomography scan revealed bilateral extensive small nodular infiltrates with negative serial acid-fast sputum smears. Acid-fast bacilli were detected in sputum culture at four weeks and were identified by DNA probe as *Mycobacterium tuberculosis*.

**Conclusion:** Miliary tuberculosis is a potentially lethal form of tuberculosis that mostly affects immunosuppressed patients, although in rare occasions can also affect immunocompetent adults.



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CASE REPORT

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## ABSTRACT

**Introduction:** Miliary tuberculosis (TB) is a disseminated form of tuberculosis which may involve the lungs and other organs. It is a rare but potentially lethal form of tuberculosis seen mostly in immunocompromised patients. It is, however, not commonly reported in immunocompetent hosts. **Case Report:** We present a case of a 67-year-old African-American male who presented with persistent non-productive cough for three weeks, diarrhea, fatigue and weight loss. There was no history of active TB contacts, HIV infection, or other predisposing factor for immunosuppression. Physical examination was also unremarkable. Chest X-ray and computed tomography scan revealed bilateral extensive small nodular infiltrates with negative serial acid-fast sputum smears. Acid-fast bacilli were detected in sputum culture at four weeks and were identified by DNA probe as *Mycobacterium tuberculosis*. **Conclusion:** Miliary tuberculosis is a potentially lethal form of tuberculosis that mostly affects immunosuppressed patients, although in rare occasions can also affect immunocompetent adults.

**Keywords:** Miliary tuberculosis, *Mycobacterium tuberculosis*, HIV/AIDS.

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## INTRODUCTION

Miliary tuberculosis (TB) is a rare form of TB infection that results from massive lympho-hematogenous dissemination of *Mycobacterium tuberculosis* bacilli. [1] It involves mostly the lungs but may also affect several other organs in the body. It is more likely to occur in immunocompromised patients due to their depressed cellular immunity and is rarely reported in immunocompetent hosts. In this report, we present a case of Miliary TB in an otherwise immunocompetent patient.

## CASE REPORT

A 67-year-old African-American male with a history of hypertension for 10 years, atrial flutter on Coumadin for four years, localized prostate cancer status post radiation therapy in remission came to the emergency room for persistent non-productive cough for 2–3 weeks and watery diarrhea with colicky abdominal pain for about 10 days for which he was prescribed antibiotics and antitussives by his primary medical care provider with no relief. He also complained of fatigue, malaise, poor appetite, and significant weight loss (about 9.07 kg in 2–3 months). He denied fever, chills, night sweats, dyspnea, chest pain, nausea or vomiting. He also denied any history of smoking, alcohol or illicit drug use, recent travel, sick contacts or exposure to industrial dusts. He worked as a

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mail-man for the postal service and traveled to Bahamas in 2010. His current medications were metoprolol and Coumadin.

On physical examination, the patient was alert and in no pain or distress. Vital signs were normal except mild tachycardia of 101/minute. Physical examination was unremarkable including respiratory system examination. Laboratory evaluation, normal range is given in parenthesis, revealed mild leukocytosis WBC count of 14,300/ $\mu$ L (4,500–11,000/ $\mu$ L), mild anemia with of hemoglobin of 12.3 g/dL (13.5–17.5 g/dL) and mean corpuscular volume (MCV) of 88.3 (80–100), Erythrocyte sedimentation rate (ESR) 29 (0–15), hypokalemia (serum potassium of 2.9 mmol/L (3.6–5.1 mmol/L), abnormal LFT's (total bilirubin 0.9 mg/dL (0.3–1.2 mg/dL), aspartate aminotransferase (AST) 77IU/L (15–41 IU/L), alanine aminotransferase (ALT) 89 IU/L (17–63 IU/L), alkaline phosphatase 103 IU/L (32–91 IU/L), mild elevations of serum amylase 150U/L (28–100) and lipase levels 59 U/L (22–51 U/L). Coagulation profile was as follows: Prothrombin time (PT) 16.4 s (9.7–11.3 s), international normalized ratio (INR) 2.19 (1.1–1.7) and partial thromboplastin time (PTT) 26.5 s (24.7–34.4 s) as the patient was on warfarin for atrial flutter. Electrocardiography (EKG) showed atrial flutter with variable atrioventricular block at 94 bpm. Chest X-Ray showed bilateral extensive small nodular infiltrates. Computed tomography (CT) scan of the chest, abdomen, and pelvis showed innumerable very small nodules (2–3 mm) seen throughout both lungs, small bilateral pleural effusions, small pericardial effusion and multiple small low attenuation lesions scattered throughout the liver. There were no adrenal or pancreatic lesions or retroperitoneal lymphadenopathy seen. Abdominal sonogram was unremarkable. Differential diagnosis included metastatic lung cancer, hypersensitivity pneumonitis, pneumoconiosis, rheumatoid nodules, vasculitis and fungal pneumonia among others. Three sets of acid-fast bacilli (AFB) sputum smears were negative. Purified Protein Derivative (PPD) skin test, HIV Elisa, urine legionella antigen, hepatitis serology, basic autoimmune work-up (antinuclear, anti-Ds DNA, anti CCP-antibodies, rheumatoid factor), tumor markers (AFP, CEA, CA 19-9, PSA), blood, stool and urine cultures were all unremarkable. Patient was offered bronchoscopy for further diagnostic evaluation but he declined. The diagnostic possibility of miliary TB and possible anti-TB treatment was discussed with the patient owing to the classic radiologic findings despite negative serial AFB smears. He refused treatment at the time because he felt relatively well and had never had any contact with TB. He was then discharged to outpatient clinic for further evaluation.

Acid-fast bacilli were detected in sputum culture at 4 weeks and were identified by DNA probe as *Mycobacterium tuberculosis*. The patient was readmitted and repeat serial induced sputum acid-fast bacilli smears revealed 1+ AFB. He was started on antituberculous



Figure 1: Chest X-ray (posterior-anterior view) showing bilateral small nodular infiltrates.

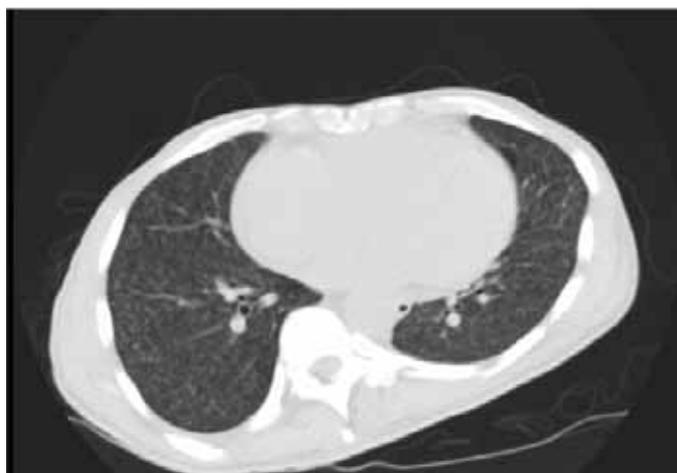


Figure 2: Computed tomography scan of the chest without contrast (axial view).

therapy with isoniazid (INH), rifampin, ethambutol, pyrazinamide and pyridoxine. No immediate drug side effects were observed and he was discharged after a week of treatment and negative serial sputum AFB smears. Susceptibility testing revealed pansensitivity to INH, rifampin, ethambutol and pyrazinamide. The patient completed the therapy with two months of INH, rifampin, ethambutol and pyrazinamide and four more months INH and rifampin. At follow-up, the patient was asymptomatic, liver function tests were normal and repeat chest X-rays were normal.

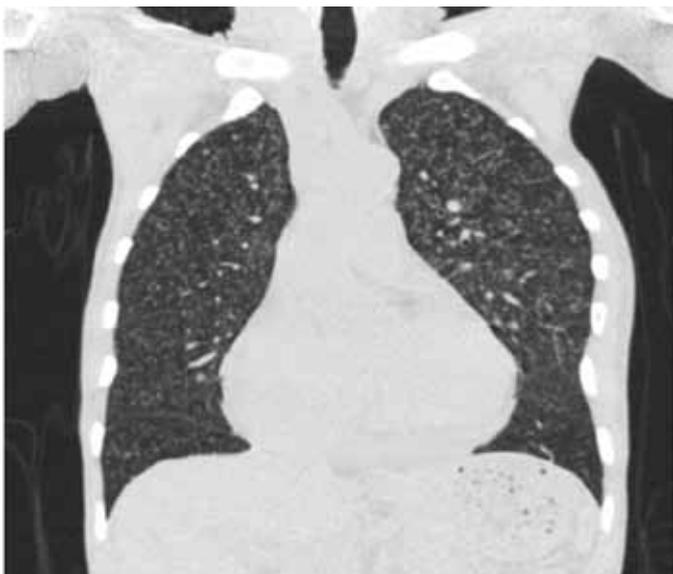


Figure 3: Computed tomography scan of the chest without contrast (coronal view) showing multiple diffuse tiny nodules (2–3 mm) seen throughout both lung fields.

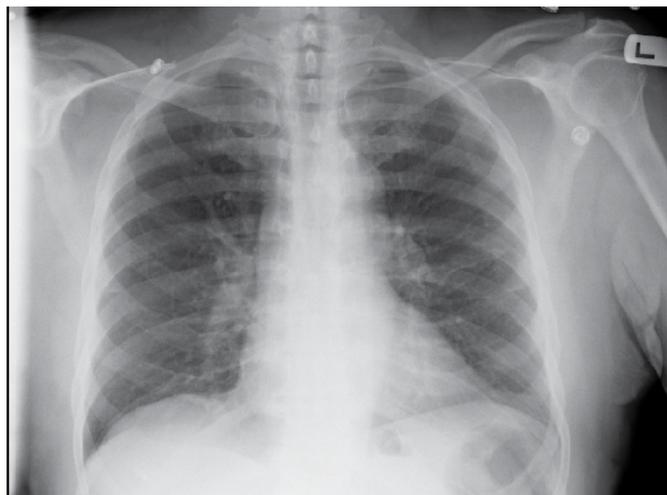


Figure 5: Chest X-ray (posterior-anterior view) after anti-TB treatment.

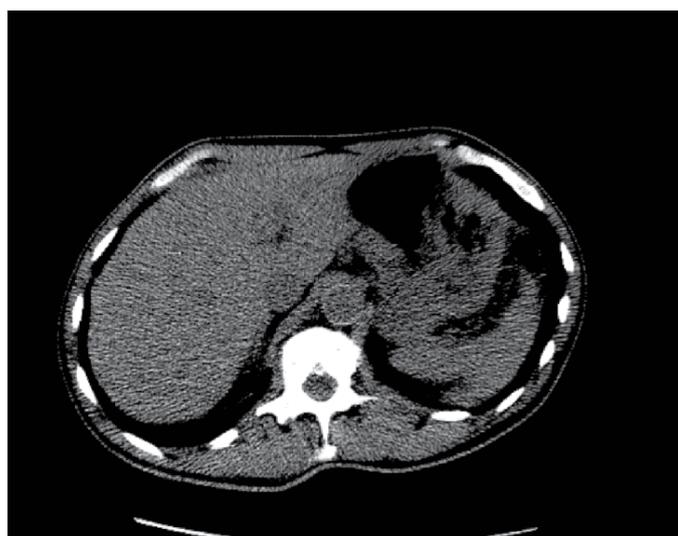


Figure 4: Computed tomography scan of abdomen showing multiple low attenuation lesions in the liver (axial view— Liver window).

## DISCUSSION

Miliary TB is defined as widespread millet-like (1–5 mm) seeding of *Mycobacterium bacilli* in the lung and possibly in other organs of the body, mostly liver, spleen, lymph nodes, pleura, pericardium, meninges and bone marrow [2]. It is a very rare form of tuberculosis and in literature reviews its frequency is estimated at 2.8% of all TB infections [3]. In the United States 11,182 incident cases of tuberculosis were reported in 2010. Of these, extrapulmonary TB accounted for approximately 22% of cases while miliary TB was reported in only 2.7% [4, 5].

Miliary TB usually occurs in the presence of immunocompromising conditions such as advanced age, cancer, organ transplantation, immunosuppressive and cytotoxic therapy (including biologic agents antitumor necrosis factor), malnutrition, alcoholism, corticosteroids, poorly controlled diabetes, silicosis, end-stage renal disease, and most importantly HIV/AIDS [6].

Among immunocompetent adults, miliary TB accounts for less than 2% of all TB cases and 20% of all extra-pulmonary TB cases in clinical studies [6]. In contrast, in patients with HIV/AIDS, miliary TB accounts for about 10% of all TB cases [3] and more than 50% of all extra-pulmonary TB cases [6]. Although miliary tuberculosis is rare in the immunocompetent population, it is important to recognize that certain genetic defects may predispose immunocompetent individuals to disseminated tuberculosis such as abnormalities in the production or metabolism of interferon-gamma and interleukin-12, which are essential for granuloma formation and protective immunity to *M. tuberculosis*. Unfortunately, quantitative or qualitative tests for these cytokines are not widely available in clinical practice [7].

The clinical presentation of miliary tuberculosis can be acute, subacute or chronic. Acute disease is rare and may occur in advanced HIV/AIDS or other immunocompromised states [6]. It is usually fulminant, including multiorgan system failure, septic shock and acute respiratory distress syndrome (ARDS) [8, 9]. Therefore, miliary tuberculosis should always be considered in patients with ARDS of unknown etiology especially if risk factors are present [10–12]. The subacute or chronic presentations of miliary TB are more common than acute disease and patients may present with failure to thrive, fever of unknown origin, night sweats or dysfunction of one or more organ systems.

The most common laboratory abnormalities include anemia, leukopenia, thrombocytopenia and lymphopenia. Other lab abnormalities may include

elevated ESR and C-reactive protein, hyponatremia, hypercalcemia and sterile pyuria [13]. Advanced age (> 60 years), lymphopenia, thrombocytopenia, pancytopenia, hypoalbuminemia, elevated transaminase levels and delayed treatment have been identified as independent predictors of mortality [9, 14].

The classic chest radiograph appearance is a faint, reticulonodular infiltrate distributed fairly uniformly throughout the lungs. This miliary pattern of infiltrates is seen in about 84% of cases [15]. Other chest radiograph abnormalities include pleural effusion, hilar/mediastinal adenopathy, interstitial or alveolar infiltrates, or cavities. Chest CT scan is a more sensitive test for evaluating miliary TB.

Acid-fast microscopy and culture of body fluids, tissue, or drainage from an infected focus establishes the diagnosis especially if organisms or caseating granulomas are seen. The cumulative diagnostic yield of different body fluids and tissues in the diagnosis of miliary TB has been reported as follows: Sputum (41%), Fiberoptic bronchoscopy (47%), urine (33%), cerebrospinal fluid (21%), lymph node biopsy (91%), liver biopsy (89%) and bone marrow aspirate/biopsy (67%) [6]. Fiberoptic bronchoscopy is usually warranted if acid-fast bacilli are not detected at multiple sites (sputum, gastric aspirate, pleural fluid, ascites, urine, etc.) and there is evidence of pulmonary involvement on chest radiography [9].

The tuberculin skin test (PPD) can be a supportive diagnostic tool if positive, but anergy is observed more frequently among patients with miliary TB (up to 68% of cases) than those with pulmonary or isolated extrapulmonary involvement. PPD conversion may often occur following treatment [15].

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

## CONCLUSION

Miliary tuberculosis is a potentially lethal form of tuberculosis arising from hematogenous dissemination of *Mycobacterium tuberculosis* bacilli. It mostly presents in immunosuppressed patients but can also affect immunocompetent adults. Diagnosis of miliary tuberculosis is often difficult due to variable clinical presentations, poorly sensitive smears and diverse radiologic findings. Although positive chest radiographic findings or a positive tuberculin skin test may support the diagnosis, negative results. However, do not exclude extrapulmonary tuberculosis. A high index of clinical suspicion is needed and antimycobacterial therapy should be administered urgently to prevent an otherwise fatal outcome.

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## Author Contributions

Chidozie Charles Agu – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content and final approval of the version to be published

Patolia Setu – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content and final approval of the version to be published

Hiba Basheer – Substantial contributions to conception and design, acquisition of data, Analysis and interpretation of data, drafting the article, Revising it critically for important intellectual content and final approval of the version to be published

## Guarantor

The corresponding author is the guarantor of submission.

## Conflict of Interest

Authors declare no conflict of interest.

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