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CASE REPORT

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Miliary tuberculosis in an immune-competent Bangladeshi man—A case report

Susanta Kumar Paul[1] | **Shamim Ahmed**[1] | **Rajashish Chakrabortty**[1] | **Shamrat Kumar Paul**[2] | **Mohammed Atiqur Rahman**[1]

[1]Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh

[2]Department of Physics and Astronomy, Clemson University, Clemson, South Carolina, USA

Correspondence
Susanta Kumar Paul, Department of Respiratory Medicine, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka-1000, Bangladesh.
Email: susantapaul723@gmail.com

Abstract

Miliary tuberculosis is a disseminated and active form of tuberculosis caused by *Mycobacterium tuberculosis*. It frequently affects immunocompromised patients. However, immune-competent hosts are reported rarely. Herein, we reported a case of miliary tuberculosis of a 40-year-old immune-competent Bangladeshi man presented with pyrexia of unknown origin.

KEYWORDS

Bangladeshi, immune-competent, miliary tuberculosis, PUO

1 | INTRODUCTION

Miliary tuberculosis (MTB) is a rare and fatal infectious disease that occurs due to the lympho-hematogenous spread of *Mycobacterium tuberculosis* bacilli.[1] According to the world health organization (WHO) 2021 reports, the incidence of tuberculosis in Bangladesh and Malaysia is around 221 and 97 per 100,000 people, respectively. It involves commonly the lung but may also affect other systems in the body. In all forms of tuberculosis cases, MTB occurs in 1%–2%, and in extrapulmonary tuberculosis, it is approximately 8%.[2] Clinical features of MTB are nonspecific, such as prolonged pyrexia, night sweats, weight loss, lassitude, anorexia, hepatomegaly, and abdominal pain. When the lungs are, an affected patient presents with cough, dyspnea, and chest pain. Occasionally, patients with miliary tuberculosis can present with "pyrexia of unknown origin" (PUO).

Atypical clinical manifestation often delays the diagnosis and may cause a fatal outcome. Therefore, a high index of clinical suspicion is needed to diagnosing of MTB. Chest radiography plays a vital role in the initial detection and final diagnosis of MTB, but miliary mottling is seen in only 50% of cases of miliary tuberculosis.[3] Only one-third of MTB patients are sputum smear-positive. Histological demonstration of granulomatous inflammation in biopsy tissue (e.g., liver, lung, and bone marrow) is usually required to make a prompt diagnosis.[4] The molecular diagnosis of mycobacterium tuberculosis DNA by polymerase chain reaction is helpful, and it is rapid, sensitive, and specific.[5] MTB is more likely to see in an immune-compromised patient due to suppression of their cellular immunity and is rarely affected in an immune-competent patient.

Herein, we reported a case of miliary tuberculosis in an immune-competent Bangladeshi man presented with pyrexia of unknown origin and hyponatremia.

2 | CLINICAL PRESENTATION

A 40-year-old nonsmoker from a middle-class family with a rural background presented with periumbilical pain with weight loss for 3 months and high-grade fever with cough for 21 days. He worked in Malaysia from 2006 as a manual worker in a furniture factory. His disease started in Malaysia and continued here. He had gradual, dull, aching pain at the periumbilical area that came and went without any radiation. The pain was typically made worse after meals, alleviated for 2 h by using a proton pump inhibitor, and then recurred. He denied any vomiting, diarrhea, or alternation of bowel habits. He had around 12 kilograms of weight loss during this illness. With the above complaint, he consulted with a physician in Malaysia and was treated with some medication but did not improve. So, he returned to Bangladesh and was admitted to our department with a high-grade fever for 21 days. Fever was intermittent mostly coming in the evening and night associated with chills and rigors, and subsided after taking the tablet paracetamol 500 mg with profuse sweating. The highest recorded temperature was 103F. Along with fever, patient developed a cough that was dry and occasionally becomes productive which was whitish, not foul-smelling, or had any hemoptysis. He had no chest pain, shortness of breath, joint pain, rash, photosensitivity, and burning sensation during micturition. His bowel and bladder habits were normal. He had no previous history of pulmonary tuberculosis or contact with a smear-positive pulmonary tuberculosis patient. On general examination, the patient was toxic and emaciated, the temperature was 102°F, and vitals were normal with Spo_2 98% at room temperature. Systemic examination revealed no abnormality.

On investigation, CBC showed mild anemia (hemoglobin 10.9 g/dL) with leukocytosis (total WBC count 11,200/cumm). The ESR (80 mm/1st hour) and CRP (75.87 mg/L) were elevated. Serum electrolytes showed hyponatremia (sodium 125 mmoL/L) but normal serum cortisol level. Complete urine analysis, liver, thyroid, and renal function, RBS, serum amylase, lipase, calcium, lactate dehydrogenase (LDH), angiotensin-converting enzyme (ACE), and lipid profile were normal. ICT for Kala-azar, malaria, dengue, and *Mycobacterium tuberculosis* was negative. Blood and urine culture was sterile. RT-PCR for COVID-19 was negative. HBsAg, Anti-HCV, and anti-HIV 1 and 2 were negative. Upper GI endoscopy, colonoscopy, ultrasonography, and CT scan abdomen found no abnormality. Chest X-ray showed pleural reaction (Figure 1) and a high-resolution CT scan chest showed miliary infiltrates (Figure 2). Mantoux test, sputum for AFB, and Gene X-pert MTB/RIF were negative. Bronchoscopy with bronchoalveolar lavage fluid for MTB culture and Gene X-pert MTB/RIF was not possible due to a lack of facilities. So, with the symptoms of prolonged fever, cough, weight loss, abdominal pain, and miliary shadows in the HRCT scan, we diagnosed this patient as a case of miliary tuberculosis. Immediately oral anti-tuberculous treatment with isoniazid (INH), rifampicin, ethambutol, pyrazinamide, and pyridoxine with steroids (30 mg/day) was started. After 3 days of starting anti-tuberculous drugs, the patient becomes afebrile and the cough improved. No immediate drug side effects were observed. So, patient was discharged with anti-tuberculous drugs with steroids and advised to follow up after 1 month.

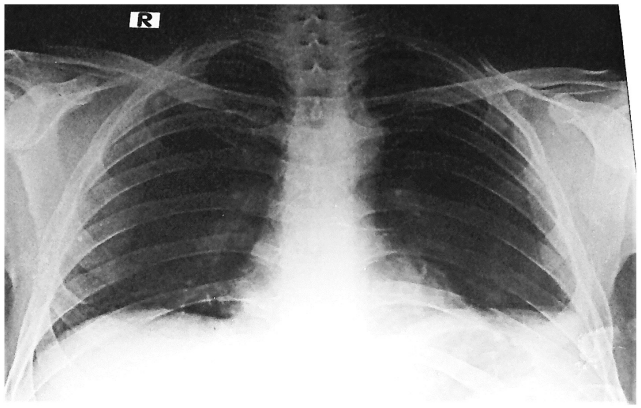

FIGURE 1 Chest X-ray showing the presence of left-sided pleural reaction.

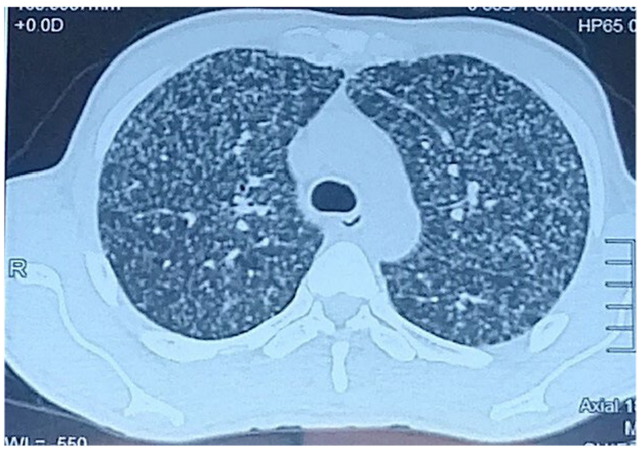

FIGURE 2 HRCT of the chest (noncontrast) shows the presence of innumerable miliary nodules scattered throughout both lungs.

At the follow-up, the patient was asymptomatic, and liver and renal function tests and chest X-ray were normal. After 6 months of antitubercular treatment, the patient improved significantly without any side effects.

3 | DISCUSSION

Miliary tuberculosis is a rare, but lethal infectious disease caused by the lympho-hematogenous spread of

Mycobacterium tuberculosis bacilli. MTB most commonly occurs in an immune-compromising condition such as advanced age, uncontrolled diabetes mellitus, cancer, malnutrition, immunosuppressive and cytotoxic drugs, corticosteroids, end-stage renal failure, and most importantly HIV/AIDS.[6] Among the immune-competent individuals, miliary tuberculosis occurs in less than 2%, but in the case of HIV/AIDS, MTB accounts for more than 10% of all tuberculosis cases.[7] Although miliary tuberculosis is rare in immune-competent patients, certain genetic defects such as abnormalities in the production or metabolism of interferon-gamma and interleukin-12 may be responsible for the immune-competent individuals developing disseminated tuberculosis.[8] In the miliary tuberculosis, mortality is around 25%–30% either delay in diagnosis or no diagnosis.

The clinical manifestation of miliary tuberculosis can be acute, subacute, and chronic. Acute presentation is rare and seen in advanced HIV/AIDS patients or immune-compromised conditions. Subacute or chronic presentation is more common in miliary tuberculosis than acute presentation and Patients can present with pyrexia of unknown origin, night sweats, failure to thrive, or dysfunction of one or more organ systems. Therefore, a high index of suspicion is required for the diagnosis of MTB attributable to unusual symptoms, and nonspecific clinical signs, and it can mimic several other disorders.[9]

Our patient presented with periumbilical pain with weight loss for 3 months, high-grade fever, and cough for 21 days but no response to different medications. He was no lymphadenopathy or organomegaly except at high temperatures (102°F). There were no systemic examination findings even in the respiratory system. Before admission to our department, he visited several physicians and did several investigations including CBC, ESR, CRP, urine routine microscopic examination, sputum for Gram stain and culture sensitivity, ultrasonography of the abdomen even upper GI endoscopy, and colonoscopy, but there was no conclusive diagnosis.

We diagnosed him with pyrexia of unknown origin before doing further investigation. A study by Mart et al. found that 50% of patients with miliary tuberculosis presented as pyrexia of unknown origin.[10] There are so many causes of pyrexia of unknown origin but infections, inflammations, malignancy, and miscellaneous are the main categories ultimately responsible for the majority of the cases of PUO. Extrapulmonary tuberculosis or miliary tuberculosis is the single most common infection, among the infectious cause in most PUO series.[11]

However, for the diagnosis of tuberculosis in our patient, the initial negative point was the patient's complaint of periumbilical pain and weight loss later developed a high-grade fever, but he had no history of contact with a smear-positive pulmonary tuberculosis patient, presence of BCG mark, no history of chest pain, lymphadenopathy, and organomegaly. Chest X-ray showed an absence of lung findings for tuberculosis. In miliary tuberculosis, hepatomegaly is present in 20% of cases, and splenomegaly in 19% of cases among 269 adults diagnosed cases.[12] Study by Sayantan et al. described that lymphadenopathy and organomegaly are more common in children compared with adults.[13] However, BCG vaccination protects miliary tuberculosis but it is controversial. A study conducted by Hussey et al. stated that the incidence of military tuberculosis was approximately 88% among BCG-vaccinated patients.[14]

In miliary tuberculosis, several hematological and biochemical abnormalities have happened among them anemia, leukopenia, thrombocytopenia, lymphopenia, elevated ESR and CRP, sterile pyuria, and changes in plasma electrolyte levels such as hyponatremia and hypercalcemia. In pulmonary tuberculosis, hyponatremia may occur in up to 50% of patients. It occurs as a result of either dysregulation in ADH (Antidiuretic hormone) release or involvement of the adrenal gland.[15] In our patient anemia, elevated ESR and CRP, sterile pyuria, and hyponatremia were observed. Hyponatremia was due to dysregulation in ADH releases because of normal serum cortisol levels, and liver, renal, and thyroid function, ultrasonography, and CT scan of the abdomen exclude Addison's disease.

The classical radiological presentation consists of miliary pattern shadow in chest imaging. However, in the primary stage, the chest X-ray may be found normal or with other various radiological patterns such as reticulonodular/interstitial, cavities, mediastinal or hilar lymphadenopathy, or even pleural effusion may be present. For that reason, diagnosis of miliary tuberculosis by a chest X-ray is challenging. The miliary pattern of infiltrates is found in around 84% of cases.[16] High-resolution CT scan of the chest is more sensitive to assess miliary tuberculosis. The most common HRCT chest features of miliary tuberculosis that a radiologist has defined are miliary mottling,[17] reticular opacity, and ground-glass attenuation. It is also different in images between patients with or without HIV/AIDS.[18] Our patient chest X-ray showed only pleural reaction (Figure 1), but the CT scan chest showed numerous tiny nodules evenly distributed in all segments of both lungs (Figure 2) suggestive of miliary tuberculosis.

In suspected MTB, to confirm the histopathological and/or microbiological diagnosis appropriate samples should be collected according to organ involvement. Microscopic examination and culture of sputum, body fluids, and tissue confirm the diagnosis if acid-fast bacilli or caseating granulomas are seen. Among the biological specimens, microscopically AFB was found in sputum (41.4%), bronchoscopic aspirates (46.8%), urine (32.7%),

cerebrospinal fluid (21.2%), lymph node biopsy (91%), liver biopsy (89%), and bone marrow biopsy (67%).[6] Fiber-optic bronchoscopy (FOB) is usually indicated if acid-fast bacilli are not detected in sputum or body fluid and chest radiography shows miliary shadow infiltrates.[19] In our patient, sputum for AFB and Gene X-pert MTB/RIF was negative. The sensitivity of sputum smear for acid-fast bacilli is only 35%–70%, requiring 5000–10,000 bacteria/mL of sputum. The nucleic acid amplification (NAA) method is quick with high specificity and low sensitivity for M. tuberculosis. The sensitivity of the NAA test in a smear-negative patient is only 60%–70%.[20]

Transbronchial lung biopsy (TBLB) may have a potential role in the diagnosis of miliary tuberculosis. In TBLB, granulomatous inflammatory lesions can be demonstrated in up to 60% of cases.[21] For a patient with miliary tuberculosis, a tuberculin skin test (PPD) can be a supportive diagnostic tool if positive, but anergy is observed frequently in up to 68% of cases. Unfortunately, many patients with miliary tuberculosis remained undiagnosed before their death and were confirmed during autopsy.[22]

Mantoux test was negative in our patient and FOB with bronchoalveolar lavage (BAL) fluid for MTB culture, Gene X-pert MTB/RIF, and TBLB were not possible because of a lack of facilities.

4 | CONCLUSION

Miliary tuberculosis can affect both the immune-compromised and the immune-component individual. Though variable clinical symptoms and diverse radiological findings make the diagnosis of MTB difficult. However, a high index of suspicion and a judicious investigation should be performed to confirm or refuse the diagnosis of miliary tuberculosis when a patient presents with pyrexia of unknown origin. To avert the fatal outcome antimycobacterial treatment should be started immediately.

AUTHOR CONTRIBUTIONS

Susanta Kumar Paul: Conceptualization; data curation; investigation; writing – original draft; writing – review and editing. **Shamim Ahmed:** Conceptualization; writing – original draft; writing – review and editing. **Rajashish Chakrabortty:** Conceptualization; writing – original draft; writing – review and editing. **Shamrat Kumar Paul:** Software; visualization. **Mohammed Atiqur Rahman:** Project administration; supervision.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this case report are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

Written informed consent was obtained from the patient in our study. The purpose of this research was completely explained to the patient and was assured that their information will be kept confidential by the researcher.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Susanta Kumar Paul https://orcid.org/0000-0002-2766-9471
Rajashish Chakrabortty https://orcid.org/0000-0001-9060-6185

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