Case Report

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Internal Medicine Section

Disseminated Multidrug-resistant Tuberculosis with Rare Extrapulmonary Manifestations and Pulmonary Thromboembolism: A Case Report

KUNDAN MEHTA[1], PRATIKSHA DUTTA[2]

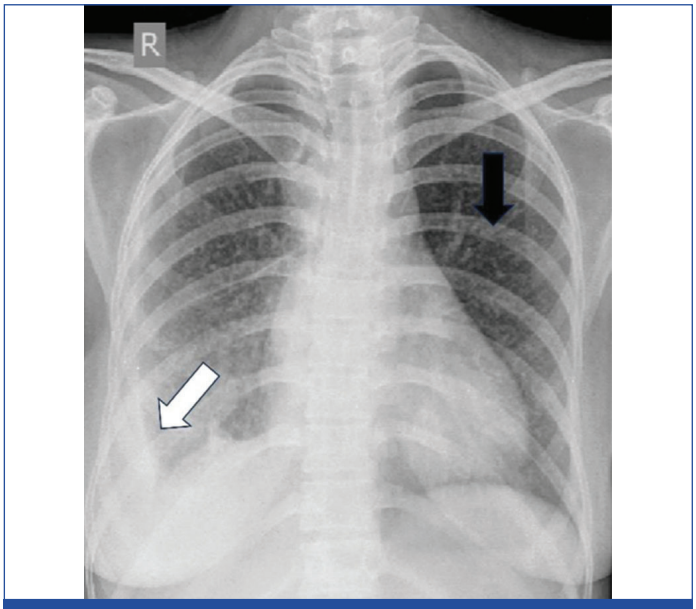
ABSTRACT

Tuberculosis (TB) remains a leading global cause of illness and death. In 2023, 10.8 million individuals worldwide were diagnosed with TB, including 6.0 million men, 3.6 million women and 1.3 million children. That year, TB caused 1.25 million deaths. Disseminated TB is characterised by the involvement of two or more non contiguous sites due to the haematogenous spread of Mycobacterium Tuberculosis (MTB), arising from progressive infection, reactivation of latent foci, or, rarely, iatrogenic causes. Disseminated TB represents less than 2% of all TB cases and up to 20% of extrapulmonary TB cases in immunocompetent adults. Commonly affected sites include lymph nodes, pleura, bones, joints and meninges, with rarer sites such as the breast, pericardium and skin. Breast TB accounts for less than 0.1% of breast pathologies and 3-4.5% of surgical breast cases in developing countries. Tuberculous pericarditis affects 1-2% of pulmonary TB patients. Delayed diagnosis of disseminated TB can lead to life-threatening complications, including meningitis, pericarditis, intestinal perforation, osteomyelitis, sepsis and pulmonary thromboembolism. TB is a prothrombotic condition due to elevated levels of procoagulants (fibrinogen, Factor VIII), decreased anticoagulants (protein C, protein S) and platelet activation, which can contribute to thrombosis. The present case of a 25-year-old female describes disseminated Multidrug-Resistant Tuberculosis (MDR-TB) involving the lungs, pleura, abdomen, brain and rarer sites such as the breast and pericardium, complicated by pulmonary thromboembolism. The present case emphasises the necessity of a comprehensive diagnostic approach in patients with atypical presentations and underscores the importance of early, intensive treatment for disseminated TB, especially MDR-TB, to prevent severe complications and improve outcomes.

Keywords: Pleural effusion, Pericardial effusion, Thrombosis, Tuberculoma, Tuberculous mastitis

CASE REPORT

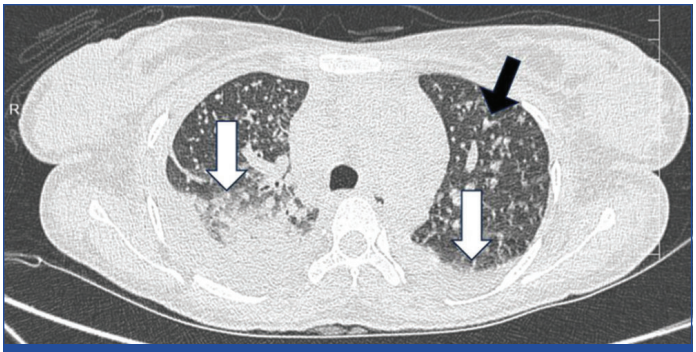
A 25-year-old female with no known co-morbidities presented with a low-grade fever and bilateral nipple discharge persisting for seven months, along with a cough, dyspnoea (Modified Medical Research Council Grade I) [1], weight loss and loss of appetite for the past month. Upon examination, the patient was pale and tachycardic (pulse: 121 bpm), with a respiratory rate of 24 breaths per minute, blood pressure of 90/60 mmHg and oxygen saturation of 96% on room air. Respiratory examination revealed decreased breath sounds in the right infrascapular, infra-axillary and interscapular areas, along with bilateral diffuse fine crepitations. A breast examination revealed swelling, redness, warmth and pus discharge from both nipples, more pronounced on the left-side. A chest radiograph showed bilateral nodular shadows, more pronounced on the left-side, accompanied by right pleural effusion [Table/Fig-1].



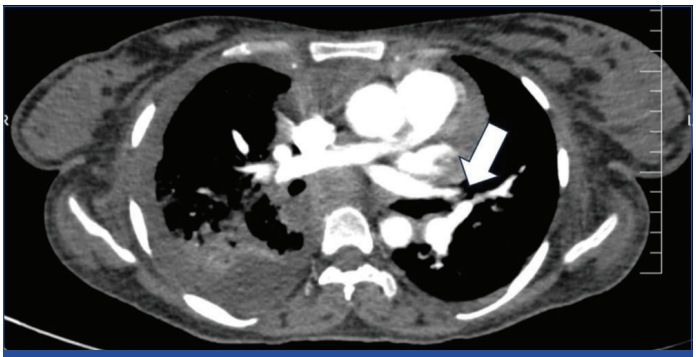
[Table/Fig-1]: Chest radiograph (posterior-anterior view) white arrow pointing at right costophrenic angle blunting suggestive of right pleural effusion and black arrow pointing at diffuse nodular opacities.

The patient was admitted to the ward from the Outpatient Department and all routine investigations (complete blood count, liver function test, renal function test, serum electrolytes, serology and total proteins) were sent. The haemoglobin level was 9.2 mg/dL. In view of the persistent tachycardia and disproportionate dyspnoea, a D-Dimer level was also measured, which was 7194 ng/mL (normal=0-500 ng/mL) [2]. Other blood indices were within normal limits. Subsequently, due to the elevated D-Dimer, a Computed Tomography Pulmonary Angiography (CTPA) was performed, which revealed thromboembolism in the sub-segmental branches of the anterior segment of the left upper lobe, lung parenchymal changes suggestive of necrotic mediastinal lymphadenopathy, bilateral pleural effusion (right: moderate, left: mild) and moderate pericardial effusion [Table/Fig-2,3].

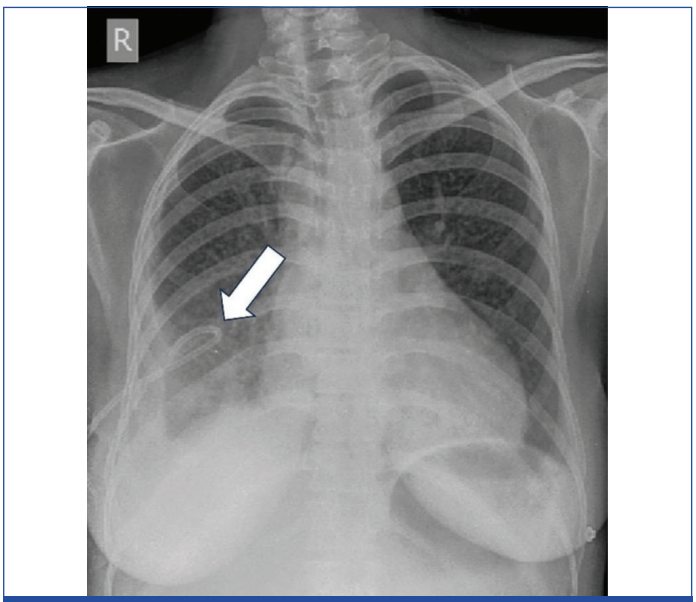
An echocardiogram suggested a large pericardial effusion with diastolic compression of the right atrium and early diastolic compression of the right ventricle, along with moderate pulmonary hypertension. A diagnostic thoracentesis followed by right-sided ultrasonography-guided pigtail insertion was performed [Table/Fig-4]. The pleural fluid drained was sent for routine microbiology, Cartridge-Based Nucleic Acid Amplification Test (CBNAAT), Gram stain, Ziehl-Neelsen (ZN) stain, malignant cytology and culture sensitivity and all reports were negative. The pleural fluid was exudative and lymphocyte-predominant as per Light's criteria,



[Table/Fig-2]: Computed tomography pulmonary angiography (lung window) white arrow pointing to bilateral pleural effusion (right > left) and black arow pointing to centrilobular nodules.



[Table/Fig-3]: Computed tomography pulmonary angiography (mediastinal window) white arrow pointing to filling defect in subsegmental branches of anterior segment of left upper lobe.



[Table/Fig-4]: Chest radiograph (posterior- anterior view) white arrow pointing to right-sided pigtail in-situ.

with an adenosine deaminase value of 40.8 IU/L [Table/Fig-5]. The pericardial fluid revealed on computed tomography pulmonary angiography was drained (700 mL) and its analysis showed a protein level of 4.26 g/dL [Table/Fig-6].

Sputum CBNAAT was performed, which revealed MTB detected at a low level, with rifampicin resistance. Ultrasonography of the bilateral breasts showed a well-defined collection measuring approximately 32×15×45 mm (CC×AP×Tr) in the right breast, predominantly involving the upper inner quadrant and an ill-defined collection measuring approximately 40×16×31 mm {Craniocaudal (CC), Anteroposterior (AP), and Transverse (TR)} noted in the left breast, predominantly involving the inner and outer lower quadrants. Fine needle aspiration cytology of the left breast abscess showed caseous necrosis with lymphocytes, suggestive of tuberculous mastitis. The left nipple discharge CBNAAT also revealed MTB detected with rifampicin resistance.

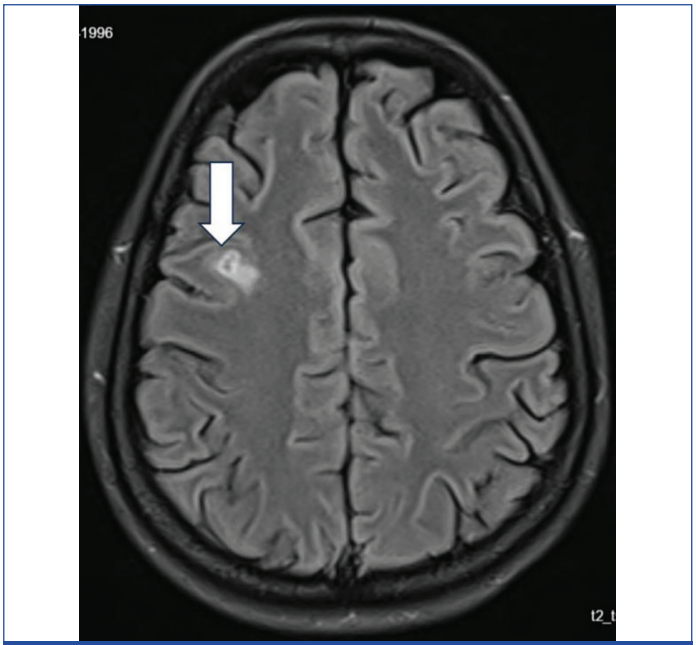
Ordered test	Pleural fluid examination
Proteins by Biuret method	4 g/dL
Glucose by hexokinase method	42 mg/dL
Total leucocyte count	1100
Adenosine deaminase	40.8 IU/L
CBNAAT	MTB not detected
Lymphocytes	90%

[Table/Fig-5]: Pleural fluid analysis.

Test	Pericardial fluid examination
Proteins by Biuret method	4.26 g/dL
Glucose by hexokinase method	38 mg/dL
Total leucocyte count	550
Adenosine deaminase	129.3 IU/L
CBNAAT	MTB not detected
Lymphocytes	80%

[Table/Fig-6]: Pericardial fluid analysis.

Further work-up was conducted to evaluate other sites of disseminated TB. An Magnetic Resonance Imaging (MRI) brain (contrast-enhanced) revealed 3-4 ring-enhancing granulomas in the frontal lobe, with surrounding oedema, consistent with tuberculoma [Table/Fig-7]. Abdominal ultrasound showed enlarged mesenteric, aortic, para-aortic and iliac lymph nodes ranging from 8-22 mm. CTPA, MRI brain, left nipple discharge analysis, abdominal ultrasound, pleural fluid analysis and pericardial fluid analysis were all suggestive of lung parenchymal, cerebral, breast, abdominal, pleural and pericardial TB, respectively. A diagnosis of disseminated MDR-TB was made, involving TB at six non contiguous and rare sites in the body.

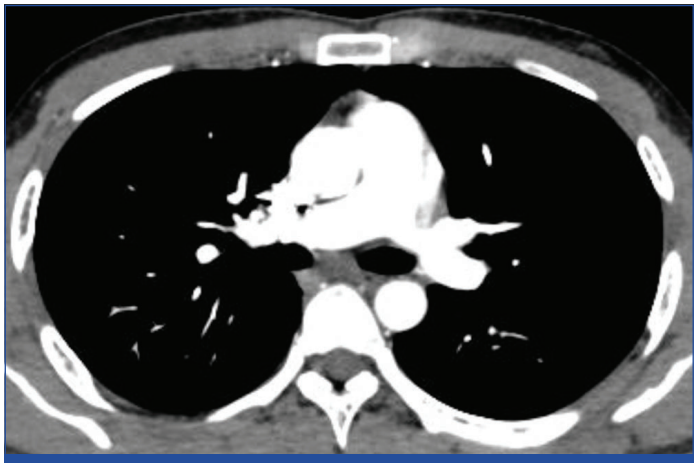


[Table/Fig-7]: MRI brain (contrast enhanced) white arrow pointing to ring enhancing lesion with surrounding oedema.

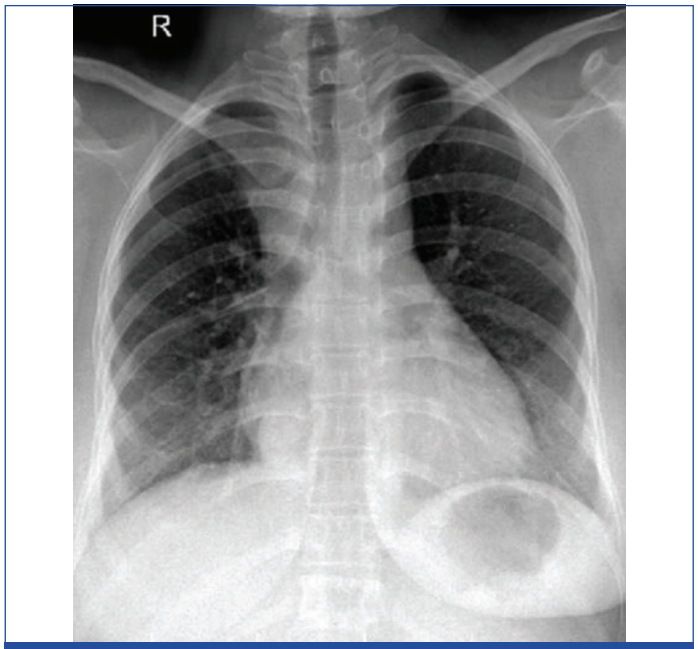
In view of the above reports, the patient was started on antitubercular drugs (all oral longer regimen) according to her weight band, as per the Programmatic Management of Drug-Resistant TB (PMDT) guidelines [3], along with anticoagulation therapy due to the pulmonary thromboembolism noted in the CTPA. The patient was also started on tablet levetiracetam 500 mg once a day prophylactically to avoid seizures. She was admitted for a week and was closely monitored. Upon initiation of the antitubercular and anticoagulation therapy, she showed clinical improvement. The patient was then discharged and advised to follow-up regularly with repeat chest radiographs, sputum Ziehl-Neelsen stains, sputum

cultures and ultrasound examinations of the breast and abdomen to assess both clinical and radiological resolution.

At the end of six months post-initiation of anticoagulation, a repeat CTPA [Table/Fig-8] and echocardiography were performed, which showed resolution of the thromboembolism as seen previously. After 18 months of receiving the all-oral longer regimen, a repeat chest radiograph showed complete resolution of pleural effusion and inhomogeneous opacities [Table/Fig-9]. Repeat ultrasonography of the abdomen and pelvis, as well as the breast, also demonstrated complete resolution. Both repeat sputum Ziehl-Neelsen stain and culture were negative, showing no growth, respectively. Antitubercular Therapy (ATT) was stopped and the patient was advised to return for follow-up after six months.



[Table/Fig-8]: Computed tomography pulmonary angiography (mediastinal window)-Normal study, showing resolution of right pleural effusion and no filling defect noted.



[Table/Fig-9]: Chest radiograph (posterior-anterior view) showing complete resolution of bilateral pleural effusion and diffuse nodular opacities.

DISCUSSION

Disseminated TB refers to the involvement of two or more non contiguous sites caused by the haematogenous spread of MTB. This condition may arise from progressive primary infection, reactivation of a latent focus followed by subsequent dissemination, or, in rare cases, through iatrogenic origins [4,5]. TB, a disease recognised for centuries, primarily targets the respiratory system. However, it can disseminate to other organs, including the brain, heart, abdomen and bones, resulting in serious complications such as meningitis, pericarditis, intestinal perforation, osteomyelitis and life-threatening sepsis [6]. Breast TB constitutes less than 0.1% of all breast pathologies [7,8] and accounts for 3-4.5% of surgically managed breast conditions in developing countries [9,10]. In rare cases, it may also lead to pulmonary thromboembolism [11].

The exact underlying mechanism remains unclear, but it is described in the literature as multifactorial. Thromboembolism in TB may be associated with all three components of Virchow's triad: hypercoagulability, venous stasis and endothelial dysfunction. Additionally, factors such as reactive thrombocytosis, anaemia and the release of proinflammatory cytokines that damage the vascular endothelium during the disease process also contribute to the thrombogenic state of TB [12]. Active TB is associated with a hypercoagulable state, resulting from an imbalance between pro-coagulant and anticoagulant factors. This includes elevated levels of fibrinogen, factor VIII and plasminogen activator inhibitor-1, along with reduced levels of antithrombin III and protein C, particularly during the first month of treatment [13]. The early initiation of antitubercular medications has been reported to reduce the prothrombotic state in patients with TB, highlighting the need for prompt treatment [14].

Literature reports a similar case published four years ago involving a 51-year-old male with pulmonary TB who developed bilateral sub-massive pulmonary thromboembolism and deep vein thrombosis, likely due to TB-induced hypercoagulability [15].

CONCLUSION(S)

The present case highlights a rare and complex presentation of disseminated MDR-TB involving multiple non contiguous sites, including the lungs, brain, breasts, abdomen, pleura and pericardium, complicated by pulmonary thromboembolism. The timely initiation of ATT alongside anticoagulation for pulmonary thromboembolism was critical in managing this complicated case. The present case underscores the importance of a thorough diagnostic approach in patients with unusual presentations and highlights the need for early, aggressive treatment of disseminated TB, particularly MDR-TB, to prevent severe complications and achieve favourable outcomes.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Respiratory Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.
2. Junior Resident, Department of Respiratory Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pune, Maharashtra, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Pratiksha Dutta,
Junior Resident, Department of Respiratory Medicine, Dr. D. Y. Patil Medical College, Hospital and Research Centre, Sant Tukaram Nagar, Pimpri Colony, Pimpri-Chinchwad, Pune-411018, Maharashtra, India.
E-mail: drpratikshadutta@gmail.com

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