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Case Report

Miliary tuberculosis related Acute Respiratory Distress Syndrome: Early diagnosis can save life

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Abstract
Miliary tuberculosis is an uncommon cause of Acute Respiratory Distress Syndrome (ARDS) with a high mortality. Early diagnosis and timely initiation of treatment are important for good outcome. We report a case of 23 years old female who needed admission to intensive care unit (ICU) due to ARDS. On routine investigations, the cause of ARDS could not be ascertained. Finally, high resolution computed tomography of chest and bronchoscopic guided lung biopsy were done which confirmed the etiology to be miliary tuberculosis. Patient showed improvement after starting anti-tubercular therapy with steroids. One week later, the patient's condition was stabilized and was shifted out of ICU. This case report emphasizes that miliary tuberculosis, though difficult to diagnose, should always be considered a differential diagnosis in patients with ARDS, as early initiation of treatment can prove to be lifesaving.
Keywords: *Miliary tuberculosis, acute respiratory distress syndrome, intensive care unit, antitubercular drug.*

Introduction

Massive lympho-hematogenous dissemination of mycobacterium tuberculosis bacilli lead to miliary tuberculosis. It is a potentially lethal disease if not diagnosed and treated early. It accounts for less than 2% of all tuberculosis cases and 20% of all extra-pulmonary tuberculosis cases in immune competent adults; the infection rate in immune-compromised patients is much higher.[1] Miliary tuberculosis can sometimes lead to acute respiratory distress syndrome (ARDS).[2,3] Patients of miliary tuberculosis with ARDS have a high mortality of 33-90%.[4,5] We present a case of miliary tuberculosis with ARDS and discuss its diagnosis and management.

Case Report

A 23-year-old female at eight weeks of gestation was diagnosed with hydatiform mole for which she underwent suction and evacuation of uterus. After an uneventful postoperative period, she was discharged from the hospital but returned back

after 4 weeks with complaints of high-grade fever and dry cough. For investigating the possible source of infection; culture of blood, sputum, urine and high vaginal swab were sent; and broad-spectrum antibiotics were started. Patient's haematological investigations were normal except for low haemoglobin of 7.7 gm% for which one unit packed red cells was transfused. Her chest X-ray was unremarkable and culture reports were negative, but fever persisted in spite of antibiotic therapy.

Two weeks later, the patient developed tachypnoea and her chest X-ray showed fluffy infiltrates over bilateral lung fields. Her arterial blood gas analysis was indicative of ARDS (PaO_2 of 55mmHg atFiO_2 of 0.6; PaO_2/ FiO_2=92.5). She was transferred to Intensive Care Unit (ICU) and non- invasive mask ventilation with pressure support of 15 cm of H_2O and FiO_2 of 0.6 was started. Repeat cultures (blood, sputum and urine) were sent which were again negative for any bacteriological growth. Other tests including widal, malaria antigen and dengue serology were also negative. In spite of broad-spectrum antibiotic therapy, her condition did not improve. On day 5 of ICU admission, a High Resolution Computed Tomography (HRCT) scan of chest was done which showed diffuse ground glass opacity with septal thickening in bilateral lung parenchyma along with basilar consolidation and miliary nodules pathognomic of military tuberculosis (Fig. 1, 2). Bronchoscopy guided lung tissue sample was taken and sent for microscopic examination which showed epithelial cell granuloma with caseating necrosis confirming tuberculosis (Fig. 3). Sputum for AFB was however negative. Anti-tubercular drugs and steroids were started; thereafter there was improvement in patient's symptoms with resolution of fever and breathlessness. After one week of initiating anti-tubercular therapy, the patient was transferred to ward on room air oxygen and later discharged with an advice to continue anti-tubercular therapy.

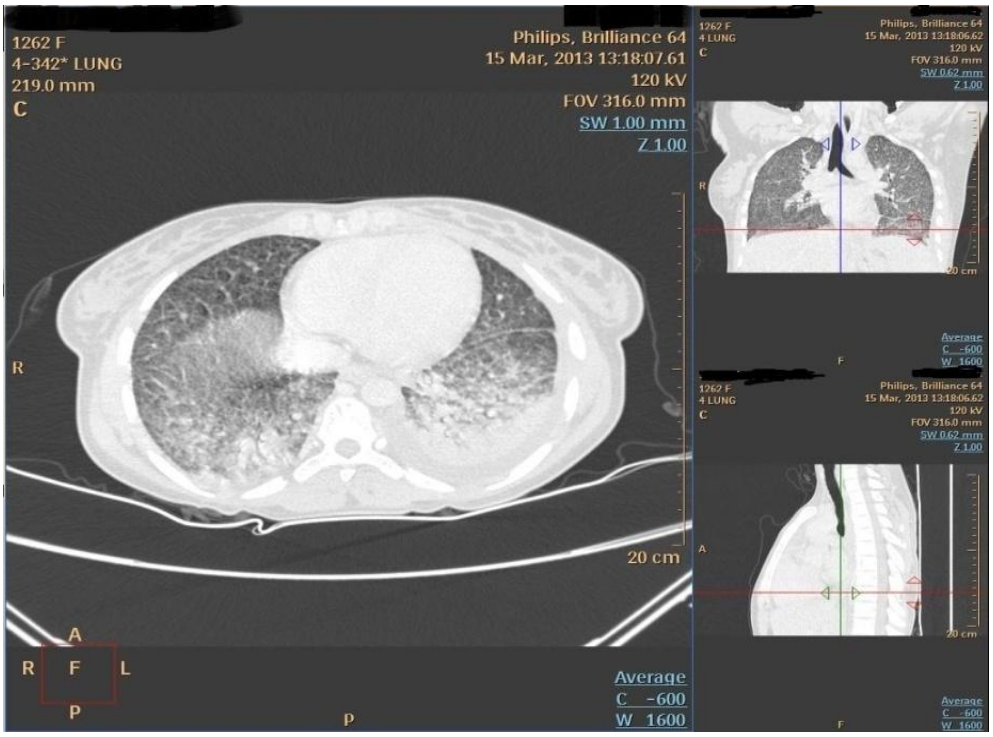

Figure 1: HRCT film showing chest in coronal section with septal thickening and miliary nodules

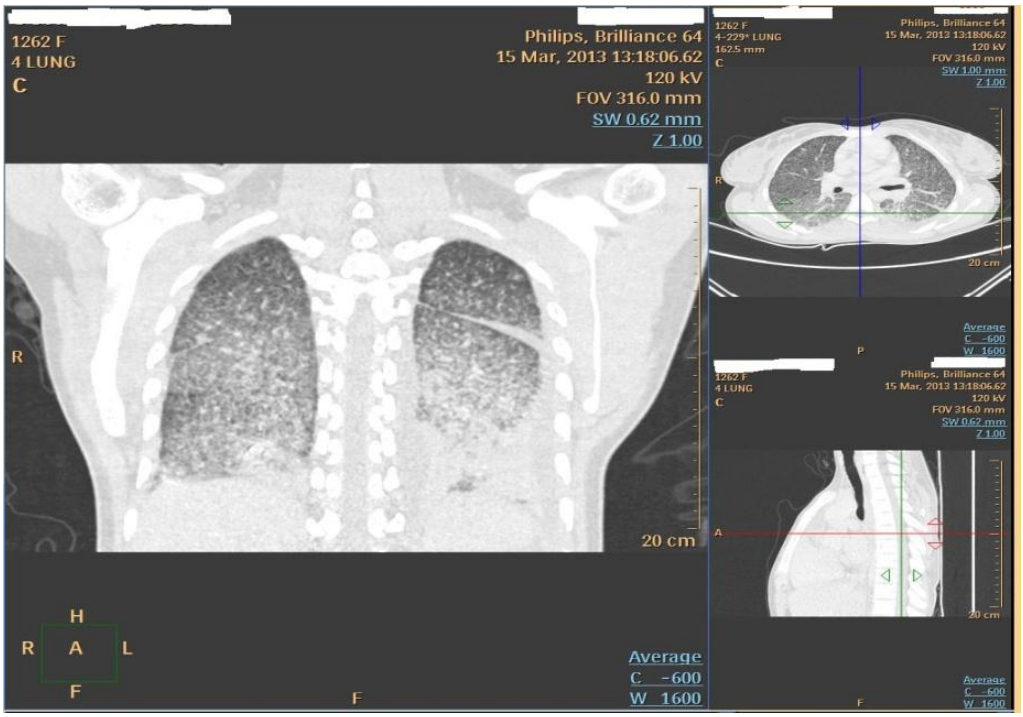

Figure 2: HRCT film showing chest in transverse section with bilateral military nodules and basal consolidations

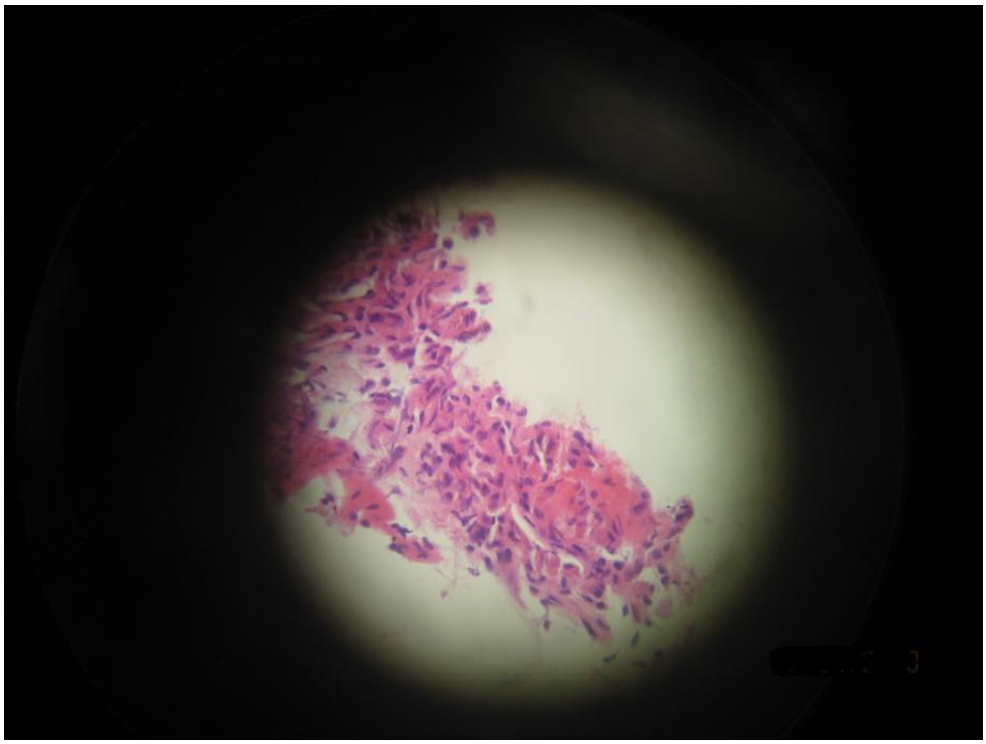

Figure 3 – Histopathology slide of lung tissue showing epithelial cell granuloma with necrosis.

Discussion

ARDS is a life-threatening reaction to injuries or infections of the lung with a high mortality rate of 30-40%.[6] Miliary tuberculosis is being increasingly recognized as a cause of ARDS in India.[3]

The pathogenesis of ARDS in military tuberculosis is not completely understood, the suggested mechanisms include massive release of mycobacterium into pulmonary circulation resulting in inflammation, obliterative endarteritis and alveolo-capillary membrane damage.[7] In

addition, lipo-arabinomannan component of mycobacterium cell wall is thought to act in a manner similar to lipopolysaccharide in bacterial sepsis causing activation of macrophages and massive release of cytokines like tumour necrosis factor-α and interleukin-1β.[8] Finally, the development of lung injury in infected individuals is also influenced by the host's immunologic responses independent of pathogen burden or virulence of the *Mycobacterium* strain.[4]

The criteria used for diagnosing miliarytuberculosis include presence of clinical symptoms of tuberculosis, classical miliary pattern or bilateral diffuse reticulonodular lesions on background of miliary shadows on plain chest X-ray or HRCT scan; histopathological or microbiological evidence of tuberculosis; and favourable clinical or radiographic response to anti-tubercular treatment.[9] Though military tuberculosis can cause ARDS, its diagnosis may be challenging and often missed by clinicians due to atypical clinical presentation of the disease or absence of classical miliary pattern on chest X-ray. The differentiating clinical features between military tuberculosis and bacterial pneumonia include thelonger duration of constitutional symptom such as fever with malaise, cough with breathlessness and weight loss; and the absence of response to empirical antibiotic therapy.[10-12]

The classical miliary pattern on chest radiograph is present in only 50 % of patients with military tuberculosis and may be apparent only weeks after tubercular infection.10,13 Also, the miliary pattern on chest X-ray may get masked once ARDS has developed. In these situations, HRCT is the useful radiological investigation for diagnosis of active disease.1 Though mycobacterial culture is gold standard for diagnosis of tuberculosis, this cannot be relied upon for initiating the treatment in ARDS with miliary tuberculosis as culture results take as long as 6–8 weeks. In our patient, the diagnosis of miliarytuberculosis was made on the basis of findings of HRCT and microscopic pathological examination of bronchoscopic tissue sample which showed caseating granulomas (Fig.3).

Treatment with anti-tubercular drugs is an important factor that can affect patient outcome. Higher mortality within 1 year is found amongst patients who do not receive appropriate anti-tubercular treatment.14,15 In patients with ARDS with suspicion of miliary tuberculosis as the ethology, anti-tubercular treatment should be started empirically, even before the availability of confirmatory test results, as it increases the survival likelihood.16 In treatment of military tuberculosis with ARDS, therapy with corticosteroid is shown to be beneficial.1 Corticosteroids act by inhibiting the release of lymphokines and cytokines, which are responsible for constitutional symptoms and tissue damage. In addition, corticosteroids allow the penetration of anti-tubercular drugs into the granulomas and its disruption.10 Administration of corticosteroids in early stages has shown to improve pulmonary and extra pulmonary organ dysfunction in patients with ARDS.17

In conclusion, prognosis of miliary tuberculosis with ARDS can be improved by maintaining high index of suspicion of tuberculosis in cases of acute respiratory failure of unknown origin, particularly in immunocompromised individual. Additionally, HRCT and bronchoscopic guided lung biopsy are useful modalities in difficult to diagnose cases. Early initiation of treatment with anti-tubercular drugs can improve the outcome.

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