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Case Report

Miliary Tuberculosis presenting with Acute Respiratory Distress Syndrome: A case report

Lalita Fernandes[*1], Rohit Vadala[2] and Anthony M Mesquita[3]

[1]*Professor, Department of Pulmonary Medicine, Goa Medical College, Goa, India*
[2]*Senior Resident, Department of Pulmonary Medicine, Goa Medical College, Goa, India*
[3]*Director, Professor, HOD, Department of Pulmonary Medicine, Goa Medical College, Goa, India*

***Correspondence Info:**
Dr. Lalita Fernandes
Department of Pulmonary Medicine,
TB and Chest Hospital,
St. Inez, P.O.Caranzalem, Goa, India
E-mail: drlalitafernandes@gmail.com

Abstract

Tuberculosis is one of the most important health problems in the developing world. Miliary tuberculosis particularly is a major killer disease if not diagnosed and treated early. The natural history of miliary tuberculosis is variable with most of the patients having sub-acute or chronic disease while some have acute presentation with rapid clinical deterioration and death. Miliary tuberculosis presenting with acute respiratory distress syndrome (ARDS) requiring mechanical ventilation is rare. Awareness of the clinical presentation helps in early diagnosis and management of the disease. We report a case of ARDS due to Miliary tuberculosis in a young immune-competent female with no co-morbidities who succumbed to her illness.

Keywords: Miliary Tuberculosis, ARDS, Mortality, Anti-tubercular therapy.

1.Introduction

Tuberculosis remains to be a major killer disease in India accounting for one-fifth of global disease burden. India accounts for an estimated 2.2 million of the 8.6 million new cases of tuberculosis that occur each year globally.[1] A significant proportion of tuberculosis patients require admission, with in-patient mortality rates ranging from 2% to 12%.[2]

Miliary tuberculosis which results from haematogenous dissemination of Mycobacterium tuberculosis is a potentially lethal disease if not diagnosed and treated early. It accounts for less than 2% of all tuberculosis cases and upto 20% of all extra-pulmonary tuberculosis cases among immune competent adults with higher rates in immune compromised patients.[3]

Miliary tuberculosis as a risk factor for ARDS is rare. We present a case of miliary tuberculosis in an immune-competent female without any co-morbidity, who succumbed to her illness due to ARDS.

2. Case report

A 36 year old female was referred from a district hospital as a case of bronchopneumonia when she failed to show response to antibiotics. She presented with history of non-productive cough of 15 days duration and exertional breathlessness which had progressed to breathlessness at rest over 4-5 days. She also complained of fever which was intermittent, low grade with no chills or rigors. She did not give history of any contact with tuberculosis nor had taken any treatment for tuberculosis in the past. She was non-hypertensive, non-diabetic with no history of smoking, alcohol consumption or substance abuse.

On examination, she had severe dyspnoea with respiratory rate of 44/min and heart rate of 150/min, blood pressure of 90/60 mmHg and oxygen saturation on room air was 72%. Auscultation of the chest revealed bilateral crepitations. Cardiovascular system examination revealed tachycardia without any murmurs, while CNS and abdomen examination was normal.

Complete haemogram showed haemoglobin of 8.6 gm%, total count of 9600/mm^3, neutrophils - 88%, lymphocytes- 8%, eosinophils -4%, platelet count of 2.7lakhs. Her renal functions were normal and fasting blood sugar was 92mg%.

Liver functions showed total serum bilirubin of 1.8gm%, total protein of 4.2gm%, SGOT- 257 IU/ml, SGPT- 37 IU/ml, alkaline phosphatase-227IU/ml. Leptospira and blood Widal antibody titres were negative. ELISA for HIV antibodies and HBsAg were negative. Her blood cultures were sterile. Blood gas analysis showed pH of 7.026, PaO_2 of 55.2 mmHg, PCO_2 of 32.7 mmHg, and HCO_3 of 8 mmHg; severe metabolic acidosis. Chest X-ray showed bilateral reticulo-nodular shadowing involving the mid-zones and the lower zones (see Fig 1a, 1b).

She was immediately managed with invasive mechanical ventilation along with broad spectrum antibiotics for a possible bronchopneumonia. Anti-tubercular therapy was also started in view of clinical and radiological suspicion of Miliary tuberculosis. However, there was clinical worsening and the patient developed septic shock requiring vasopressor support. Patient succumbed to her illness on the 3rd day of admission despite aggressive therapy.

Post mortem biopsy of lung was performed. Histopathology of the lung tissue showed granulomatous inflammation composed of epitheloid cells, langhans giant cells, lymphocytes and caseation necrosis with areas of haemorrhage (see Fig 2a, 2b). The diagnosis of tuberculosis was thus confirmed.

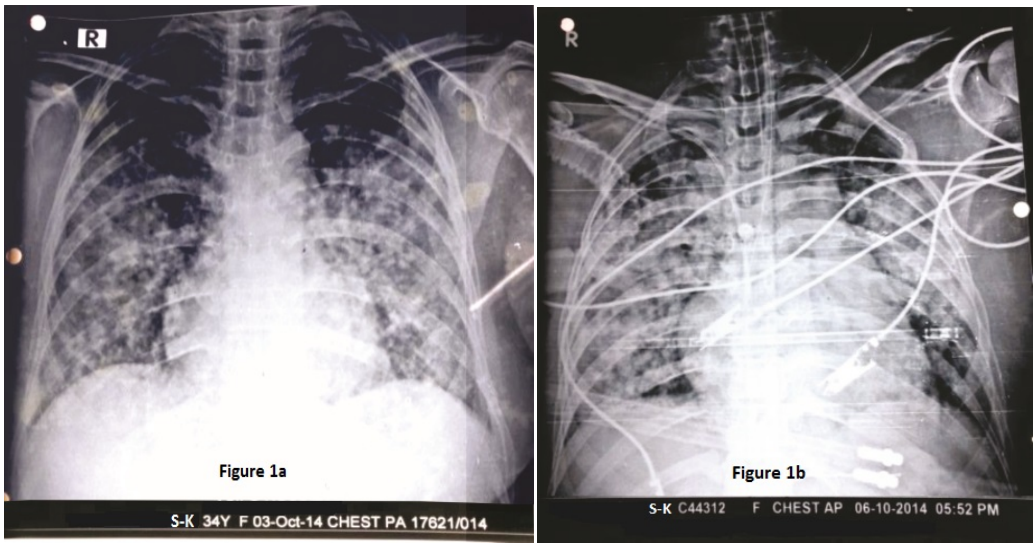

Figure 1a & 1b -Chest radiograph showing bilateral reticulo-nodular shadowing involving the mid-zones and the lower zones.

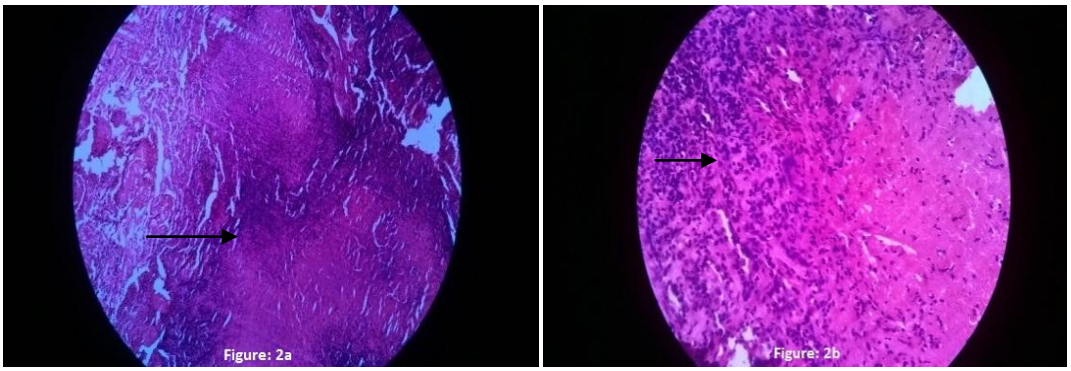

Figure 2a - Histopathology of lung tissue (low power field) showing well formed granulomas with central caseation.

Figure 2b - Granuloma (high power field) showing presence of langhans giant cells (arrow), lymphocytes, epitheloid cells and caseation necrosis

3. Discussion

Miliary Tuberculosis denotes all forms of progressive, widely disseminated haematogenous tuberculosis. In the year 1700 the term 'miliary' was first described by John Jacob Manget, who linked the appearance of the involved lung to millet seeds due to its surface being covered with firm small white nodules.[4]

It occurs due to widespread haematogenous dissemination of tubercle bacilli from an active caseous focus. This focus may be a primary progressive infection of Mycobacterium tuberculosis or the reactivation of a latent focus. Miliary tuberculosis continues to remain as a perplexing disease with difficult diagnosis and treatment due to its variable clinical presentation, atypical radiological findings and difficulties in establishing tuberculosis as the aetiological diagnosis.

ARDS was first described in 1967 as a life threatening respiratory condition characterised by hypoxia and stiff lungs. It is a severe lung syndrome wherein there is increased permeability of pulmonary capillary endothelial cells and alveolar epithelial cells leading to pulmonary edema, refractory hypoxaemia, multi-organ failure and death. It is diagnosed by the New Berlin criteria as follows.[5]

1) Acute onset: It is defined as within 7 days of a known clinical insult or new or worsening respiratory symptoms
2) Bilateral opacities on chest imaging that is not fully explained by effusions, lobar/lung collapse or nodules.
3) PaO2: FiO2 ratio ≤ 300 with a PEEP or CPAP ≥ 5 cm H_2O
4) Respiratory failure that is not fully explained by cardiac failure or fluid overload.

Miliary TB is usually a rare cause of ARDS.[6] Exact incidence of miliary TB presenting as ARDS is not known however it is estimated that 1-2% of ARDS patients are associated with disseminated tuberculosis.[7] Mortality from miliary TB is approximately 20% and miliary TB with ARDS has definitely a higher mortality.[8]

Pathogenesis of ARDS in patients with tuberculosis is not known. It is postulated that massive release of mycobacteria into pulmonary circulation results in inflammation, obliterative endarteritis and damage to alveolo-capillary membrane.[9] There is also platelet aggregation in pulmonary capillaries causing endothelial injury and leucocyte activation resulting in increased vascular permeability. Lipoarabinomannan, the mycobacterial cell wall component, acts similar to lipopolysaccharide in bacterial sepsis to activate macrophages to release tumour necrosis factor-α [TNF- α] and interleukin-1b [IL-1b]. The activation of macrophages is also thought to be a key step in the causation of lung injury.[10]

Clinical manifestations of miliary tuberculosis are non-specific, the chest radiographs do not always show classical miliary changes instead may be normal, sometimes have faint reticulonodular infiltrates uniformly distributed throughout the lung which become apparent days to weeks after presentation. HRCT is a more sensitive investigation for miliary tuberculosis which shows centrilobular nodules in random distribution scattered throughout the entire lungs. The patient may present with complications causing diagnostic dilemma. In addition, obtaining material for mycobacterial analysis can be difficult, especially in patients with extra pulmonary tuberculosis and in mechanically ventilated patients. Therefore a high degree of clinical suspicion and a systematic approach to diagnostic testing is required to establish the diagnosis of miliary tuberculosis.[11] Complications like acute kidney injury, disseminated intravascular coagulation, multi organ failure and septic shock are poor prognostic factors. Sharma et al determined that in patients with tuberculosis; prolonged illness, absolute lymphopenia and increased alanine aminotransferase (SGPT) are independent risk factors for ARDS.[12] However, our patient had only absolute lymphopenia as a risk factor for ARDS with increased aspartate aminotransferase (SGOT) and alkaline phosphatase levels.

Anti-tubercular treatment should be considered in patients with clinical suspicion of tuberculosis even before the results of diagnostic tests are available. This is due to the fact that delay in initiation of treatment can result in death. In the treatment of miliary tuberculosis, corticosteroids may be used as adjuvant. They act by allowing tubercular drugs to penetrate the granulomas and also inhibit release of cytokines and lymphokines responsible for inflammatory cascade.

Our case was a rare combination of miliary tuberculosis with ARDS. She was a young patient with no co- morbidities. She was managed in ICU with broad spectrum antibiotics, as the differential diagnosis for acute symptoms and miliary shadows can be bacterial infection, invasive ventilation and because of clinico-radiological suspicion of tuberculosis, patient was started on anti-tubercular therapy.

However, rapid deterioration and death is seen in few patients due to progressive disease despite therapy. Hence, an emphasis on early diagnosis, treatment and a clinical awareness of fatal combination of ARDS with miliary tuberculosis is the basis of this case report.

4. Conclusion

Miliary Tuberculosis constitutes one of the rare causes of ARDS with acute and atypical clinical presentation. Awareness of this presentation, early diagnosis and prompt treatment of the disease is essential to prevent mortality. Miliary TB should be considered as a possibility of ARDS in the

developing world even in the absence of co morbidities or immune suppression.

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