Case Reports

Acute respiratory distress syndrome with miliary tuberculosis

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ABSTRACT

Acute respiratory distress syndrome (ARDS) is a common disorder in the intensive care unit and is associated with high mortality. Tuberculosis (TB) continues to be a major health problem and infects approximately one-third of the world’s population. Tuberculosis is a common disease in Saudi Arabia with an increasing annual incidence rate. The diagnosis of miliary TB can be difficult due to the diversity of radiological patterns, nonspecific clinical findings, and the limitation of routine diagnostic tests, which may require invasive procedures. Most patients with TB have predisposing factors, mainly diabetes mellitus, chronic liver disease, immunosuppressed state, and malignancy. In this case report, we present a patient with ARDS caused by miliary TB. A Medline literature review did not reveal any similar cases reported from Saudi Arabia. Our objective in presenting this particular case is to highlight the important association between miliary TB and ARDS.

Case Report. A 71-year-old man was admitted to the hospital complaining of productive cough and weight loss. Physical examination showed fine bilateral basal crackles. Laboratory findings showed elevated liver enzymes. Tuberculin skin test and sputum smear for acid-fast bacilli were negative. On the fifth day of admission, he deteriorated and developed severe respiratory distress. A chest radiograph demonstrated worsening pulmonary infiltrates. He was electively intubated and was put on a mechanical ventilator. The chest CT scan revealed diffuse bilateral pulmonary nodules and airspace disease. Based upon the clinical suspicion of acute respiratory distress syndrome associated with miliary tuberculosis (TB), empiric treatment with antituberculosis and systemic steroids was started. He was extubated after 6 days. The diagnosis of miliary TB was confirmed by a thoracoscopic lung biopsy. He was discharged with a near normal chest radiograph and was followed up as an outpatient.
to persons with tuberculosis (TB). He had no personal history of any respiratory disease or malignancy. On physical examination, he appeared ill, his temperature was 37.6°C, pulse 112/min, blood pressure 160/107 mm Hg, and a respiratory rate of 20/min with oxygen saturation of 99% on room air. Lung examination revealed bilateral inspiratory crackles over the lower lung fields without signs of consolidation. His cardiac examination was unremarkable except for tachycardia. The abdomen was soft, and no organomegaly was detected. There was no lymphadenopathy or arthritis. The remainder of physical examination was unremarkable. Laboratory investigations revealed a white blood cell count of 5100/μL with a differential cell count of 65% neutrophils, 27% lymphocytes, and 8% monocytes, absolute lymphocyte count (ALC) 1400/μL (normal 1300-2900/μL), hemoglobin of 12.5 g/dl, and platelet count of 105000/μL. He had elevated liver enzymes, aspartate transaminase 158 IU/L (normal 5-34 IU/L), alanine transaminase (ALT) 68 IU/L (normal < 58 IU/L), and alkaline phosphatase 666 IU/L (normal 40-150 IU/L). Gamma glutamyl transpeptidase was 596 IU/L (normal 12-64 IU/L), total bilirubin 38.2 μmol/L (normal 3.4-20.5 μmol/L), and albumin 29 g/l (normal 34-48 g/l). Random glucose was 5.2 mmol/L (normal 4.1-9 mmol/L), erythrocyte sedimentation rate 30 mm/h (normal < 20 mm/h), and C-reactive protein 89 mg/L (normal < 10 mg/L). His blood chemistry and coagulation profile were within normal limits. Arterial blood gases, on room air were pH 7.38, partial pressure of arterial carbon dioxide (PaCO₂) 37.5 mm Hg, partial pressure of arterial oxygen (PaO₂) 88.5 mm Hg, and bicarbonate concentration 23 mmol/L. Chest radiograph showed diffuse bilateral nodular opacities with lower lobes predominance (Figure 1). Abdominal ultrasound was unremarkable. He was admitted to a general medical ward and started on ceftriaxone and azithromycin, for presumed community acquired pneumonia. He was put on airborne isolation. Tuberculin skin test was negative, and 3 sputum specimens were negative for acid-fast bacilli (AFB). Nucleic acid amplification (NAA) testing for TB was negative. Both blood and urine cultures were sterile.

Five days after admission, he deteriorated with respiratory rate 30/min and oxygen saturation 78% on room air. Blood gases showed pH 7.40, PaCO₂ 34.58 mm Hg, PaO₂ 67.88 mm Hg, and bicarbonate 21.1 mmol/L on 100% oxygen by face mask. The calculated PaO₂/fraction of inspired oxygen (FiO₂) was 68 mm Hg. At that time, he was transferred to the intensive care unit (ICU) and was intubated electively. He was put on mechanical ventilation using a lung protective strategy for acute respiratory distress syndrome (ARDS). Chest x-ray and CT scan showed worsening bilateral alveolar infiltrates (Figures 2 & 3). The HIV serology was negative. After intubation, he was started on antituberculosis medications due to the high index of suspicion of TB (initially with intravenous Moxifloxacin, Ethambutol [EMB], and Amikacin). Isoniazid (INH), Rifampicin (RIF), and Pyrazinamide
(PZA) were not started due to elevated liver enzymes. He was also given intravenous methylprednisolone. Within the next 24 hours of the intubation, bronchoscopy was carried out and bronchoalveolar lavage (BAL) was obtained. The AFB stain was negative. The NAA for TB was also negative. During ICU admission, the patient developed pancytopenia with white blood cells of 2100/μL with an ALC of 630/μL, hemoglobin 10.1 g/dl, and platelet 92000/μL. In addition, he developed hyponatremia (Na 128 mmol/L). Within the next four days, he started to improve and he was extubated on day 11. Methylprednisolone was discontinued a day earlier. On the fifteenth day of admission, when he was stabilized, a lung biopsy was obtained via video assisted thoracoscopic surgery. Histopathology examination revealed multiple areas of granulomas with occasional caseation (Figure 4). The AFB stain was negative. However, NAA was positive on the lung biopsy.

On the twenty-third day of hospitalization, he was discharged in a stable condition with near complete resolution of the chest x-ray abnormalities. Liver enzymes and pancytopenia normalized. He continued to follow up as an outpatient on 4 oral anti-tuberculosis medications: INH, RIF, EMB, and PZA. Within 5 weeks of his follow up, cultures of the lung biopsy were positive for Mycobacterium tuberculosis. The organism was fully sensitive to all first line antituberculosis medications.

Discussion. Acute respiratory distress syndrome is a severe lung disease characterized by inflammation of the lung parenchyma leading to impaired gas exchange, hypoxemia, and multi-organ failure. Identification of the primary cause of respiratory distress is vital for initiation of appropriate therapy. Miliary TB is a rare cause of ARDS. There are few case reports of ARDS in patients with miliary TB, most of which were from Japan. According to our search, there is a scarcity of reports from Saudi Arabia. The ARDS is said to occur when the ratio of $\text{PaO}_2/\text{FiO}_2 < 200 \text{ mm Hg}$, bilateral radiological lung infiltration, and pulmonary artery pressure of $<18 \text{ mm Hg}$, or no clinical evidence of elevated left atrial pressure, all of which were present in our patient.

Miliary TB is a widespread dissemination of Mycobacterium tuberculosis via hematogenous spread. There are many factors that may predispose towards the development of miliary TB including HIV infection, diabetes mellitus, immunosuppressive agents, steroids, and alcoholism. In several case reports, military TB and ARDS occurred in immunosuppressed patients. The clinical presentation of miliary TB is highly variable. It can present as fewer of unknown origin, dysfunction of one or more organs, septic shock or ARDS. In a series of 109 patients with miliary TB, 7 patients developed ARDS. The nonspecific features of the presentation may account for the diagnosis to be missed. As the diagnosis of miliary TB is frequently difficult to reach, many reported cases were diagnosed postmortem. The duration of symptoms before clinical worsening of miliary TB to ARDS is usually gradual, ranging from 5 to 90 days, but it can be unpredictably rapid. Predictors of the development of ARDS in military TB patients were demonstrated in one study. In patients with miliary TB, absolute lymphocytopenia, and elevated ALT are independently associated with ARDS development. The prognosis of miliary TB has clearly improved after the introduction of effective antituberculosis medications. However, the situation is quite different when ARDS complicates miliary TB. According to the limited number of reported articles of ARDS and miliary TB, the overall mortality rate is as high as 80%. Delayed treatment of military TB with respiratory failure may contribute to the persistently high mortality rates in ICU patients with this condition. Therefore, as carried out in our case, patients with ARDS of obscure etiology where clinical features suggest TB as the inciting cause, antituberculosis therapy should be started empirically while the diagnosis is actively pursued. The diagnosis of TB requires identification of Mycobacterium Tuberculosis. In this described case, the patient had a negative tuberculin skin test and sputum examination for AFB, both tests cannot be used to exclude TB, as tuberculosis skin test is only positive in 28-53%, and sputum for AFB smear is positive in 20-40% of patients with miliary TB. The results of smear and culture from BAL have been reported to be positive in 70% of patient with TB. The results of BAL were negative in our case. Finally, the diagnosis of our patient with miliary TB was reached by lung biopsy.

The implication of this case is to emphasize the association between miliary TB and ARDS. It will also
help future research to focus on this particular cause of ARDS where mortality remains high despite the availability of anti-tuberculosis treatment.

In summary, we reported a case of miliary TB that was complicated by ARDS. The diagnosis could not have been made without lung biopsy. In patients with unexplained ARDS, miliary TB should be considered in areas known to be endemic for TB.

Acknowledgment. We extend our thanks to Dr. Mohamed M. Fairoz, Radiologist, for reviewing the images.

References


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