CASE REPORT

Pulmonary tuberculosis presenting with acute respiratory distress syndrome (ARDS): A case report and review of literature

Ab. Hameed Raina [a,*], **Abid Bhat** [a], **Fayaz Ahmad Bhat** [a],
Khalid Hamid Changal [a], **Ghulam Nabi Dhobi** [a], **Pervaiz Ahmad Koul** [a],
Manzoor Ahmad Raina [b], **Feroz Ahmad Wani** [c]

[a] *Department of Internal Medicine, Sheri-Kashmir Institute of Medical Sciences, Soura (J&K), India*
[b] *Department of Clinical Biochemistry, Sheri-Kashmir Institute of Medical Sciences, Soura (J&K), India*
[c] *Department of Community Medicine, Sheri-Kashmir Institute of Medical Sciences, Soura (J&K), India*

Abstract   Tuberculosis is a very highly prevalent disease particularly in the developing world. In India one person dies of tuberculosis every minute. It can be a differential diagnosis of any disease ranging from infections to malignancies. But tuberculosis as a primary cause of respiratory failure requiring mechanical ventilation is an uncommon occurrence. Among patients with pulmonary tuberculosis, those with miliary or disseminated disease or having comorbidities like acquired immunodeficiency syndrome (AIDS) are especially prone to develop acute respiratory distress syndrome (ARDS). We present a case of a young female with no comorbidities or immuno suppression who presented with ARDS to us. We initially managed with mechanical ventilation and broad spectrum antibiotics, but there was no improvement. Only after anti tubercular therapy (ATT) and corticosteroids the patient recovered.

© 2013 Production and hosting by Elsevier B.V. on behalf of The Egyptian Society of Chest Diseases and Tuberculosis. Open access under CC BY-NC-ND license.

Introduction

In most countries, as ours, tuberculosis remains a major public health problem. One third of the world's population is estimated to be infected with *Mycobacterium tuberculosis*. A significant proportion of tuberculosis patients still has to be hospitalized, and in-hospital mortality remains high, with estimates ranging from 2% to 12% [1]. Some decades ago, respiratory failure resulting from tuberculosis was reported mainly in cases of miliary tuberculosis. In 1977, the first case series of

* Corresponding author. Tel.: +91 9906650955.
E-mail address: rainahameed@gmail.com (A.H. Raina).

respiratory failure in 16 patients with tuberculosis and fibro-cavitary disease was described [2]. The reported frequency of acute respiratory failure in patients with active tuberculosis ranged from 1.5% to 5.0% [3,4], although pulmonary tuberculosis is rarely the primary cause of this complication. We report a case of a patient presenting with ARDS who subsequently turned out to be a case of pulmonary tuberculosis.

Case summary

Our case was a 32 year old female, normotensive, non-diabetic, presenting with a four week history of severe breathlessness, cough with expectoration with blood tinged sputum. Initially she had followed some private practitioner outside but there was no relief and symptoms got worsened.

On examination the patient was conscious, oriented, febrile to touch, cyanosed, tachypneic with respiratory rate of 34/min, pulse of 94b/min and temperature of 100F, BP was 140/82mmHg. Oxygen saturation was 70% only. Systemic examination revealed bilateral course crepitations in the lungs. Rest of the examination was normal. Initial investigations reveal Hb of 10 g/dl, TLC of 12,000/uL, DLC of 84% neutrophils and 20% lymphocytes. Platelet count of 120,000. KFT of 40 IU urea and 1.2mg/dl of creatinine. ABG/electrolytes showed pH of 7.34, po2 = 40mmHg, pco2 = 45mmHg, Hco3 = 22-meq/L, Na = 143, k = 3.5 depicting Type 1 respiratory failure. ECG showed sinus tachycardia. Po2/FiO2 = 198. Chest X-ray (Figs. 1 and 2) showed bilateral dense reticulo-nodular pattern interspersed with fine infiltrates. The patient was immediately managed with invasive mechanical ventilation and broad spectrum antibiotics but she did not improve. Influenza retroviral and other virological serologies were negative. Blood and urine culture came sterile. There was no evidence of fungal infection. Bedside echo was done which was normal. Tracheal aspiration showed strong positivity for *M. tuberculosis* but Monteux test came negative. Subsequently computed tomography (CT) scan (Fig. 3) showed typical miliary pattern of the lungs though there was no evidence of disseminated tuberculosis. So on clinical and radiological suspicion she was put on anti-tubercular therapy. Fortunately after 7 days of treatment the patient showed signs of improvement and she was extubated on 12th day of admission. In the meantime

culture came positive for *M. tuberculosis* after 2 weeks of culture in Bactec. Hence she was diagnosed as a case of pulmonary tuberculosis presenting as acute respiratory distress syndrome (ARDS). She was discharged on 15th day. She is on our follow up and is doing well. Sputum for acid fast bacilli (AFB) is now negative and is symptomatically much better.

Discussion

Tuberculosis (TB) has been the scourge of civilization before recorded history, afflicting humans and domestic animals alike in all parts of the world. The multitude of names including "the white plague," "consumption," and "phthisis" that has been applied to TB attests to its protean manifestations. While the earliest classical descriptions of TB can be found in the writings of Hippocrates, it was the experiments of P.F.H. Klencke in 1843 and Jean Antoine Villemin in 1865 that elucidated the contagious nature of the disease. The identification of the tubercle bacillus by Kochin in 1882 allowed for the understanding of the pathogenesis of TB [2].

Tuberculosis is being increasingly recognized as a cause of acute respiratory distress syndrome (ARDS) [3–5]. Although exact figures as to what percentage of cases of ARDS are tubercular in aetiology are not available, in the Southeast Asia tuberculosis accounts for 3–16% of cases of community-acquired pneumonia. Malhotra et al. studied 185 cases of RICU admissions. Out of a total of 984, 18.8% admissions had ARDS over an 8-year period of which tuberculosis accounted for seven (3.8%) [6]. The pathogenesis of ARDS in patients with pulmonary tuberculosis has not been clearly elucidated. Postulated mechanisms include massive release of mycobacteria into the pulmonary circulation resulting in inflammation, obliterative endarteritis and damage of the alveolocapillary membrane [7]. Platelet aggregation in pulmonary capillaries causing endothelial injury and leucocyte activation resulting in increased vascular permeability are other hypotheses. In addition, lipoarabinomannan, a component of the mycobacterial cell wall, is thought to act in a manner similar to lipopolysaccharide in bacterial sepsis to activate macrophages to release tumour necrosis factor-α [TNF-α] and interleukin-1β [IL-1β] [8]. The activation of macrophages is thought to be a key step in the causation of lung injury [8]. It is yet to be determined, whether it is the individual host immunologic responses
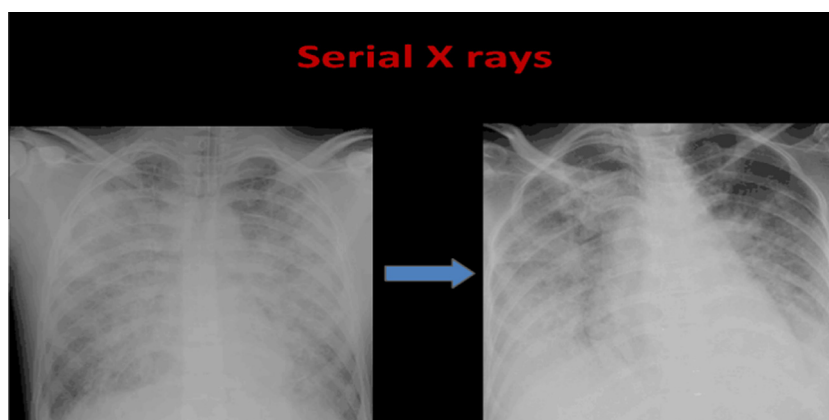
Figure 1 Chest X-ray showing bilateral infiltrates (ARDS picture).
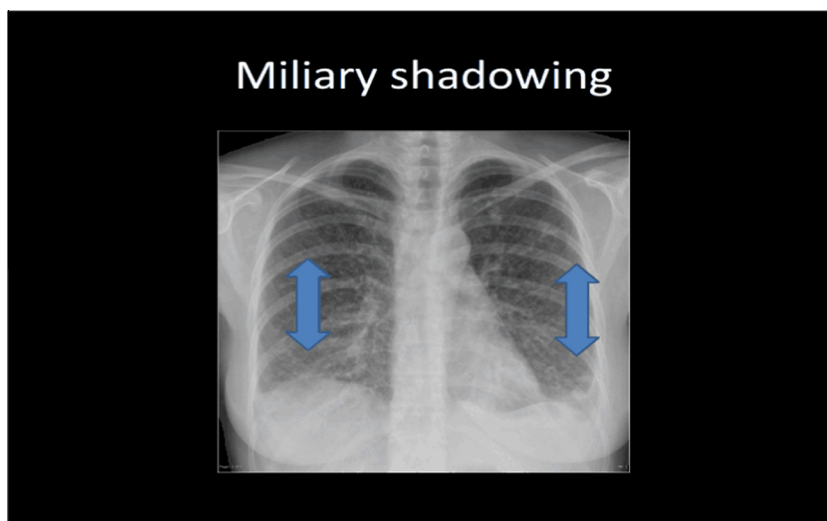
Figure 2 Chest X-ray showing features of miliary tuberculosis.
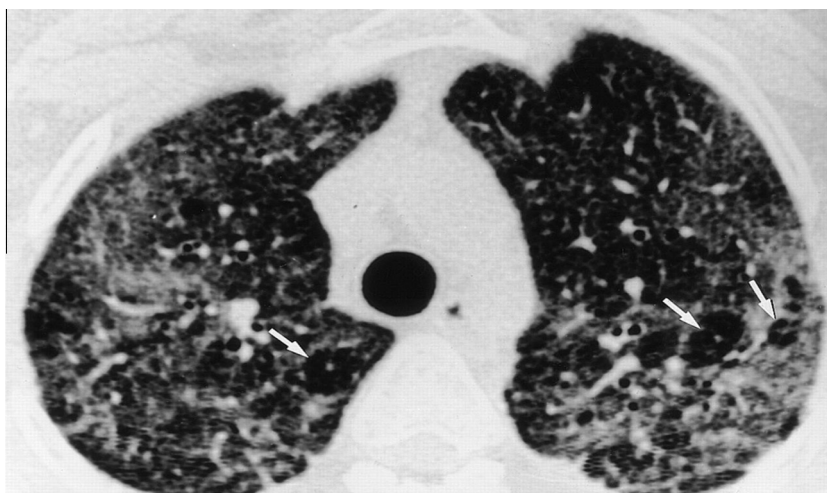
Figure 3 CT scan of the chest showing features of ARDS.

independent of organism burden or differences in the virulence of different strains of the *M. tuberculosis* which are the prime factors in the development of lung injury [6].

Acute respiratory distress syndrome (ARDS) is a life-threatening reaction to injuries or acute infection to the lung. ARDS is a severe lung syndrome with direct and indirect causes. Inflammation of the lung parenchyma leads to impaired gas exchange with systemic release of inflammatory mediators, causing inflammation, hypoxaemia and frequently multiple organ failure. This condition has a 90% death rate in untreated patients. With treatment, usually mechanical ventilation in an intensive care unit, the death rate is 50%. It is diagnosed by the following criteria: [9]

1. **Acute onset:** It is defined as within 7 days of some defined event, which may be sepsis, pneumonia, or simply a patient's recognition of worsening respiratory symptoms. (Most cases of ARDS occur within 72 h of recognition of the presumed trigger.)
2. **Bilateral opacities** consistent with pulmonary oedema must be present but **may be detected on CT** or chest X-ray.

3. PaO2: FiO2 ratio < 300. **"Acute lung injury" no longer exists**. Under the Berlin definition, patients with PaO2/FiO2 200–300 would now have "mild ARDS.
4. Respiratory failure should not be fully explained by cardiac failure or fluid overload. **There is no need to exclude heart failure in the new ARDS definition;** patients with high pulmonary capillary wedge pressures, or known congestive heart failure with left atrial hypertension can still have ARDS.

The new Berlin definition for ARDS has also categorize ARDS as being mild, moderate, or severe:

ARDS severity	PaO2/FiO2[*]	Mortality[**]
Mild	200–300	27%
Moderate	100–200	32%
Severe	< 100	45%

[*] On PEEP 5+.
[**] Observed in cohort.

The following three clinical settings account for 75% of ARDS cases:

1. Sepsis syndrome – most important cause.
2. Severe multiple trauma.
3. Aspiration pneumonia which is due to aspiration of saliva/gastric contents.
4. Complication of pneumonia if left untreated.
5. Necrotizing pancreatitis. Some cases of ARDS are linked to large volumes of fluid used during resuscitation post trauma. Other causes include shock, near-drowning, multiple transfusions and inhalation of irritants or toxic fumes that damage the alveolar epithelium and miliary tuberculosis. But pulmonary tuberculosis without dissemination causing ARDS has rarely been mentioned in literature. Our case, therefore, represents a unique cause of ARDS.

The leading cause of ICU admission of tubercular patients was respiratory failure, and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores ranged from 13 to 23 in most of the studies [1]. Some authors evaluated the factors associated with the development of respiratory failure and the need for mechanical ventilation. Gram-negative pneumonia or sepsis, COPD, history of poor compliance with tuberculosis treatment, and cancer were predictors of respiratory failure [10]. Our case had none of these. Patients with miliary/disseminated tuberculosis were more likely to require mechanical ventilation than those having only pulmonary tuberculosis. In a study conducted in Brazil investigating the pulmonary histopathological changes found in 3030 autopsies of patients who died of acute respiratory failure, tuberculosis was diagnosed as an underlying disease in 110 cases (3.6%). Among them ARDS was found in very few cases [11]. The most common radiological findings are reticular infiltrates and consolidation and cavitation can occur in 27–50% of cases [1]. The most common laboratory findings are anaemia, leucopenia, leucocytosis, and hypoalbuminemia [12]. Our patient had only anaemia among these.

Clinical characteristics and chest X-ray remain the main tools for the early diagnosis of active pulmonary tuberculosis. Mycobacterial culture takes 6–8 weeks. Therefore, the treatment of intensive care unit (ICU) patients can rarely be based on culture results. In addition, obtaining material for mycobacterial analysis can be difficult, especially in patients with extra pulmonary tuberculosis and in mechanically ventilated patients whose parameters preclude diagnostic procedures, such as bronchoscopy. Although antituberculosis treatment is potentially toxic, it is recommended that patients admitted to an ICU with tuberculosis symptoms start receiving the medications before the results of diagnostic tests are available, given that delayed treatment initiation can result in death. In immunocompromised patients, the index of suspicion should be even higher [1]. Appropriate diagnostic investigation, as well as knowledge of the clinical and radiological presentations of severe tuberculosis, can contribute to earlier diagnosis and treatment initiation. The time from onset of symptoms to initiation of anti-tuberculosis treatment has been reported to be over 30 days in 28.8–34.0% of cases [13]. In that retrospective study, the time from admission to initiation of treatment was shorter in patients with miliary tuberculosis than in those with tuberculous pneumonia. There can be a delay in diagnosis and, consequently, in initiation of treatment because it is difficult to differentiate tuberculous pneumonia from severe bacterial pneumonia on X-rays. Symptom duration longer than two weeks and the presence of micronodules or a cavitary pattern on chest X-ray were significantly associated with active pulmonary tuberculosis [14]. The introduction of new techniques, including early detection of the aetiological agent by PCR, can aid in diagnosis and contribute to early initiation of treatment. In addition, high resolution computed tomography (HRCT) has been used in situations in which chest X-ray does not contribute to the diagnosis of active disease, such as in cases of minimal parenchymal changes and in the differentiation of old fibrotic lesions from those that are characteristic of bronchogenic dissemination [15].

Appropriate antituberculosis treatment is an important factor that can affect patient outcome. Higher mortality is found among patients who do not receive optimal treatment including isoniazid and rifampin.

In the treatment of tuberculosis, corticosteroids are used as adjuvants, especially in extra pulmonary forms of the disease, such as meningeal and pericardial tuberculosis. Corticosteroids act by inhibiting the release of lymphokines and cytokines, which are responsible for constitutional symptoms and tissue damage. In addition, they allow antituberculosis drugs to penetrate granulomas, disrupting them [16]. In general, corticosteroid use is considered for selected patients with severe forms of pulmonary tuberculosis, usually for those who develop ARDS [13]. We used them in our patient and they helped.

Our case is unique in the sense that the patient was young, had no comorbidities, or superadded infection. She presented with ARDS and was managed in ICU with mechanical ventilation and broad spectrum antibiotics initially. But when she did not respond other causes were thought of. Further work up gave the diagnosis of underlying tuberculosis. It was after putting her on ant tubercular drugs and corticosteroids that she improved. So tuberculosis should always be kept a possibility of ARDS particularly in the developing world even if there are no comorbidities or immunosuppression.

References

[1] Denise Rossato Silva, Marcelo Basso Gazzana, Paulo de Tarso Roth Dalcin, Severe tuberculosis requiring ICU admission, J. Bras. Pneumol. 38 (3) (2012) 386–394.

[2] Lawrence. Chow, Paul. Stark, Miliary tuberculosis, radiographic features, Appl. Radiol. 2 (2000) 25–28.

[3] M.K. Agarwal, P.P. Muthuswamy, A.S. Banner, R.S. Shah, W.W. Addington, Respiratory failure in pulmonary tuberculosis, Chest 72 (5) (1977) 605–609.

[4] H. Levy, J.M. Kallenbach, C. Feldman, J.R. Thorburn, J.A. Abramowitz, Acute respiratory failure in active tuberculosis, Crit. Care Med. 15 (3) (1987) 221–225.

[5] C. Penner, D. Roberts, D. Kunimoto, J. Manfreda, R. Long, Tuberculosis as a primary cause of respiratory failure requiring mechanical ventilation, Am. J. Respir. Crit. Care Med. 151 (3 Pt 1) (1995) 867–872.

[6] P. Malhotra, R. Agarwal, D. Gupta, A.N. Aggarwal, Successful management of ARDS with bronchopleural fistula secondary to miliary tuberculosis using a conventional ventilator, Monaldi Arch. Chest Dis. 63 (3) (2005) 163–165.

[7] A.R. Piqureas, L. Marruecos, A. Artigas, C. Rodriguez, Miliary tuberculosis and adult respiratory distress syndrome, Intensive Care Med. 13 (1987) 175–182.

[8] Y.M. Zhang, T.C. Doerfler, B. Lee, B. Guillemin, W.N. Rom, Mechanisms of stimulation of interleukin-1β and tumour necrosis factor by *Mycobacterium tuberculosis* components, J. Clin. Invest. 91 (1993) 2076–2083.

[9] ARDS and ALI, BEST OF 2012, Critical Care; JAMA. Available from: < pulmccm.org/2012/ards-review/consensus-panel > .

[10] R.N. Frame, M.C. Johnson, M.S. Eichenhorn, G.C. Bower, J. Popovich Jr., Active tuberculosis in the medical intensive care unit: a 15-year retrospective analysis, Crit. Care Med. 15 (11) (1987) 1012–1014.

[11] Ade M. Soeiro, E.R. Parra, M. Canzian, C. Farhat, V.L. Capelozzi, Pulmonary histopathological alterations in patients with acute respiratory failure: an autopsy study, in: J. Bras. Pneumol. 34 (2) (2008) 67–73.

[12] D.R. Silva, D.M. Menegotto, L.F. Schulz, M.B. Gazzana, P.T. Dalcin, Mortality among patients with tuberculosis requiring intensive care: a retrospective cohort study, BMC Infect. Dis. 10 (2010) 54.

[13] S.M. Lin, T.Y. Wang, W.T. Liu, C.C. Chang, H.C. Lin, C.Y. Liu, et al, Predictive factors for mortality among non-HIV-infected patients with pulmonary tuberculosis and respiratory failure, Int. J. Tuberc. Lung Dis. 13 (3) (2009) 335–340.

[14] C. Hui, C.L. Wu, M.C. Chan, I.T. Kuo, C.D. Chiang, Features of severe pneumonia in patients with undiagnosed pulmonary tuberculosis in an intensive care unit, J. Formos. Med. Assoc. 102 (8) (2003) 563–569.

[15] M.B. Conde, F.A. Melo, A.M. Marques, N.C. Cardoso, V.G. Pinheiro, P.D.T. Dalcin, et al, III Brazilian thoracic association guidelines on tuberculosis, J. Bras. Pneumol. 35 (10) (2009) 1018–1048.

[16] P. Muthuswamy, T.C. Hu, B. Carasso, M. Antonio, N. Dandamudi, Prednisone as adjunctive therapy in the management of pulmonary tuberculosis. Report of 12 cases and review of the literature, Chest 107 (6) (1995) 1621–1630.