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# Clinical review of eight patients with acute respiratory distress syndrome due to pulmonary tuberculosis

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## Abstract

Pulmonary tuberculosis can lead to acute respiratory distress syndrome (ARDS) even in the absence of superinfection, and this condition requires mechanical ventilation. We describe herein the characteristics and outcomes of 8 patients with this association hospitalized in a French teaching hospital between 1997 and 2006.

**Keywords:** *Mycobacterium tuberculosis*, ARDS, multiple organ failure, ICU, nosocomial pneumonia

## Introduction

Tuberculosis (TB) is an unusual cause of acute respiratory distress syndrome (ARDS) in the intensive care unit (ICU) [1]. The mortality rate in these patients is higher than in other causes of ARDS [2,3]. Only a few studies have reported the association of ARDS with TB [4,5].

The goal of this study was to describe the characteristics and outcomes of TB with ARDS in a French teaching hospital.

## Patients and methods

A retrospective study was performed in 5 ICUs of the university hospital in Montpellier, France, between December 1997 and December 2006. Patients were identified by a cross-search of the Medical Information Department database (patients hospitalized in the ICU with a diagnosis of TB and/or ARDS) and the Mycobacteriology Department database (isolation of *Mycobacterium tuberculosis*). All adult patients with documented pulmonary TB and ARDS hospitalized in the ICU were included.

Pulmonary TB was defined by the isolation of *M. tuberculosis* in bacterial culture from bronchial aspirates or bronchoalveolar lavage fluid or pleural effusion. ARDS was defined according to the American-European Conference criteria: PaO<sub>2</sub>/FiO<sub>2</sub> ratio of  $\leq 200$ , bilateral infiltrates on chest radiography, and a pulmonary artery wedge pressure of  $< 15$  mmHg or no clinical evidence of heart failure [6].

Nosocomial pneumonia was defined according to the American Society guidelines as pneumonia occurring more than 48 h after hospital admission, and was detected by weekly surveillance tracheal aspirates.

The following data were obtained from medical records: demographic characteristics, co-morbidities, time from symptom onset to ICU admission, reasons for admission, simplified acute physiology score (SAPS) II and sepsis-related organ failure acute (SOFA) score, laboratory tests including HIV ELISA test, pulmonary investigation methods, treatments, delays between onset of symptoms and diagnosis or anti-tuberculous treatment, ICU mortality, cause of death, and ICU length of stay.

Chest radiographic patterns were interpreted by a trained radiologist, and reanalysis of the images was

done at the time of data collection by an intensivist. Miliary TB was defined in the presence of pulmonary micronodules on chest radiographs. Drug resistance was defined by phenotypic proportional methods and multidrug resistance was defined as resistance to at least isoniazid and rifampicin [7].

Results are expressed as median values and interquartile range or percentages. The statistical analyses were performed using STAT-VIEW II (Abacus Concepts Inc, Berkeley, CA, USA). We performed a descriptive analysis by computing the frequencies and the percentages for categorical data, and the means, standard deviations, quartiles, and extreme values for continuous data.

## Results

Eight patients with pulmonary TB and ARDS were identified over a 9-y period. Clinical and biological characteristics are summarized in Table I. The median age was 55.5 (interquartile range (IQR) 30–70) y. All patients were HIV-seronegative. Causes of hospitalization in the ICU were acute respiratory failure ( $n=7$ ) and digestive perforation ( $n=1$ ). Mycobacterium tuberculosis was isolated in bronchoalveolar lavage ( $n=4$ ), in tracheal aspirates ( $n=3$ ), and in pleural effusion ( $n=1$ ). Pulmonary samples at admission excluded superinfection in all cases. In 1 patient, M. tuberculosis was isolated in pulmonary and in

peritoneal samples. The diagnosis of TB was made in the ICU for 7 patients and before ICU admission for 1. The median delay between onset of symptoms and diagnosis was 43 (IQR 12–121) days.

All patients were mechanically ventilated; 6 were ventilated on admission and all were ventilated within the first 72 h. No patients received non-invasive ventilation before mechanical ventilation. The median PaO<sub>2</sub>/FiO<sub>2</sub> ratio on day 1 of ARDS was 93.5 (IQR 62–220). The duration of mechanical ventilation was a median 12 (IQR 1–73) days. Others ARDS therapeutics used were: intravenous corticosteroids ( $n=2$ ), procubitus ventilation ( $n=2$ ), neuromuscular blocking agents ( $n=5$ ), and inhaled nitric oxide ( $n=3$ ). During hospitalization 7 patients required vasopressors for a median 5.5 (IQR 1–56) days; 1 patient required inotropic agents; haemodiafiltration therapy was performed in 3 patients. A septic shock haemodynamic profile (including low systemic vascular resistance) was noted in 3 cases in the absence of other co-infections (haemodynamic monitoring by Swan–Ganz catheterization or PICCO system), and required vasopressor use.

All isolates of M. tuberculosis were susceptible to first-line anti-tuberculous drugs. Anti-tuberculosis therapy (ATT) including 3 ( $n=2$ ) or 4 ( $n=6$ ) first-line anti-tuberculous drugs was started in the ICU for 7 patients. One patient received ATT before ICU admission. The time between ICU admission and the start of ATT was a median 3 (IQR 2–11) days. ATT was administrated intravenously for 6 patients (ethambutol, isoniazid, rifampicin) and enterally via a nasogastric tube for the other 2 patients.

Six patients presented nosocomial pneumonia. The time between the start of mechanical ventilation and nosocomial pneumonia was a median 40.5 (IQR 13–53) days. Pseudomonas aeruginosa ( $n=4$ ), Enterococcus faecalis ( $n=1$ ), and Klebsiella pneumoniae ( $n=1$ ) were isolated from bacteriological cultures of respiratory tract samples.

Length of stay in the ICU was a median 18 (IQR 2–77) days. Seven patients died in the ICU. The causes of death were septic shock with multiorgan failure ( $n=5$ ), refractory cardiogenic shock ( $n=1$ ), and refractory hypoxemia ( $n=1$ ).

## Discussion

Pulmonary TB is an unusual cause of ARDS in France. At the hospital in Montpellier, we found less than 1 case per year. Zahar et al. described 22 cases of ARDS and TB that occurred in 2 ICUs over the course of 7 y in Paris [5]. A septic haemodynamic profile due to TB in the absence of co-infection has rarely been described [8]; lipoarabinomannan present in the mycobacterial wall could act as a sepsis promoter [9].

Table I. Patient clinical and biochemical characteristics on admission to the ICU.

Parameters	Results <sup>a</sup>
Age (y)	55.5 (30–70)
Male/female ratio	6/2
SOFA score	6.5 (4–9)
SAPS2	44.5 (10–60)
Thoracic radiography findings	
Bilateral infiltrates ( $n$ )	5
Miliary pattern ( $n$ )	2
Cavitation ( $n$ )	2
Pleural effusion ( $n$ )	1
Biochemistry on admission	
Creatinine (μmol/l)	53.5 (27–102)
Platelets ( $\times 10^9/l$ )	253 (139–607)
CRP (mg/l)	189 (27–255)
Bilirubin (μmol/l)	9 (8–33)
Albumin (g/l)	23 (8–27)
Co-morbidities	
COPD ( $n$ )	1
Diabetes ( $n$ )	0
Coronary artery disease ( $n$ )	1

ICU, intensive care unit; SOFA, sepsis-related organ failure assessment; SAPS, simplified acute physiology score; CRP, C-reactive protein; COPD, chronic obstructive pulmonary disease.

<sup>a</sup>Results are presented as median (interquartile range) unless stated otherwise.

In our study, the mortality rate was near 90%. This ICU mortality rate is very high, especially as all patients were HIV-negative and all isolates of *M. tuberculosis* were susceptible to first-line anti-tuberculous drugs. Global ARDS mortality has been determined to be 40% [10]. Previous studies have established the TB-ARDS mortality rate to be 60% [2,3] and have identified factors of a poor prognosis to include: multiple organ failure, low PaO<sub>2</sub>/FiO<sub>2</sub> ratio, low serum albumin, and delay of initiation of ATT [3–5]. In our study, 7/8 patients had multiple organ failure, 5/8 had undernutrition, and the delay between onset of symptoms and ATT was a median 46 (IQR 15–124) days. These factors associated with a high incidence of nosocomial pneumonia probably explain the high mortality found in our study.

Nosocomial pneumonia was present in 6/8 patients and *P. aeruginosa* was the most commonly identified pathogen. In other studies of TB and ARDS, there has been no information about nosocomial pneumonia under mechanical ventilation. There is probably a particular interest in preventing mechanical acquired pneumonia in ARDS TB patients [1].

We acknowledge limitations to our study; it was limited to a single university hospital with a relatively small sample size and was retrospective in design. This may have led to various biases.

In conclusion, pulmonary TB can lead to ARDS, a rare but specific condition, and is associated with high ICU mortality. A septic haemodynamic profile requiring vasopressors can be present without co-infections. Factors of a poor prognosis found in our study were multiple organ failure, low PaO<sub>2</sub>/FiO<sub>2</sub> ratio, low serum albumin, and a delay in initiation of ATT. Nosocomial mechanical acquired pneumonia was not rare and in our view needs to be the target of prevention strategies and needs to be treated promptly.

**Declaration of interest:** The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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