

# The adult respiratory distress syndrome and bronchogenic pulmonary tuberculosis

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**ABSTRACT** In three cases of pulmonary tuberculosis associated with the adult respiratory distress syndrome the clinical features, which were similar to those of patients with miliary tuberculosis and adult respiratory distress syndrome, included a history of cough, fever, and dyspnoea on effort, and the physical signs of fever, tachypnoea, pulmonary adventitious sounds, tachycardia, and hepatomegaly. In these cases the radiological features, though suggestive of diffuse pulmonary oedema, were more prominent on the side in which the cavitary lesion appeared. The diagnosis of tuberculosis was made easily from direct examination of sputum. Despite early ventilatory support and antituberculous therapy, two of the three patients died. Postmortem examination of the lungs in these cases showed evidence of acute alveolar damage (loss of type 1 pneumocytes and the presence of hyaline membranes within alveolar ducts) and of chronic alveolar damage (interstitial and alveolar fibrosis).

Several cases of the unusual association of miliary tuberculosis and the adult respiratory distress syndrome have been described in the past decade.<sup>1-6</sup> Acute respiratory distress may occur in chronic cavitary or bronchogenic pulmonary tuberculosis,<sup>7,8</sup> but is seldom recognised as a cause of such a deterioration.<sup>9</sup> We describe three patients with cavitary pulmonary tuberculosis who developed adult respiratory distress syndrome and were treated in the Respiratory Intensive Care Unit at Groote Schuur Hospital during 1981-1982.

## Case reports

### CASE 1

A 31 year old woman, having treatment for schizophrenia as an outpatient, was admitted to hospital with a two month history of productive cough and a three day history of dyspnoea on effort, fever, and loss of appetite. She was febrile (39.9°C), pale, and cyanosed and in severe respiratory distress (respiratory rate 60/min). There was no finger clubbing. There was dullness to percussion at the right lung base; bronchial breathing was audible over the left lung and crackles were heard throughout both

lung fields. A chest radiograph showed diffuse bilateral opacification, with a left sided air bronchogram.

The pulse rate was 156 beats/min and regular and the blood pressure 120/80 mm Hg. The central venous pressure was not raised and there was no third heart sound. An electrocardiogram showed sinus tachycardia and poor progression of R wave height across the chest leads. Abdominal and neurological examination, including fundoscopy, showed nothing abnormal.

The haemoglobin concentration was 10.5 g/dl and the white blood cell count (WBC)  $11.4 \times 10^9/l$  (54% polymorphonuclear leucocytes, 30% band neutrophils, 10% lymphocytes, 3% monocytes, 1% eosinophils, 1% metamyelocytes, and 1% myelocytes). The erythrocyte sedimentation rate was 10 mm in the first hour. No acid fast bacilli were demonstrable on direct examination of a trans-tracheal aspirate.

Arterial blood gas tensions while the patient was breathing air were PaO<sub>2</sub> 5.3 kPa (39.8 mm Hg) and PaCO<sub>2</sub> 3.7 kPa (27.8 mm Hg) with a pH of 7.56. Measurements with a Swan-Ganz catheter showed a pulmonary artery pressure (PAP) of 40/24 mm Hg, with a mean value of 32 mm Hg and a pulmonary capillary wedge pressure (PCWP) of 12 mm Hg. Adult respiratory distress syndrome was diagnosed and the patient was intubated and mechanically ventilated with a volume cycled ventilator with a tidal

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volume of 1 litre and peak inspiratory pressures of 35–55 cm H<sub>2</sub>O. Penicillin and gentamicin were given intravenously.

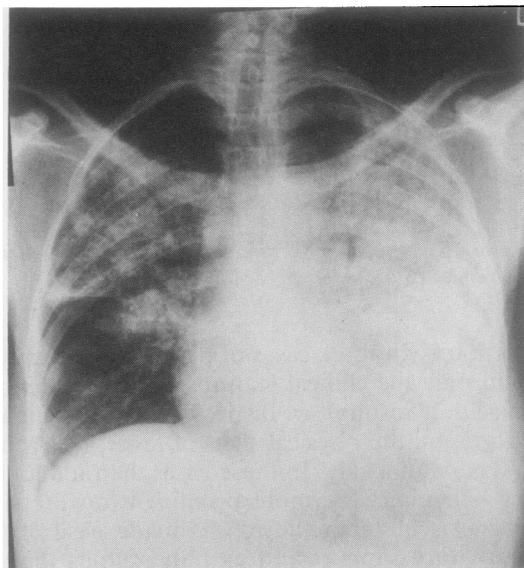
Two hours after admission she became hypotensive and required treatment with an intravenous infusion of dopamine in a dosage of 5–10 µg/kg/min for 36 hours. She required positive end expiratory pressure (PEEP) of 10 cm H<sub>2</sub>O and an inspired oxygen concentration (F<sub>IO</sub><sub>2</sub>) of 0.6 to maintain oxygenation.

Antituberculous treatment (streptomycin, isoniazid, pyrazinamide, and rifampicin) was started after acid fast bacilli had been demonstrated on direct examination of a tracheal aspirate two days after admission. Review of the initial chest radiograph, together with subsequent films, showed a cavity 4 cm in diameter in the left upper lobe (fig 1). A high, swinging fever persisted, but blood cultures, cerebrospinal fluid, and sputum were negative for pathogens. Four days after admission she developed disseminated intravascular coagulation (platelet count  $46 \times 10^9/l$ , a prothrombin index (PI) less than 10%, and a fibrinogen degradation product concentration greater than 160 µg/ml). On the ninth day after admission she developed status epilepticus, which was not controlled despite treatment with phenobarbitone, carbamazepine, phenytoin, and clonazepam in dosages sufficient to give serum concentrations in the upper limit of the therapeutic range. She remained comatose until her death 23 days later. During this period she was adequately ventilated, with representative blood gas tensions (with F<sub>IO</sub><sub>2</sub> 0.4 and 5 cm PEEP) of 12.0 kPa (90 mm Hg) for PaO<sub>2</sub> and 4.8 kPa (36 mm Hg) for PaCO<sub>2</sub>.

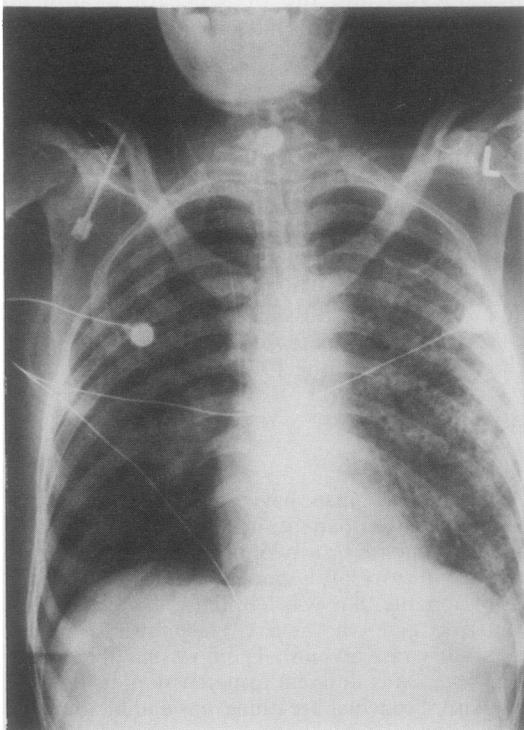
Post mortem examination of the lungs showed the appearance of left upper and right lower lobe cavitory tuberculosis, with reactive, non-caseous hilar lymph nodes and no evidence of extrapulmonary haematogenous or lymphatic spread. Histological examination showed extensive alveolar and to a lesser extent interstitial fibrosis. Hyaline membranes were recognisable within alveoli, together with desquamation of alveolar lining cells. There was a predominantly mononuclear infiltrate throughout both lungs, together with scattered tuberculous granulomas. There was no evidence of tuberculous involvement of the brain or meninges.

#### CASE 2

A 22 year old black woman, who had previously been completely well, was admitted to hospital after two weeks of increasing dyspnoea on effort and cough productive of white sputum. She was found to be well nourished but acutely ill and febrile (37.4°C). She was cyanosed and tachypnoeic (respiratory rate 35/min). The left hemithorax



(a)



(b)

Fig 1 Case 1: Chest radiograph (a) on admission and (b) four days after admission.

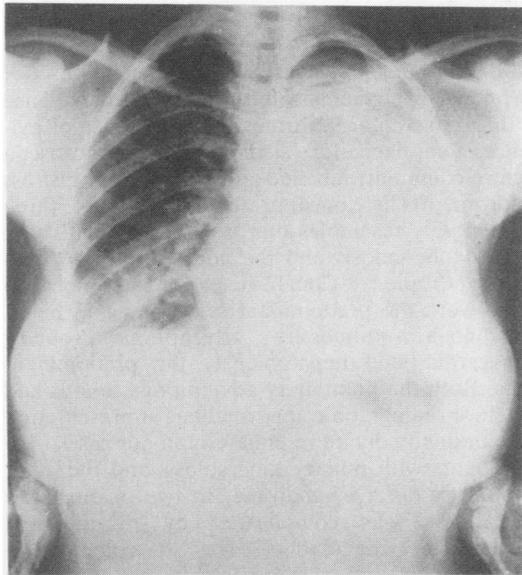


Fig 2 Case 2: Chest radiograph on admission.

moved poorly on inspiration. There was bronchial breathing throughout the left lung and diffuse crackles were heard in the right lower zone posteriorly. A chest radiograph showed diffuse bilateral opacification, more prominent on the left side (fig 2). Arterial blood gas levels while she was breathing 40% oxygen by face mask were  $\text{PaO}_2$  4.3 kPa (32.3 mm Hg) and  $\text{PaCO}_2$  6.1 kPa (46 mm Hg), with a pH of 7.25. The heart rate was 120 beats/min and blood pressure 120/60 mm Hg. No third heart sound was heard and there was no other evidence of cardiac failure. An electrocardiogram showed sinus tachycardia. The liver was palpable 7 cm below the costal margin. Neurological examination, including fundoscopy, showed nothing abnormal. The haemoglobin concentration was 9.5 g/dl and the white blood cell count  $22.4 \times 10^9/l$  (70% polymorphonuclear leucocytes, 4% metamyelocytes, and 3% myelocytes). There was haematological evidence of disseminated intravascular coagulation. The platelet count was less than  $10 \times 10^9/l$ , the prothrombin index 52%, and the fibrinogen degradation product concentration greater than 320  $\mu\text{g/ml}$ . Acid fast bacilli were found on direct examination of sputum. Despite commencement of treatment (streptomycin, isoniazid, pyrazinamide, and rifampicin), her condition deteriorated and she required intubation and mechanical ventilation 48 hours later.

A chest radiograph showed bilateral diffuse opacification and adult respiratory distress syndrome was diagnosed. A Swan-Ganz catheter

showed a PAP of 50/35 mm Hg with a PCWP of 14 mm Hg. Adequate oxygenation required an  $\text{FIO}_2$  of 0.5 and PEEP of 20 cm  $\text{H}_2\text{O}$ , with a tidal volume of 800 ml and peak inspiratory pressures of 50–55 cm  $\text{H}_2\text{O}$ . Six days after admission *Acinetobacter* sp was cultured from a tracheal aspirate, and treatment with co-trimoxazole was started. The clinical course was complicated by a left pneumothorax on the 16th day of ventilation, which precipitated a cardiac arrest. Resuscitation was successful but she remained hypercapnic and hypoxic with an  $\text{FIO}_2$  of 0.9. High frequency ventilation was instituted as an adjunct to intermittent positive pressure ventilation, which improved ventilation, allowing the  $\text{FIO}_2$  to be reduced to 0.6 over the following two days. Seven days after the start of high frequency ventilation, pulmonary function again deteriorated and she died of respiratory failure.

Post mortem examination of the lungs showed the appearances of tuberculous bronchopneumonia of the right upper lobe and the entire left lung, as well as a tuberculous bronchopleural fistula in the left lower lobe, with an empyema. The hilar lymph nodes were caseous and the right atrium and right ventricle were dilated. There was histological evidence of acute alveolar damage, with loss of type 1 pneumocytes, an increase of type 2 pneumocytes, and the presence of hyaline membranes in alveolar ducts. There was an increase in fibrous tissue in the alveolar walls and in the pulmonary interstitium generally.

### CASE 3

A 45 year old black man, who was known to smoke heavily and drink alcohol to excess, was admitted to hospital after one month of weight loss, nausea, vomiting, fever, and cough productive of white sputum. He had coughed up small amounts of blood on the day before admission. He had become increasingly short of breath over three days and on admission he was dyspnoeic at rest. There was no history of tuberculosis or cardiac disease, and effort tolerance had been normal.

A chest radiograph showed extensive bilateral opacification, with a left apical cavity and a small right sided pleural effusion (fig 3). Direct examination of the sputum showed acid fast bacilli and anti-tuberculous treatment was started with streptomycin, isoniazid, rifampicin, and pyrazinamide. He rapidly deteriorated during the following 24 hours becoming acutely ill, pale, and febrile (38°C). He was cyanosed and tachypnoeic (respiratory rate 40/min). There was dullness to percussion at the left lung base, and considerable inspiratory and expiratory crackles were audible, particularly in the left mid and lower zones and in the right lower zone.

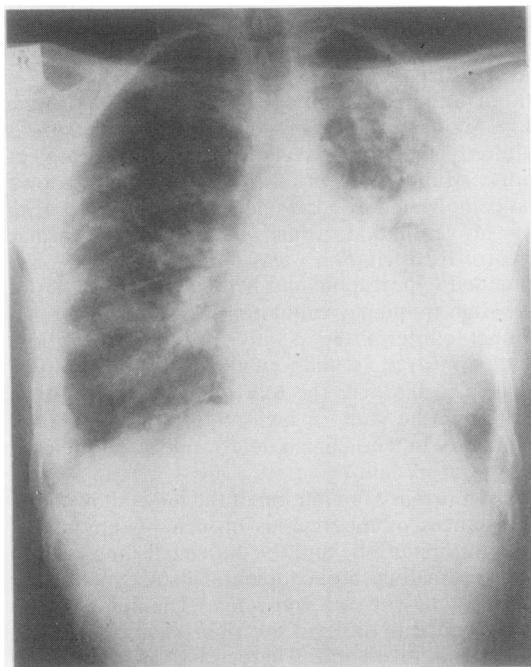


Fig 3 Case 3: Chest radiograph on admission.

Arterial blood gas tensions while the patient was breathing 40% oxygen by face mask were 6.7 kPa (50 mm Hg) for PaO<sub>2</sub> and 4.4 kPa (33 mm Hg) for PaCO<sub>2</sub>, with a pH of 7.47. The heart rate was 130 beats/min and regular and the blood pressure was 140/80 mm Hg. There was no evidence of cardiac failure. An electrocardiogram showed a sinus tachycardia and non-specific T wave flattening in the inferolateral leads. The liver was palpable 4 cm below the costal margin. Neurological examination showed nothing abnormal.

A clinical and radiological diagnosis of adult respiratory distress syndrome secondary to bronchogenic tuberculosis was made, and continuous positive airway pressure given by face mask with a PEEP of 5 cm H<sub>2</sub>O and an FIO<sub>2</sub> of 0.5. Hydrocortisone was given intravenously in a dosage of 200 mg six hourly. After eight hours arterial blood gas tensions improved, the PaO<sub>2</sub> rising to 15.7 kPa (118 mm Hg) and the PaCO<sub>2</sub> to 6.1 kPa (46 mm Hg), so that the FIO<sub>2</sub> could be reduced to 0.4. After 48 hours he was given oxygen via nasal prongs with a flow of 4 l per minute, and when he left the intensive care unit a day later arterial blood gas tensions were unchanged. Although he was not yet ambulant, his respiratory rate had decreased to 20/min. He was discharged to a local tuberculosis hospital, where he made a good recovery.

## Discussion

All three patients presented with the acute onset of dyspnoea, hypoxaemia, and radiographic evidence of diffuse alveolar infiltrates in the absence of evidence of cardiac failure as the precipitating cause, a picture commonly labelled adult respiratory distress syndrome.<sup>10</sup> The clinical presentation of these three cases closely resembles that found in patients with miliary tuberculosis and the adult respiratory distress syndrome.<sup>1-4</sup> Cough, fever, and dyspnoea on effort were the predominant symptoms and fever, tachypnoea, pulmonary adventitious sounds, tachycardia, and hepatomegaly the predominant signs. Both the pulmonary adventitious sounds and the chest radiographic abnormalities at presentation were undoubtedly more unilateral in our cases than in patients with miliary tuberculosis and the adult respiratory distress syndrome. In two of our cases the illness was complicated by disseminated intravascular coagulation. This is common in patients with miliary tuberculosis and the adult respiratory distress syndrome.<sup>1-6</sup> If the adult respiratory distress syndrome is recognised, any respiratory deterioration should be treated by early administration of PEEP with the dual aim of preventing a reduction in functional residual capacity and improving oxygenation, thereby allowing support with a lower inspired oxygen concentration and reduction in mortality.<sup>11</sup>

There is strong laboratory evidence that administration of corticosteroids protects cells from damage due to sepsis. For example, in vitro data suggest that glucocorticoids might inhibit complement induced granulocyte aggregation, thought to be implicated in pulmonary endothelial injury in adult respiratory distress syndrome.<sup>12</sup> Clinical studies also indicate the value of steroid treatment in adult respiratory distress syndrome due to sepsis. In nine out of 10 patients with the syndrome, four of whom had sepsis as a cause, administration of methylprednisolone was associated with a favourable outcome.<sup>13</sup> Furthermore, in a two part study of 500 patients with septic shock glucocorticoids were shown both retrospectively and prospectively to reduce mortality significantly.<sup>14</sup>

The role of corticosteroids in ensuring a favourable outcome in tuberculosis, either bronchogenic or miliary, is controversial. There is evidence that treatment with corticosteroids appears to be effective in reducing systemic toxicity and the intensity of the pulmonary inflammatory response, as well as hastening radiographic resolution in cases of pulmonary tuberculosis.<sup>15-17</sup> The danger of infections in patients immunocompromised by steroid treatment, however, as well as the complications of gastrointes-

tinal haemorrhage, may outweigh the benefits of corticosteroids in tuberculosis.<sup>18 19</sup> In case 3 we considered administration of steroids reasonable. Possibly steroids are beneficial in adult respiratory distress syndrome due to tuberculosis, as they are in cases of the syndrome due to other types of bacterial sepsis.

The diagnosis of tuberculosis was easily made from direct examination of sputum in two cases and of tracheal aspirate in the other. Necropsy in two cases confirmed the presence of pulmonary tuberculosis but yielded no macroscopic or histological evidence of dissemination. In these cases there was good evidence of adult respiratory distress syndrome, with the demonstration of both acute alveolar damage (loss of type 1 pneumocytes and the presence of hyaline membranes within alveolar ducts) and chronic alveolar damage (interstitial and alveolar fibrosis).<sup>20</sup> In case 2 a high inspired oxygen concentration and superadded acinetobacter pneumonia may have contributed to the progressive severity of adult respiratory distress syndrome and the histological appearance at necropsy, and in cases 1 and 2 disseminated intravascular coagulation may have played a part. The clinical and radiological sequence of events, however, supports pulmonary tuberculosis with bronchogenic spread as the main cause of adult respiratory distress syndrome in both cases.

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