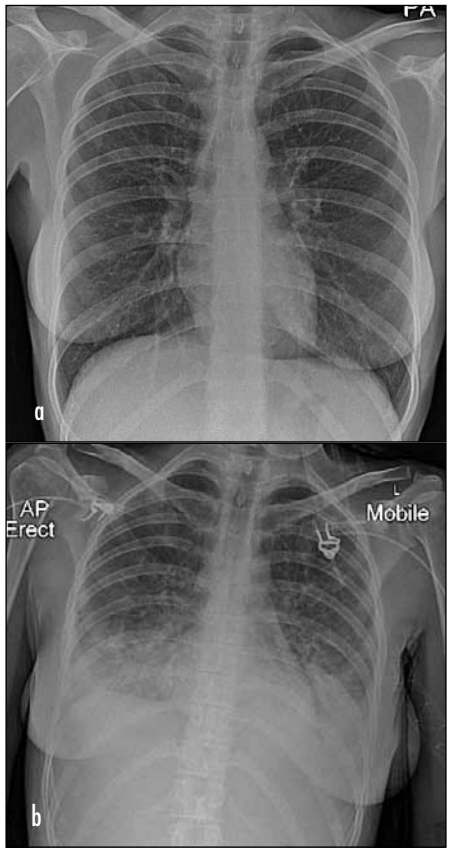
'This medical student just gets sicker'

Introduction

This case report highlights the cryptic onset and complications, such as pancytopenia, non-cardiac pulmonary oedema and hepatitis, of miliary tuberculosis infection. In addition it draws attention to liver biopsy as the investigation with greatest diagnostic yield.

Figure 1. a. Normal chest radiograph. b. Chest radiograph showing bilateral mid-zone infiltrates and pleural effusions.



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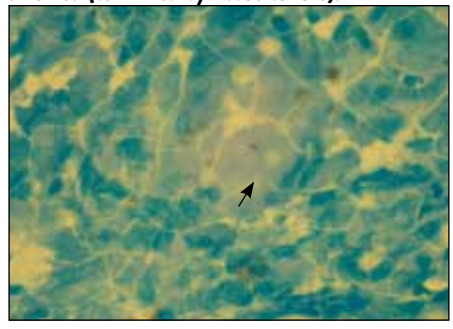
Discussion

This case illustrates the presentation of miliary tuberculosis, which is frequently insidious and should be considered in patients presenting with fever and pancytopenia despite normal chest radiology and negative sputum smears. The liver is almost always involved, with caseating granulomata seen in 90–100% of cases. For this reason liver biopsy gives the greatest diagnostic yield. It is unusual to see acid-fast bacilli in bone marrow and liver biopsies and they were not seen in any such specimens in one series by Maartens et al (1990).

Dyer et al (1985) have demonstrated that *Mycobacterium tuberculosis* release lipoarabinomannan that stimulates tumour necrosis factor release from monocytes and macrophages. This cytokine release results in vascular leak, which can cause adult respiratory distress syndrome, as suggested by Moreno et al

Figure 2. Ziehl–Neelsen stain of liver biopsy (x600) with* Mycobacterium tuberculosis *complex arrowed (confirmed by tissue culture).



Case Report

A 26-year old female medical student presented to hospital with a 2-week history of abdominal pain, fevers and vomiting. There was no history of smoking, alcohol, foreign travel or animal contact. Examination revealed hepatomegaly and temperature of 38°C. Initial blood results were haemoglobin 9.1 g/dl, white cell count 2.7×10^9/litre, platelets 130×10^9/litre, alanine aminotransferase 199 IU/litre, aspartate aminotransferase 62 IU/litre, alkaline phosphatase 247 IU/litre, international normalized ratio 1.4, sodium 133 mmol/litre. Admission chest radiograph was normal (*Figure 1a*). Hepatitis screen showed prior infection with hepatitis A and cytomegalovirus. Human immunodeficiency virus and autoimmune profile serology were negative. On day 4 the patient developed a dry cough and hypoxia. Chest radiograph revealed basal pulmonary infiltrates (*Figure 1b*). The patient was treated for 'atypical' pneumonia with co-amoxiclav, clarithromycin and continuous positive airway pressure on the intensive care unit. Over the next 48 hours she deteriorated, requiring intubation and ventilation; teicoplanin was added. Computed tomography scanning showed patchy pulmonary air space shadowing, pleural effusions, ascites and normal pelvic images. Pleural fluid aspiration and drainage revealed transudate effusions and a bronchoscopy and bronchoalveolar lavage was performed. Exhaustive microbiology investigations of blood (including multiple serological studies for bacteria and viruses), CSF (<1 white blood cell, glucose 3.8 mmol/litre, protein 460 mg/litre), urine, stool, sputum, nasopharyngeal aspirate, pleural and bronchoalveolar lavage fluid failed to identify an infectious cause for the patient's illness. She was extubated after 36 hours with complete resolution of chest radiological infiltrates. Lack of clinical improvement, persisting pyrexia, deteriorating pancytopenia and liver function tests prompted further investigation with liver and bone marrow biopsies.

Ziehl–Neelsen staining of a liver biopsy (*Figure 2*) and bone marrow demonstrated the presence of granulomatous inflammation and acid-fast bacilli. Acid-fast bacilli were abundantly seen in under 5 minutes of starting histological inspection of tissue sections. *Mycobacterium tuberculosis* was confirmed by tissue culture, and found to be sensitive to rifampicin by the reference laboratory using rapid reverse hybridization. A good clinical response was seen with non-hepatotoxic anti-tuberculous therapy, including amikacin, ofloxacin and ethambutol, since standard therapy resulted in marked hepatitis. First-line anti-tuberculous drugs were then gradually introduced. The patient made a full recovery with resolution of liver function tests and blood counts.

(1989) and Ahuja et al (1992), and is the likely cause of the non-cardiogenic pulmonary oedema and ascites that was seen in this case. Pancytopenia is another recognized complication and a case series by Maartens et al (1990) reported its occurrence in 5% of patients with miliary tuberculosis. A direct effect of granulomatous inflammation and tumour necrosis factor-inhibited haematopoiesis give rise to this haematological picture, however, haematological malignancy, as a cause of both pancytopenia and miliary tuberculosis, should be excluded. **BJHM**

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