CASE REPORT

Adult respiratory distress syndrome as a severe immune reconstitution disease following the commencement of highly active antiretroviral therapy

N R Goldsack, S Allen, M C I Lipman

We report a patient who developed adult respiratory distress syndrome (ARDS) secondary to Mycobacterium tuberculosis as an immune reconstitution disease. This complication occurred 14 days after the commencement of highly active antiretroviral therapy (HAART) for advanced HIV infection. The case emphasises that immune reconstitution can be an extremely aggressive complication of HAART.

Immune reconstitution disease is a well recognised complication of highly active antiretroviral therapy (HAART). It is believed to occur as a consequence of treatment related increases in blood CD4 T cells, with subsequent inflammation in tissues affected by ongoing opportunistic infection.1 We report a patient who developed adult respiratory distress syndrome (ARDS) shortly after the commencement of HAART as a manifestation of severe immune reconstitution disease secondary to pulmonary tuberculosis.

CASE HISTORY

A 41 year old black Kenyan male with known HIV infection presented to our emergency clinic with breathlessness 2 weeks after the commencement of HAART. He had previously tested HIV positive in 1991, following an episode of oral candidiasis. Since that time he had remained well with no other opportunistic infections, and his CD4 count had been consistently above 450 cells × 10^6/l while his viral load was less than 36 000 copies/ml. However, after an absence of 1 year, in April 2000, he returned to the HIV clinic for further management. Routine investigation at that time revealed a normal chest radiograph (fig 1) but his CD4 count had dropped to 121 cells × 10^6/l (12%) with an elevated viral load of 413 000 copies/ml. Clinical examination at this time was normal.

In view of his low CD4 count he started HAART using two nucleoside reverse transcriptase inhibitors (AZT 300 mg twice daily and 3TC 150 mg twice daily) with a non-nucleoside reverse transcriptase inhibitor (efavirenz 600 mg at night). In addition, he was given co-trimoxazole (960 mg once daily) as prophylaxis against Pneumocystis carinii pneumonia (PCP). He tolerated this regimen extremely well and reported greater than 95% adherence.

Fourteen days later he returned to the clinic with a 2 day history of fevers and night sweats, and a 24 hour history of worsening shortness of breath. His CD4 count had increased to 298 cells × 10^6/l (19%) and his viral load had successfully fallen to 23 000 copies/ml. It was noted that he desaturated on exercise breathing air from 96% to 89%. A chest radiograph taken at this time revealed gross abnormality with evidence of widespread miliary shadowing (fig 2). A provisional diagnosis of community acquired pneumonia or PCP was made, and he was treated with intravenous antibiotics (benzylpenicillin 1.2 g 4 hourly and clarithromycin 500 mg four times daily) and high dose intravenous co-trimoxazole (120 mg/kg per day).

Over the next 12 hours he developed worsening respiratory failure. An arterial blood gas on air indicated a pH 7.38, PaO_2 4.2 kPa, PaCO_2 4.9 kPa. He was, therefore, transferred to the intensive care unit for mechanical ventilation, and intravenous corticosteroids (hydrocortisone 100 mg four times daily) were added into his treatment regimen. A Swan Ganz catheter was inserted, and a pulmonary wedge pressure of 14 mm Hg was noted. Over the next 4 days he continued to be ventilated and required increasing amounts of positive pressure support. During this period his chest radiograph revealed increased alveolar shadowing in keeping with his clinical deterioration (fig 3).

He underwent a fibroptic bronchoscopy with bronchoalveolar lavage. This yielded no evidence for PCP; however, acid fast bacilli were seen on the direct smear. His therapy was

Figure 1 Normal chest x ray before commencing HAART.

Figure 2. Chest x ray 2 weeks after commencing HAART. This chest x ray demonstrates the presence of widespread miliary shadowing.
In this case, subclinical tuberculosis was probably present in the patient’s lungs, and HAART resulted in a severe inflammatory response with resultant respiratory failure and ARDS.

Immune restoration disease has also been reported with other infectious agents including tuberculous lymphadenitis secondary to *Mycobacterium-avium-intracellulare* (MAI), in cytomegalovirus (CMV) pulmonary and non-pulmonary infections, hepatitis B and C viruses, and *Cryptococcus neoformans* infections. In these cases immune reconstitution produced localised inflammation and the appearance of systemic disease in patients who had beneficial immunological and virological responses to HAART. These diseases usually occur in patients with lower baseline CD4 T cell counts and higher plasma HIV RNA levels than those who don’t develop disease.

There have been a number of previous reports of worsening of tuberculosis following the initiation of HAART. In one case a patient developed miliary tuberculosis with paradoxical expansion of an intracranial tuberculoma. In another, cerebral tuberculosis was the manifestation of this condition. However, this is the first case of ARDS secondary to tuberculosis occurring as a consequence of this phenomenon. Chest radiographic changes are also well documented in patients after HAART, although they are rarely as dramatic as described in this patient. In summary, immune restoration illness needs to be considered in patients with the new onset of symptoms following the commencement of antiretroviral therapy. Although it is often associated with a typical history and rapid preceding blood CD4 T cell increases, it must remain a putative diagnosis until opportunistic disease has been excluded.

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**REFERENCES**

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