Acute respiratory failure due to miliary tuberculosis in a patient with idiopathic CD4+ T-lymphocytopenia

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Introduction

In 1992, the Centers for Disease Control and Prevention (CDC) defined idiopathic CD4+ T-lymphocytopenia (ICL) as a reproducible CD4+ lymphocytopenia (<300 mm^-3) in the absence of human immunodeficiency virus (HIV) infection or other known cause of immunodeficiency (1). Ten of the 47 patients with ICL reported by Smith and coworkers developed opportunistic pulmonary infections (2), and only three cases of pulmonary tuberculosis were found. On the other hand, CD4+ T-lymphocyte level is occasionally reported to be reduced in various infectious diseases including pulmonary tuberculosis (3,4).

Case Report

A 49-year-old man was admitted to a local hospital in March 1993 because of fever and increasing dyspnoea. He had been well until 1 month prior to admission. He had no risk factors and had never taken immunosuppressive therapy. A chest roentgenogram on admission showed reticulonodular shadows (2-5 mm) distributed throughout both lungs with a pleural effusion in the left chest (Plate 1).

Arterial blood gas analysis on room air showed severe hypoxaemia with a respiratory alkalosis (PaO_2=4.64 kPa, PaCO_2=3.31 kPa, and pH=7.50). Although antibiotics were administered, his hypoxaemia progressively worsened and he developed acute respiratory failure. Three days later, he was transferred to our hospital. On physical examination the patient appeared acutely ill, and dyspnoeic. There was severe lip and peripheral cyanosis. Inspiratory crackles were heard over both lungs. He required mechanical ventilation due to severe hypoxaemia.

Laboratory studies revealed a white blood cell count of 12,200 mm^-3 (lymphocytes; 3%). The CD4+ cell count was 51 mm^-3 and the CD8+ cell count 181 mm^-3 (a CD4:CD8 ratio of 0.28) (Fig. 1). Serum immunoglobulin levels were normal except for a slightly low IgM level. A sputum smear was positive for acid-fast bacilli and subsequently grew colonies of Mycobacterium tuberculosis on culture. A skin test with purified protein derivative was negative. Serological tests for HIV-1 and HIV-2 antibodies were negative as determined by both ELISA and...
Western blot. Antibody to human T-cell lymphotrophic virus Type 1 was also not detected. He was diagnosed as having miliary tuberculosis and idiopathic CD4+ T-lymphocytopaenia. He was begun on antituberculous chemotherapy: isoniazid, rifampicin, ethambutol and streptomycin sulfate, plus oral kanamycin.

The M. tuberculosis organisms isolated were sensitive to these antituberculous drugs. He had a good response to this regimen and his hypoxaemia gradually improved. On chest roentgenogram reticulonodular shadows gradually cleared. However, the CD4+ cell count and CD4:CD8 ratio remained low (Fig. 1). He was discharged from hospital in December 1993. In August of 1994, the CD4+ cell count was 247 mm\(^{-3}\), the CD8+ cell count was 804 mm\(^{-3}\) and the CD4:CD8 ratio was 0.31. Repeated HIV tests were negative. His clinical status remains unchanged at time of writing.

Discussion

In pulmonary tuberculosis with acquired immune deficiency syndrome (AIDS), the roentgenographic pattern of primary tuberculosis and postprimary tuberculosis was observed in 64% of the patients and that of a miliary pattern was 3% (5). In ICL, however, the clinical picture of pulmonary tuberculosis is poorly understood. In a review by Smith and coworkers (2), pulmonary tuberculosis was found in only three patients. To our knowledge, acute respiratory failure due to miliary tuberculosis in ICL has not been previously reported. This patient had no prior history of pulmonary tuberculosis. However, on a chest roentgenogram taken several years prior to admission, several calcified nodules and pleural thickening of the right apex were observed, suggesting that he may have had primary pulmonary tuberculosis. It is likely that suppression of cell-mediated immunity by ICL may reactivate a site of old tuberculosis, resulting in miliary tuberculosis. The patient likely acquired pulmonary tuberculosis, because in Japan the morbidity of pulmonary tuberculosis is still high, three or more times that in the U.S.A. or the U.K. (6).

It has been reported that pulmonary tuberculosis is occasionally linked to deletion of CD4+ T-lymphocytes, usually within the low normal range (4). In our patient, the CD4+ cell count on admission was extremely low, comparable to the values in ICL patients reported by Smith and coworkers (2). Effective antituberculous treatment is reported to normalize tuberculous CD4+ T-lymphocytopaenia (7). After 6 months of antituberculous treatment, our patient clinically and radiographically improved, but the CD4+ cell count remained below 300 mm\(^{-3}\) (Fig. 1). However, total lymphocyte and CD8+ cell counts were initially decreased, and returned to the normal range within 1 month. CD8+ T-lymphocytopaenia (<250 cells mm\(^{-3}\)) is observed in some patients with ICL (2,8). In pulmonary tuberculosis without HIV infection, CD8+ cell counts can be decreased similar to CD4+ cells, preserving a normal CD4:CD8 ratio (3,7). With antituberculous treatment, both CD4+ and CD8+ cell counts usually normalize (7). In our patient, CD8+ cell counts were low on admission, and with antituberculous treatment, CD8+ cell counts recovered, while CD4+ cell counts remained low, preserving the low CD4:CD8 ratio.

CD4+ T-lymphocyte depletion in the absence of HIV infection is known to occur in certain bacterial, viral and fungal infections, lymphoproliferative disorders and autoimmune disorders (3,7,9). Our patient had no evidence of any of these conditions, and had never received any immunosuppressive drug. We cannot find any cause for
this patient's CD4⁺ T-lymphocyte depletion, including HIV infection. Thus, our patient with idiopathic CD4⁺ T-lymphocytopenia had suffered from miliary tuberculosis with acute respiratory failure.

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References


Diagnosis of pulmonary veno-occlusive disease: new criteria for biopsy


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Introduction

Pulmonary veno-occlusive disease (PVOD) is a rare condition in which the predominant anomaly is the stenosis or occlusion of the lumen of small pulmonary veins due to fibrosis of the intima (1). Its aetiology is unknown, although it is sometimes associated with viral infection, environmental toxins, chemotherapy, autoimmune disease, use of contraceptives, intracardiac shunts or radiation injury, and some cases suggest genetic predisposition (2). In spite of a variety of therapies having been tried, it is usually fatal within a few years; lung transplant is currently the treatment of choice. Its definitive diagnosis requires demonstration of the above-mentioned anatomopathological features in pulmonary biopsy material, although pulmonary biopsy is not always possible. The diagnostic difficulties associated with three cases of PVOD seen in our centre in recent years have led us to examine what clinical criteria constitute sufficient grounds for carrying out pulmonary biopsy to confirm PVOD.

Case Reports

For all three patients, cardiac and pulmonary circulation parameters measured by cardiac catheterization are listed in Table 1, and pulmonary function parameters in Table 2.