CASE REPORT

MASSIVE PULMONARY CRYPTOCOCCOSIS IN AN IMMUNOCOMPETENT PATIENT

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Abstract. A 64-year-old man presented with progressive dyspnea. The symptom of severe hypoxia requiring mechanical ventilator, and bilateral pulmonary infiltrates on the chest film led to the clinical diagnosis of adult respiratory distress syndrome. Autopsy demonstrated widespread cryptococci and mucinous material in alveoli with mild inflammatory response.

Pulmonary cryptococcosis is a disease with variable clinical presentation and pathologic features (Feigin, 1983; Emmon *et al*, 1995). It usually occurs as a part of disseminated disease in immonosuppressed patients (Kerkering *et al*, 1981). Isolated pulmonary involvement, however, is not uncommon (Lewis and Rabinovich, 1972) and the clinical course may lead to either spontaneous resolution (Hammerman *et al*, 1973; Kerkering *et al*, 1981) or progressive fatality (Tenholder *et al*, 1992). Herein, we report a case of massive isolated pulmonary cryptococcosis of which clinical manifestations were similar to adult respiratory distress syndrome (ARDS) in an apparent immunocompetent host.

A 64-year-old man was hospitalized because of fever, cough, and progressive dyspnea for 7 days. Past history revealed chronic hepatitis B and infective endocarditis of mitral and aortic valves. After treating the latter condition with cloxacillin for 32 days, he had been doing well.

On admission, he was febrile and tachypneic with signs of congestive heart failure. A pansystolic murmur was heart in the mitral valve area. A chest x-ray showed cardiomegaly with bilateral infiltration. An ECG revealed atrial fibrillation with rapid ventricular response. Initial laboratory results were as follows: 12.2 g% of Hb, 22,200 WBCs/mm^3 with 93% granulocytes, 183,000 thrombocytes/mm^3, 113 mg% plasma glucose, 42 mg% BUN, and 1.7 mg% creatinine. Echocardiogram showed moderate mitral regurgitation without vegetation. The presumptive diagnoses were pneumonia and congestive heart failure; therefore penicillin G sodium (PGS) 6 million units per day, plus diuretic and inotropic drugs were given.

One day after admission, his dyspnea increased. Moreover, hypoxemia and hypotension developed. Mechanical ventilation thus was started with FiO_2 of 1 and positive end expiratory pressure (PEEP) of 10 cm H_2O in order to maintain oxygenation (PaO_2 65.6 mmHg and 93.5% O_2 saturation). The pulmonary capillary wedge pressure (PCWP) was 8 mmHg. Follow-up chest film exhibited bilateral increasing alveolar infiltrates (Fig 1) leading to the diagnosis of ARDS. Blood culture was sterile. Organisms were not identified in sputum by Gram, acid-fast bacilli (AFB) and modified AFB stains. Anti-HIV

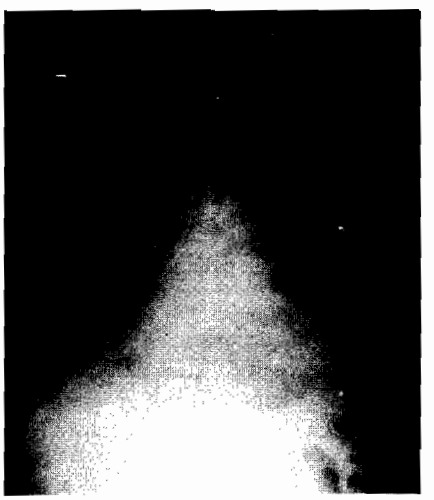

Fig 1–Chest X-ray on the forth day of hospitalization shows bilateral alveolar infiltrations.

was negative. Multiple changes of antibiotics were made in order to treat suspected infective endocarditis (PGS 18 mUs/day plus gentamicin 180 mg/day) and later Gram negative sepsis (ceftacidime 3 g/day). Nevertheless, the patient progressively deteriorated and died 7 days after admission.

At autopsy, the main pathology was in the 4,100g lungs which sank in water and showed total consolidation, with a gray gelatinous cut surface (Fig 2A). Microscopically, widespread prolifera-tion of encalsulated cryptococci was noted in almost all alveoli. Mayer's mucicarmine stain highlighted the fungal capsules as well as mucinous material in the alveoli (Fig 2B). Budding yeast cells were apparent (Fig 2C). The relatively preserved pulmonary parenchyma showed minimal inflammatory reaction. Hyaline membrane, however, was not detected. The organisms were not identified in other organs.

Cryptococcosis was a relatively rare disease before the advent of AIDS (Diamon *et al*, 1995). Typically, it occurs in such conditions as impaired T-cell mediated immunity (*eg* organ transplant recipients), lymphoreticular malignancy, administration of high dose corticosteroid and immunosuppressive drugs (Kerkering *et al*, 1981). Currently, AIDS is the major risk factor for cryptococcosis accounting for more than 80% of cases (Diamon *et al*, 1995). The disease, however, does occur in patients without apparent immunosuppression (Hammerman *et al*, 1973; Kerkering *et al*, 1981; Campbell, 1996).

The clinical presentation, radiographic features, and natural history are highly variable and seem to be influenced chiefly by the host immune status (Campbell, 1966; Hammerman *et al*, 1973; Kerkering *et al*, 1981; Khoury *et al*, 1984). Patients with defects in cell-mediated immunity usually have severe disseminated disease requiring systemic antifungal therapy. On the other hand, isolated pulmonary infection with self-limited disease occurs in immunocompetent hosts.

Our patient was a unique example of massive pulmonary cryptococcosis in an immunocompetent host. The radiographic feature of bilateral alveolar infiltrations, clinical course of severe hypoxemia requiring mechanical ventilation with PEEP, and low PCWP led to the erroneous diagnosis of ARDS. Without appropriate antifungal treatment due to nonrecognition of the condition, the patient deteriorated and died within 2 weeks after the onset.

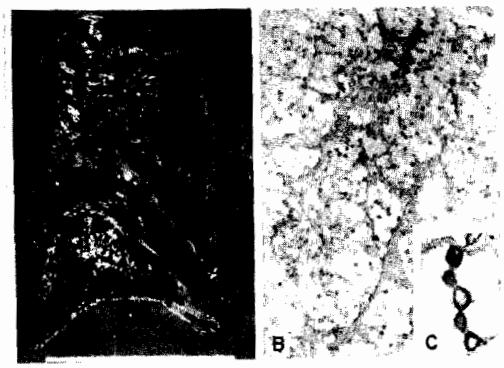

Fig 2–Pathologic features of pulmonary cryptococcosis
(A) The lung reveals total consolidation and gray mucoid cut surface.
(B) Abundant cryptococci and mucinous material distend the alveoli. (Mayer's mucicamine stain x 40)
(C) Encapsulated budding yeasts of cryptococci are connected together by strand of mucin into chain. (Mayer's mucicamine stain x 400)

The pathology of the lungs was interesting. Both lungs weighed about 12 times normal weight. Microscopic detection of numerous cryptococci and abundant mucinous material in almost all alveoli explains the feature of diffuse alveolar infiltrates on the chest x-ray and the clinical respiratory symptoms. Hyaline membrane, a characteristic morphology of ARDS, however, was not encountered. Moreover, the inflammatory reaction in the lungs was quite strange. Generally, the cellular response in pulmonary cryptococcosis is related to the host immune status (Sobonya, 1995). In immunologically intact individuals like our patient, the reaction should be distinctive but we observed only a few cellular infiltrates.

In conclusion, this is an unusual case of pulmonary cryptococcosis in an apparent immunocompetent host. The presentation was severe and progressively fatal within a short period. The postmortem findings revealed widespread pulmonary involvement with minimal inflammation and no dissemination beyond the lungs.

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