Fatal Disseminated Cryptococcosis Resembling Miliary Tuberculosis in a Patient with HIV Infection

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Abstract

A 51-year-old man was transferred to our hospital due to acute respiratory failure that had progressed over four days. A chest X-ray and thoracic computed tomography scan showed multiple faint micronodules randomly distributed throughout both lungs with ground glass opacity, suggesting miliary tuberculosis or Pneumocystis jirovecii pneumonia with acute respiratory distress syndrome. Six hours after admission, the patient died of septic shock. Later, the cryptococcal antigen titer was found to be markedly elevated (1/65,536), with a positive result for anti-human immunodeficiency virus and a low CD4 cell count (12/μL). The present case is reminder that disseminated cryptococcosis with HIV infection can be misdiagnosed as miliary tuberculosis based on radiological findings.

Key words: HIV infection, miliary cryptococcosis, micronodule

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Introduction

The detection of a miliary pattern based on radiological findings is associated with a wide range of differential diagnoses; however, only five cases of pulmonary cryptococcosis in patients with a miliary pattern on either thoracic computed tomography (1, 2) or chest X-ray (3-5) scans have been reported to date. We herein report a case of fatal pulmonary cryptococcosis resembling miliary tuberculosis in a patient with HIV infection.

Case Report

A 51-year-old man was transferred to our department due to progressive acute respiratory failure worsening over four days. He had been treated for mental retardation and depression for 10 years. He had experienced a dry cough for the last five months in addition to weight loss of 10 kg over a one-month period. He appeared very sick, thin and dyspneic. He was drowsy, with the following vital signs: blood pressure = 60/mmHg under vasopressor therapy, temperature =38.4°C, respiratory rate = 36 breaths/min, pulse rate = 142 beats/min and oxygen saturation = 86% on 10 L/min of oxygen via a mask, suggesting acute respiratory failure with shock. On a physical examination, late inspiratory crackles were heard in the left lower lung field posteriorly, and neck stiffness with Kernig’s sign was detected. Serum laboratory examinations showed a normal white blood cell count of 5,300/μL (myelocytes: 0.5%, bands: 4.5%, segs: 85%, lymphs: 6.5%, and monos: 3.5%) and β-D-glucan level, although hypoalbuminemia (1.6 g/dL), moderate anemia (9.7 g/dL) and mild elevation of glucose (144 mg/dL), HbA1c (6.5%), procalcitonin (5.94 ng/mL), C-reactive protein (7.4 mg/dL) and KL-6 (731 U/mL) were also noted. A chest X-ray (Fig. 1A) obtained two days earlier at a local hospital demonstrated diffuse multiple nodular infiltrates throughout the lungs, while thoracic computed tomography (CT) (Fig. 1B) showed multiple faint micronodules randomly distributed throughout both lungs, suggesting hematological spread, as observed in cases of miliary tuberculosis. A chest X-ray obtained on admission (Fig. 1C) showed rapid deterioration presenting as diffuse infiltration with multiple nodules throughout all lung fields, and thoracic CT (Fig. 1D) disclosed geographic ground glass opacity with randomly scattered faint micronodules, as well as interlobular septal

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thickening, suggesting acute respiratory distress syndrome (ARDS). Although head magnetic resonance imaging performed two days prior to admission to our hospital was normal, the patient displayed neck stiffness and Kernig’s sign, with radiological findings indicative of hematological spread. These findings were consistent with a diagnosis of septic shock and meningitis. The patient’s clinical course was indolent, although acute exacerbation was observed during the last several days. Therefore, he was tentatively diagnosed with miliary tuberculosis or Pneumocystis jirovecii pneumonia (PCP) associated with ARDS, and urgent lumbar puncture was performed, which showed a normal opening pressure of 15 cmH₂O, normal cerebrospinal fluid (CSF) findings (1 leukocyte/mm³, protein: 51 mg/dL, glucose: 41 mg/dL) and no bacteria on Gram staining.

Despite the administration of intensive treatment, including intravenous meropenem or pentamidine and prednisolone (1,000 mg/day) with vasopressor therapy, the patient died six hours after admission due to septic shock.

After the patient’s death, all samples obtained from the sputum (Fig. 2A), urine (Fig. 2B) and blood (Fig. 2C) were found to be positive for Cryptococcus neoformans on Gram staining and culture. In addition, a careful examination of the CSF using India ink staining showed positivity for Cryptococcus (Fig. 2D). Furthermore, serum anti-human immunodeficiency virus (HIV) antibodies measured using both an enzyme-linked immunosorbent assay and Western blotting were positive, with a low CD4 cell count (12/μL), while the serum cryptococcal antigen titer was markedly elevated (1/65,536). The patient was thus ultimately diagnosed with disseminated cryptococcosis with HIV infection.

Discussion

In HIV-positive patients, the differential diagnosis of a miliary pattern on chest X-ray scans includes Mycobacterium tuberculosis, PCP and histoplasmosis (3). Rigby et al. (2) reported that the major radiological findings of cryptococcal pneumonia can be divided into three groups: the presence of pulmonary nodules or masses, segmental or lobar consolidation and the presence of a small nodular or reticulonodular pattern. However, to the best of our knowledge, only five cases of pulmonary cryptococcosis with a miliary pattern on thoracic CT (1, 2) or chest X-ray (3-5)
scans have been reported to date (Table). All of the patients were HIV-positive, and the CD4 lymphocyte counts were low in the two patients whose data were available [our case: 12 cells/μL, other case: 59 cells/μL (3)]. The initial symptoms were nonspecific, including dyspnea, fever, coughing, night sweats, headaches and weight loss, occurring over several weeks to months. None of the reports involved examinations of the lung pathology, and no authors described the
correlation between the radiologic and pathological findings. On chest X-ray scans, diffuse interstitial infiltrates and bronchial wall thickening were also noted, together with the miliary pattern (3-5). Thoracic CT showed diverse findings, including ground glass opacity, interlobular septal thickening, thick-walled cavity formation and mediastinal lymphadenopathy, as well as the presence of scattered micronodules (1, 2). Importantly, all patients were HIV-positive, which may suggest that hematogenous seeding of Cryptococcus in the lungs is required in order to generate a miliary pattern, as observed in the present case.

This case highlights the radiological pattern of disseminated pulmonary cryptococcosis mimicking that of miliary tuberculosis. The detection of a miliary pattern on chest X-ray scans should raise suspicion of HIV infection.

The authors state that they have no Conflict of Interest (COI).

References