LETTER TO THE EDITOR

Disseminated Pulmonary Cryptococcosis Complicated with Cryptococcemia in an AIDS Patient

Cryptococcosis is a potentially fatal fungal disease. Its risk factors include lymphomas, sarcoidosis, liver cirrhosis, long-term corticosteroid therapy, and AIDS. The prevalence of cryptococcosis has been increasing over the past 20 years due to increases in the incidence of human immunodeficiency virus (HIV) infections and the use of immunosuppressive drugs. The most common opportunistic infection of lungs in AIDS patients is Pneumocystis jiroveci pneumonia (PJP). Here, we report a newly diagnosed AIDS patient who suffered from disseminated pulmonary cryptococcosis complicated with cryptococcemia as initial pulmonary opportunistic infections.

A 21-year-old male homosexual patient presented himself to our clinic with intermittent fever, dry cough, body weight loss, and general malaise for 1 month. On admission, his vital signs were as follows: body temperature 39.2°C, pulse rate 137 beats/minute, and respiratory rate 20 breaths/minute. The findings of physical examination showed clear consciousness and no evidence of neck stiffness, and Kernig or Brudzinski sign. However, he had rhonchus breathing sounds in the bilateral lungs and severe oropharyngeal candidiasis. Chest X-ray revealed the findings of interstitial infiltrations of bilateral lower lobes of lungs (Figure 1A). Results of laboratory tests included the following: white blood cell count 3450/mL, neutrophil 69%, lymphocyte 20%, hemoglobin 11.5 g/dL, and platelet 135,000/μL. The serum biochemical study revealed blood urea nitrogen 6 mg/dL, creatinine 1.07 mg/dL, alanine aminotransferase 16 U/L, and aspartate aminotransferase 17 U/L. The result of serology tests showed a high titer of anti-HIV antigen 1:1024 (enzyme-linked immunosorbent assay test) and confirmed HIV infection by Western blot test (positive P34/pol, P52/pol, P55/gag, and P68/pol). The CD4/CD8 ratio was 0.092, CD4 absolute count 32, and HIV viral load 2,689,776 (copy/mL).

Laboratory data also revealed a high titer of Mycoplasma pneumoniae, immunoglobulin G (lgG 1:320×) and Cryptococcus Ag (1:1024×). The patient received initially empirical antibiotic therapy with a daily intravenous administration of levofloxacin 750 mg and fluconazole 400 mg. He also received 80 mg trimethoprim/400 mg sulfamethoxazole orally twice daily for prophylaxis of PJP. His clinical condition improved transiently, but his fever flared up again 3 days later. Blood culture for Cryptococcus neoformans was reported on the following day. Brain computed tomography (CT) scan images revealed faint leptomeningeal enhancement of bilateral cerebral hemispheres (Figure 1B), suggesting congested pia vessel or meningitis. He underwent lumbar puncture examination with an open pressure of 11 cmH2O. Results of the cerebral spinal fluid study revealed the following: glucose 51 mg/dL (blood glucose 97 mg/dL), protein 39 mg/dL, white blood cell count 1/μL, mononuclear cell 100%, and negative finding for India ink stain of cerebrospinal fluid (CSF). However, the CSF cryptococcal antigen was positive (1:4×). Therefore, he was highly suspected to have septic encephalopathy due to cryptococcosis. Cryptococccemia still persisted, as revealed by a blood culture, even after a 10-day course of fluconazole treatment. Moreover, the treatment regimen was adjusted to daily intravenous administration of fluconazole 600 mg and amphotericin B 40 mg. A chest CT scan showed the findings of multiple small nodules of bilateral lung fields, being compatible with disseminated cryptococcosis (Figure 1B). The findings of blood culture were negative after complete therapy with a 25-day fluconazole and a 14-day amphotericin B regimen. The patient continued to receive oral fluconazole 400 mg/d at our clinic for 3 months, and he maintained in stable condition.

This typical patient lived in an area full of pigeons. This is an important environmental risk factor for infection. Cryptococcus is believed to enter the body through the respiratory tract, causing pulmonary disease and infection of the central nervous system. Cryptococcus neoformans is found frequently in soils contaminated with avian excreta and can easily be recovered from shaded and humid soils contaminated with pigeon excreta. The polysaccharide capsule, which is a surrounding membrane, is a major virulence factor for Cryptococcus. AIDS patients are especially susceptible to cryptococcal infection due to their immunocompromised status. Over 80% of cryptococcal infection occurs in HIV-infected patients. About 60–70% of patients with cryptococcosis infection are manifested clinically with fever and weight loss. Cryptococcosis most commonly involves the central nervous system (83.7%). Headache and vomiting are the most frequent symptoms. The second most common presentation is respiratory manifestation (50%), and a few patients have cutaneous skin lesions. In our patient, the initial presentations were high fever, weight loss, oropharyngeal candidiasis, cough, and dyspnea on exertion, which may lead the clinician to suspect PJP infection and miss the differential diagnosis of pulmonary cryptococcal infections.

A definitive diagnosis of cryptococcosis requires the demonstration of yeast cells in normally sterile tissues, e.g., blood or CSF. A positive cryptococcal antigen test can provide strong evidence for cryptococcosis. India ink stain of the CSF is a useful, rapid diagnostic technique. Cryptococcal cells in India ink have a distinctive appearance because their capsules exclude ink particles. However, the CSF India ink examination may yield negative results in patients with a low fungal burden. In cryptococcal meningitis, CSF examination usually shows evidence of chronic meningitis with mononuclear cell pleocytosis and increased protein levels. We excluded CNS as the primary infection in our patient, because C. neoformans was
isolated from the blood culture, he did not have pleocytosis, and he had negative CSF India ink stain and fungal culture. However, the chest CT scan picture revealed bilateral multiple cryptococcoma, and he had a high serum to CSF cryptococcal antigen titer ratio (1:1024/1:4). All those findings suggest that disseminated cryptococcosis in our patient was originated from the lungs with septic encephalopathy.

In summary, PJP is the most common pulmonary infection among AIDS patients. However, our patient had an unusual clinical picture of disseminated pulmonary cryptococcosis, with cryptococcemia manifested initially as a pulmonary opportunistic infection. Based on our experience of this case and the findings of the published papers, we suggest that clinicians should be aware of cryptococcal infection being the initial pulmonary infection in AIDS patients.

References


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