Progressive Pulmonary Cryptococcal Infection in a Nonimmunocompromised Host

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Abstract

This case report describes a 29-year-old, non-immunocompromised patient who presented with pulmonary and central nervous system (CNS) cryptococcosis. While the neurological infection responded to systemic antifungal therapy, the pulmonary infection progressed, necessitating an excision of the pulmonary lesion. Subsequently the patient had a fatal relapse of cryptococcal meningitis. We are reporting this interesting and informative case because of extensive pulmonary and CNS cryptococcosis in the presence of a normal immune status.

Key words: *Cryptococcal infection, pulmonary infection.*

A 29-year-old, white male patient was admitted to the Psychiatry Service at Nassau County Medical Center in New York with complaints of increasing depression, somnolence, anorexia, and weight loss. The patient was treated for "major depression and possible schizoaffective disorder." During the course of the investigation for continued weight loss and dysphagia, an asymptomatic left-sided lung mass was found on chest roentgenogram (Figure 1). Over the course of the ensuing two weeks, multiple diagnostic studies including CAT scan of the head and chest, lumbar puncture, fiberoptic bronchoscopy with biopsy led to the diagnosis of cryptococcal meningitis and cryptococcal brain and lung masses.

Because of the severity of the cryptococcal infection, laboratory evaluation for human immunodeficiency viral (HIV) infection was performed. HIV antibody test and T cell studies were normal. Therapy with amphotericin B was promptly started; by clinical and laboratory criteria, the patient's meningeal infection slowly improved, with no improvement of the pulmonary lesion. After a course of several weeks of amphotericin therapy with no clinical change in the size of the lung mass (Figure 2) and a persistent suspicion of an underlying pulmonary neoplasm, a left-sided pneumonectomy was performed, which was well tolerated by the patient. Approximately two weeks after discharge, the patient returned with headache and lethargy. Repeat CAT scan of the head revealed worsening of cryptococcal lesions. The patient continued to deteriorate in spite of amphotericin B and 5 flucytosine therapy and eventually he expired.

An autopsy revealed:

1. 5x4x3 cm mediastinal cryptococcal mass encasing the aorta;
2. extensive chronic cryptococcal meningoencephalomyelitis with intracerebral mass lesions and pituitary involvement;
3. pulmonary emboli;
4. no evidence of neoplasia.

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Discussion

Cryptococcus neoformans is a unimorphic fungus which can cause a granulomatous disease in humans known as cryptococcosis. Th organism occurs as a single budding yeast and has a thick capsule which is responsible for its characteristic visualization by India ink. The asexual yeast form of C. neoformans is of two varieties. The first is C. neoformans var

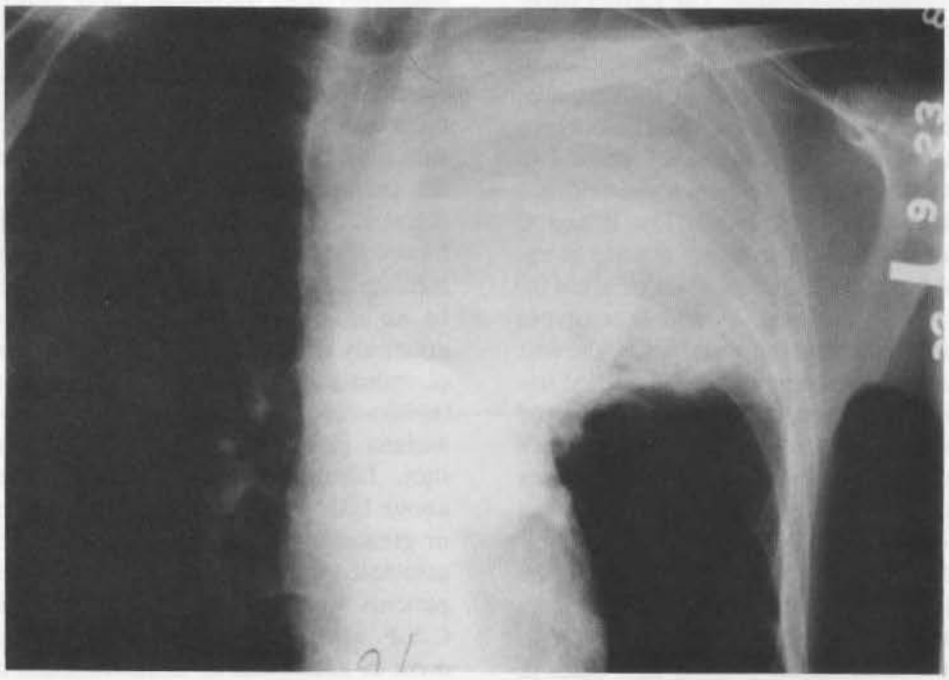

Figure 1. Chest roentgenogram reveals large homogenous mass in left upper lobe.

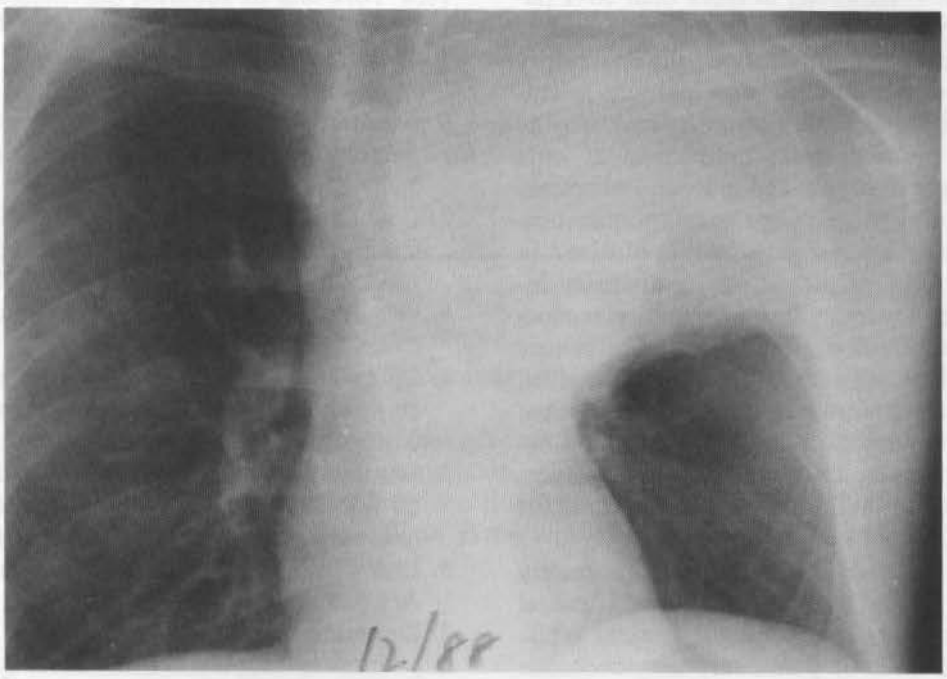

Figure 2. No discernible change observed in the left upper lobe mass after eight weeks of systemic antifungal (amphotericin) therapy.

neoformans which includes strains of serotype A or D. These strains represent the most common isolates from clinical infections worldwide. The second variety is C. neoformans var gattii which includes strains that are serotype B or C. These latter serotypes commonly cause infection in areas of Australia, Southeast Asia, Central Africa and Southern California. The clinical significance of these two varieties remains unclear, but there is some evidence to suggest a difference in virulence. The B and C serotypes appear more likely to cause disease in apparently normal hosts, and the incidence of brain invasion may be higher. Although A and D serotypes can cause disease in apparently normal hosts, the vast majority of patients have some type of identified immune suppression. It is interesting that serotypes of C. neoformans isolated from AIDS patients have been almost exclusively A and D, even when patients come from areas where serotype B and C are known to exist.[1]

Factors predisposing to infection: Because the organism is ubiquitous, it is presumed that exposure to C. neoformans is common. There must be a high natural resistance to infection because new cases in normal hosts are still rare (3000 per year in the U.S.). There is an increased incidence of infection and dissemination in patients with lymphoreticular malignancies, patients on large doses of steroids, and in patients with HIV infection (16% of patients with AIDS and pulmonary infiltrates had cryptococcosis).[2,3] However, in more than 50% patients no apparent predisposing factors are found.[4]

C. neoformans enters the body by the respiratory tracts and in two-thirds of the cases infection is confined to the lungs. Pulmonary cryptococcosis may be asymptomatic or may cause production of only scant, sometimes blood-streaked sputum. Pulmonary cryptococcosis may progress or regress spontaneously or may remain stable for long periods of time.[1] In most cases of CNS cryptococcosis, pulmonary involvement is not apparent. In pulmonary cryptococcosis, the most common roentgenographic picture resembles tumor: single or multiple cirumscribed masses or nodules, more often in the upper lobes without hilar involvement. Various other patterns are segmental pneumonia, thick-walled single cavities, lymphadenopathy, pleural effusion and generalized miliary disease.

The patient described herein was an apparently normal host, yet he manifested several unusual features of pulmonary cryptococcal infection. While the majority of cases of pulmonary cryptococcosis resolve without antifungal therapy,[5] systemic antifungal therapy had no discernible effect on the pulmonary cryptococcal lesion in this patient, and he required resection. Because sputum cultures are often negative or may be falsely positive, confirmation of diagnoses often necessitates lung biopsy. Since meningeal involvement may be clinically asymptomatic, lumbar puncture and CAT scan of the head is an essential part of the evaluation of a patient with cryptococcal disease confined to the lungs.[6] Total excision may be curative but is usually not required, as the pulmonary lesions respond well to antifungal therapy. In fact, a normal host with pulmonary cryptococcosis need not be treated unless he develops meningeal or disseminated cryptococcal infection.[7] In an immunocompromised host, one would aggressively treat pulmonary cryptococcosis to prevent disemination and relapses.[7] In cryptococcal meningitis, the presence of high titers of C. neoformans antigen in blood and C.S.F. is a poor prognostic sign. Diamond and Bennett suggested that titers above 1:32 in serum before therapy and a titer of 1:8 or greater in serum and C.S.F. after treatment was associated with amphotericin B treatment failure.[4] In patients with titers of less than 1:8 in serum and C.S.F. after treatment, cure is more likely. Development of antibodies of C. neoformans occurs later in the course with successful therapy, and may be a useful guide to therapeutic response.

Our patient represents an example of extensive cryptococcosis in the setting of a normal immune status, evidenced by the normal T cell studies and negative HIV antibody tests. In urban areas such as New York and its suburbs, disseminated cryptococcal infection is usually associated with AIDS, with an incidence of up to 7%.[3]

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