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Pulmonary cryptococcosis mimicking tuberculosis in an immunocompetent host

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ABSTRACT

Pulmonary cryptococcosis is usually underdiagnosed entity due its highly variable clinical presentation. In tuberculosis (TB)-endemic countries like Pakistan, its diagnosis is easily overlooked as there is a high degree of overlap in clinical, laboratory and radiographic presentation with TB. For definitive diagnosis fungal culture or molecular identification is required.

1. Introduction

Cryptococcus was initially considered as opportunistic pathogen, is recently being reported as a cause of severe infection in immunocompetent population as well[1]. Pulmonary cryptococcosis is an underdiagnosed entity due to its highly variable clinical presentation[2]. However it can frequently lead to disseminated infection with adverse outcomes[3].

We report a case of pulmonary cryptococcosis in an immunocompetent adult patient which was initially misdiagnosed and treated as a case of smear-negative pulmonary tuberculosis (TB) and initiation of appropriate antifungal therapy was delayed. The importance of timely and accurate diagnosis of cryptococcosis is highlighted in this case report.

2. Case

A 55-year-old nonsmoker male, with no known co-morbid presented to the outpatient clinic with 2-month history of low grade fever and weight loss. On basis of suspicion of pulmonary TB sputum was sent for acid fast bacilli (AFB) smear and he was started empirically on first line antituberculous therapy (ATT). Sputum AFB smear later turned out to be negative. After three weeks of ATT he presented to emergency room with shortness of breath. Chest X ray showed right sided pleural effusion (Figure 1A). Thoracentesis revealed exudative effusion with predominant lymphocytes (70%). Further hospital course was complicated by development of cardiac tamponade, requiring pericardiocentesis followed by spontaneous pneumothorax and subcutaneous emphysema. He was intubated and shifted to intensive care unit. Laboratory workup showed decreased total leukocyte count of 2800 with 87% neutrophils in complete blood count. CT of the chest showed right lower lobe consolidation (Figure 1B). Multiple patches of air lucent areas were identified in right lower lobe consolidation suggestive of necrosis. CT guided biopsy of right lower lobe of lung was taken and sent for histopathology and cultures. AFB smear and fungal smears of biopsy specimen were negative. Fungus culture grew rounded yeast, later identified as *Cryptococcus neoformans* based on India ink positivity, urease production, morphology on corn meal agar and bioMerieux API 20 C AUX (API #2107133). Histopathology showed inflammatory infiltrate of predominantly of lymphocytes, in and around blood vessels. On periodic acid schiff staining, rounded encapsulated budding yeast cells were seen (Figure 2). Serum cryptococcal antigen was negative. Patient refused lumbar puncture for cerebrospinal fluid examination however HIV serology was negative. He was started on intravenous amphotericin B 1 mg/kg per day. He

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was discharged home on intravenous amphotericin B therapy. Two weeks later he expired because septic shock secondary to *Pseudomonas* urinary tract infection and bacteremia.

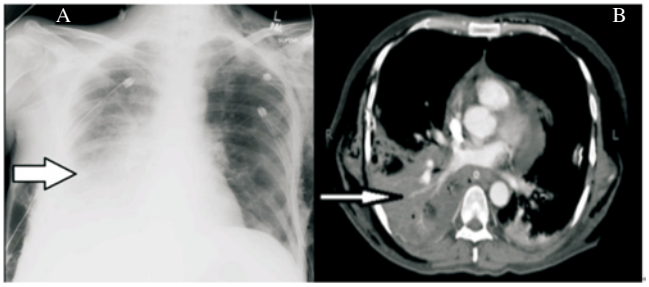

Figure1. Left 1A: Chest X ray AP view shows right lower lung zone opacification; Right 1B: CT scan chest shows right lower lobe consolidation.

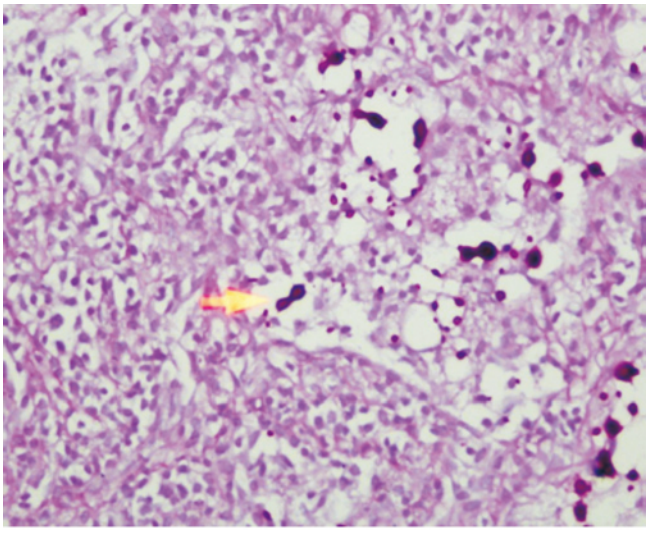

Figure 2. Periodic acid schiff staining of lung biopsy at 40 × 10 magnifications; Arrow shows round encapsulated budding yeast cells.

3. Discussion

Pulmonary cryptococcal infection can range from a localized disease to a progressive and disseminated illness[3,4]. The Infectious Disease Society of America has recommended the exclusion of the central nervous system infection in all symptomatic pulmonary cryptococcosis immunocompetent patients by lumbar puncture[5]. New Infectious Disease Society of America guidelines have endorsed antifungal therapy in mild to severe pulmonary cryptococcosis with the intention to treat not only the infection but also to prevent dissemination[5]. This raises the need of correct and timely diagnosis to avoid poor outcomes. However as noted in our case, in TB-endemic countries like Pakistan, the diagnosis of pulmonary cryptococcal infection is often overlooked as there is a high degree of overlap in clinical, laboratory and radiographic presentation with TB leading to misdiagnosis as smear negative TB.

Pulmonary cryptococcosis is often reported to be misdiagnosed as pulmonary TB. In an autopsy series of 589 out of 8 421 South African miners who had pulmonary cryptococcosis about 52% of cases were misdiagnosed as pulmonary TB[6].

Additional evidence that supports pulmonary cryptococcosis is often empirically treated as TB is the finding in a large African cohort on treatment for TB, in which cryptococcosis was found to be the commonest cause of late mortality at autopsy[7]. Jarvis *et al.*[8] reported a case of pulmonary cryptococcosis, misdiagnosed as smear-negative pulmonary TB and advanced to fatal cryptococcal meningitis. They further shared their experience from a public sector referral hospital in South Africa, where 37% of with cryptococcal meningitis have pulmonary symptoms and 15% have been misdiagnosed with smear-negative TB. This advocates that delay in diagnosis and therapy may lead to the development of cryptococcal meningitis.

In a TB-endemic region, if patient is not responding to ATT, other differential diagnosis should be promptly considered. This case report stresses the need for appropriate clinical studies and guidelines to guide the diagnosis of cryptococcosis in a TB-endemic country like Pakistan.

Conflict of interest statement

We declare that we have no conflict of interest.

Acknowledgments

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