

A case of disseminated cryptococcosis in an immunocompromised host

Sir,

We report the case of a 37-year-old woman, known to be HIV positive and on antiretroviral therapy for 9 months, who presented to us with breathlessness. She also had dry cough, weight loss, vomiting, loose stools, and progressive fatigue of 3 weeks' duration. She was hardly able to walk 30 m when she got admitted with us. Vitals were as following: SPO₂: 87% on room air, hear rate: 112/min, and respiratory rate: 34/min. Respiratory system examination revealed bilateral basal crepitations. Laboratory investigations were as following: Hb: 9.3 g/dL, total white cells: 4.43×10^9 cells/L, platelets 133×10^9 cells/L, lactate dehydrogenase: 173 U/L; C-reactive protein: 128.5 mg/L, and procalcitonin: 28.36 ng/ml. Absolute CD4 count was 65 cells/ μ . She was COVID reverse transcription–polymerase chain reaction negative. The patient was admitted to the intensive care unit and initiated on noninvasive ventilation with 60% FiO₂.

Chest radiograph showed bilateral miliary nodules with a cavity in the right upper lobe of lung [Figure 1a]. Computed tomography showed a thick-walled cavity in the right upper lobe of the lung with ground-glass opacity and a few pneumatoceles and multiple enlarged necrotic mediastinal lymph nodes [Figure 1b and c]. Ultrasound abdomen showed hepatosplenomegaly. Sputum for acid-fast bacilli (smear) and Xpert mycobacterium tuberculosis (MTB)/RIF ultra assay was negative. Fiberoptic bronchoscopy [Figure 2a] and bronchoalveolar lavage (BAL) were obtained from the right upper lobe. BAL mycobacterial culture

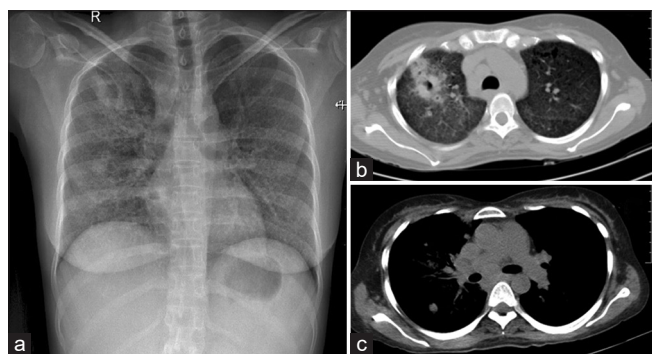


Figure 1: (a) Chest radiograph showing right upper zone cavity with bilateral miliary nodularity computed tomography. (b) Lung window showing right upper lobe apical segment thick-walled cavity and left upper lobe multiple pneumatocele. (c) Mediastinal window: showing multiple enlarged mediastinal lymph nodes with lung nodules

and Xpert MTB/RIF Ultra assay were negative. BAL cytology by Papanicolaou smear showed unstained round structures with occasional budding, suspicious for *Cryptococcus* [Figure 2c] which was confirmed with special stain for fungus Gomori methenamine silver. India ink staining showed capsulated budding yeast cells [Figure 2b]. A cryptococcal antigen lateral flow assay (BIOSYNEX Crypto PS) was performed on BAL. Both low and high-titer bands were positive [Figure 2d]. Blood culture also grew *Cryptococcus neoformans*. She was diagnosed with disseminated cryptococcosis and initiated on oral isavuconazole. The patient improved clinically and was discharged on oral antifungals.

C. neoformans is an opportunistic pathogen in immunocompromised hosts and usually causes meningitis and less commonly pulmonary infections.^[1] The patient under discussion had *Cryptococcus* in BAL and blood which is an uncommon finding.^[2] *C. neoformans* may also cause pneumonia in immunocompetent patients, but mostly, it will resolve without therapy. But in the immunocompromised patient, *C. neoformans* which is initially localized to the lung can eventually cause disseminated infection as found in our patient.^[1] The only chance of early recovery and cure in such cases will be an early diagnosis. The detection of cryptococcal antigen

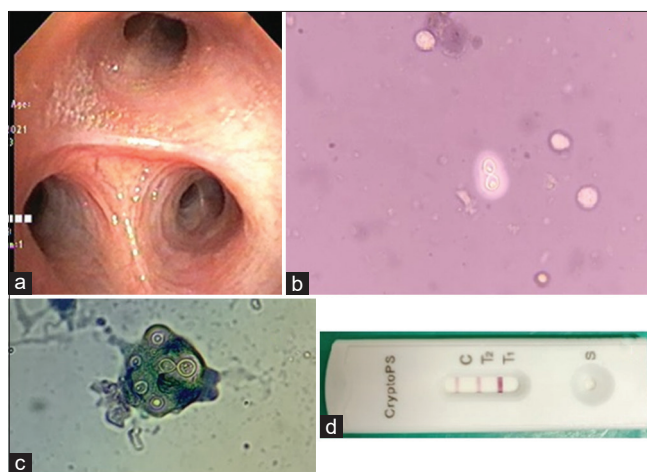


Figure 2: (a) Fiberoptic bronchoscope image showing right upper lobe normal bronchial mucosa. (b) Bronchoalveolar lavage showing capsulated budding yeast cell on India ink staining. (c) Bronchoalveolar lavage cytology Papanicolaou-stained smear showed pale staining rounded structure with a clear halo and focal suspicious budding. (d) Rapid immunochromatographic test for cryptococcal antigen (CryptoPS assay) showing positive T1 (low titer) and T2 (high titer) bands

has been found to be a useful adjunct to diagnosis in patients with *C neoformans* meningitis and fungemia.^[1,2] Bronchoscopy with BAL has become a standard part of assessment in immunocompromised patients with respiratory symptoms.^[3] Although the examination of the BAL specimen may aid in the diagnosis of *C neoformans* infection,^[2,3] there may be a delay in diagnosis unless the organism is seen on cytologic examination of the BAL specimen. If not seen, cultures take about a week for a definitive diagnosis. Cryptococcal antigen test enhances the ability to rapidly diagnose *C neoformans* infection in the lung.^[3] In the present case, BAL cytology showed *C neoformans* on Grocott methenamine silver stain, which was immediately confirmed with antigen test and eventually blood culture grew *C neoformans*.

Liposomal amphotericin B (LAB) is a drug of choice for the treatment of disseminated *C neoformans*. She presented when India was facing an acute shortage of LAB and was started on isavuconazole (ISAV). ISAV is a drug with a broad-spectrum antifungal activity that is approved for the treatment of invasive aspergillosis and mucormycosis by the US Food and Drug Administration. In a study by Thompson *et al.*, ISAV was validated as a valuable alternative to currently available agents for dimorphic fungi like *Cryptococcus*.^[4] Our patient improved with treatment and was discharged on oral ISAV.

The current case is an exception in many ways. Tuberculosis (TB) would be the most likely cause of a thick-walled cavity and miliary opacity in an endemic country like India. However, the patient repeatedly tested negative for pulmonary TB. BAL cytology and Crypto PS were positive which clinched the diagnosis. We would like to conclude that, though rare, cryptococcosis should be considered in the differential diagnosis of miliary opacity on chest X-rays, especially in immunocompromised hosts.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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