Disseminated Cryptococcosis with Endobronchial Lesions

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Learning Objectives

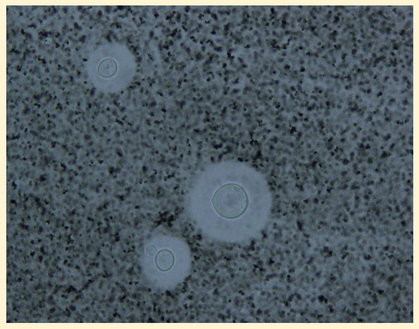
1) Describe the clinical presentation of disseminated cryptococcosis
2) Discuss the appropriate treatment of disseminated cryptococcosis

Case Presentation

A 52-year-old man with HIV/AIDS and recent CD4+ T-cell count of 11/µL (CD4+ percent of 3%) presented with shortness of breath and non-productive cough for 3 months. He was otherwise asymptomatic, denying headaches, photophobia, fevers, chills, night sweats, and hemoptysis. He had no concerning environmental exposures, and denied tobacco, alcohol, and recreational drug use. Medications included darunavir/cobicistat and emtricitabine/tenofovir.

Physical Exam:
Vital signs and physical examination were normal with the exception of several 1 mm umbilicated flesh-toned non-tender papules spread across his face.

Labs:
Laboratory analysis revealed a positive Cryptococcal serum antigen titer of 1:16,000 and CSF antigen titer of 1:32,000.



A B
Figure 1. A: Cutaneous lesions due to disseminated Cryptococcosis (patient's forehead). B: India ink staining of CSF fluid demonstrating Cryptococcal organisms.

Imaging:
Chest X-ray on admission showed a diffuse reticular pattern. Computed tomography of the thorax without contrast showed a tree-in-bud nodularity pattern with peribronchovascular thickening in addition to a large cavitary lesion within the right lower lobe.

A B
Figure 2. A: CT scan of patient's chest showing evidence of a cavitary lesion. B: Bronchoscopy image demonstrating ulcerated lesions on patient's endobronchus.

Pathology:
Bronchoscopy showed ulcerated erythematous endobronchial plaques within the right segmental bronchi. The lesions were biopsied and mucicarmine stain revealed diffuse encapsulated yeast forms. Cryptococcus *neoformans* was cultured from bronchioalveolar lavage fluid, cerebrospinal fluid, and blood.

Treatment:
The patient was treated with a combination of amphotericin B and flucytosine with improvement in his facial rash, symptoms, and Cryptococcal antigen titer.

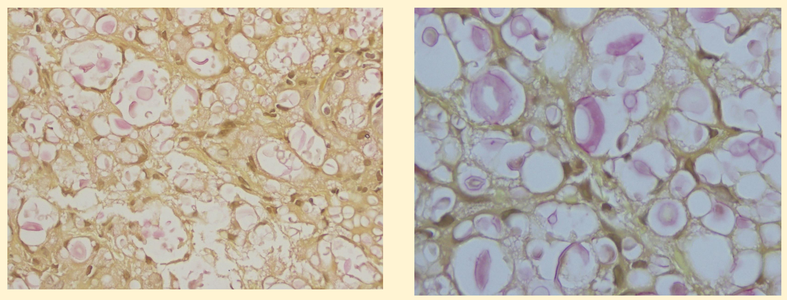


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Figure 3. A: Biopsy of right mainstem endobronchus with mucicarmine staining showing Cryptococcus *neoformans*. B: Biopsy of right mainstem endobronchus with mucicarmine staining showing Cryptococcus *neoformans* (higher power).

Discussion

This case demonstrates an AIDS patient with disseminated cryptococcosis who presented with pulmonary and meningeal involvement, and was found to have endobronchial lesions harboring Cryptococcus *neoformans* and cutaneous umbilicated papules across his face. Although these findings are typical, disseminated Cryptococcosis was more common in the pre-HAART era, and today's physicians may not readily identify it.

Cryptococcal infections primarily affect the lungs, however the most common extrapulmonary site of infection is the central nervous system, often seen in patients with AIDS. In these patients, management includes long-term treatment with anti-fungal medications, as in the table below.

Induction Phase	Consolidation Phase	Maintenance Phase
Amphotericin B 3mg/kg IV daily and Flucytosine 25 mg/kg PO q6h	Fluconazole 400mg PO daily	Fluconazole 200mg PO daily
2 weeks, or until CSF cultures negative	10 weeks	Until CD4+ count is above 200/µL for 6 months

Anti-retroviral medications are typically held for five weeks after initiation of anti-fungal therapy to decrease the risk of immune reconstitution inflammatory syndrome (IRIS). Interestingly, our patient had started anti-retroviral therapy for several weeks prior to admission, which may have precipitated an immune reconstitution phenomenon, causing his presenting symptom.

References

1) Gilbert D, Chambers H, et al. *The Sanford Guide to Antimicrobial Therapy 2015*, 45th Edition. Antimicrobial Therapy, Inc. Sperryville, VA; 2015

2) Perfect J, Dismukes W, et al. Practice Guidelines for the Management of Cryptococcal Disease. Infectious Diseases Society of America. *Clinical Infectious Diseases.* 2010 ; 50: 291 -322