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Disseminated cryptococcosis in HIV due to different species — dissimilar yet alike!

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Objective: To present two cases of disseminated cryptococcosis caused by two different species in HIV patients, presenting from the same geographical location.

Introduction: Cryptococcal meningitis is the most frequent cause of adult meningitis in areas with a high prevalence of human immunodeficiency virus (HIV) and is one of the leading causes of HIV-related deaths worldwide. *Cryptococcus gattii*, the lesser prevalent species, 'conventionally' known to affect the non-HIV and otherwise immunocompetent population, may also cause disseminated infection in HIV patients. High MICs of antifungals, especially fluconazole, may pose challenges in the management. Here, we present two cases of HIV patients with disseminated cryptococcosis, who presented from the same geographical area of India in the months of February and March 2022, respectively.

Case 1: A 34-year-old patient from the state of Rajasthan with a past history of abdominal tuberculosis and a defaulter of ART (ABC/3TC/EFV) presented with headache and vomiting for 3 weeks. After an MRI brain and CT scan of the thorax, he was diagnosed to have pulmonary and meningeal cryptococcosis based on CSF examination with a positive Gram's, and India ink stain (Fig. 1), positive cryptococcal antigen (CRAG) by lateral flow assay, and fungal culture positive for *C. gattii* (MALDI-TOF); and a paratracheal lymph node biopsy showing granulomatous inflammation with cryptococci (Fig. 2). Fluconazole MIC was 16 μg/ml. He was treated with liposomal amphotericin B with flucytosine for 2 weeks. After good clinical recovery and negative fungal culture, a high dose (1200 mg) of fluconazole was started. He is asymptomatic with repeated negative fungal culture on 2 months follow-up.

Case 2: A 37-year-old patient from Rajasthan, on ART (TDF/3TC/DTV) for HIV-1 diagnosed a month ago, presented with cough, weight loss, and fever for 2 months with severe chest pain on drinking and eating. He was diagnosed to have cytomegalovirus esophagitis based on the CMV inclusion bodies in a biopsy from the esophageal ulcers and a positive quantitative serum CMV DNA PCR. Bronchoscopy with EBUS-guided lymph node biopsy was done to investigate cavitary lung consolidation and mediastinal lymphadenopathy. BAL CRAG was positive and biopsy showed inflammation with histiocytic aggregates and necrosis, and many encapsulated yeasts form suggestive of *Cryptococcus*, which was identified by MALDI-TOF as *Cryptococcus neoformans*. Serum CRAG was positive. Though patient did not have any neurological complaints, CSF examination was done and CRAG was positive. He was treated with injection of liposomal amphotericin B, flucytosine, and ganciclovir, along with ART.

Conclusion: Default of ART by the patients, initiation of ART without investigation and treatment of opportunistic infections, and co-existence of multiple opportunistic infections, are still major challenges in the management of HIV, especially in developing countries. Though *C. neoformans* is the commonly isolated species, more and more cases of *C. gattii* are being reported. Identification of the species is important as there are differences in the epidemiology, clinical presentation, antifungal susceptibilities, and hence the treatment and prognosis.