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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 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 past history of abdominal tuberculosis and a defaulter of ART (ABC/3TC/EFV), presented with weight loss, headache and vomiting for 3 weeks.
- MRI brain showed prominent Virchow-Robin spaces (Fig 1), CT scan of thorax showed right upper lobe consolidation with enlarged supraclavicular, mediastinal and axillary lymph nodes.
- He was diagnosed to have pulmonary and meningeal cryptococcosis based on CSF examination which showed 30 cells (90% lymphocytes), with an opening pressure of 35cm of H<sub>2</sub>O, protein of 32.3 mg/dl, glucose of 56.1 mg/dl (RBS: 149mg/dl) with a positive gram's and India ink stain (Fig 2), positive cryptococcal antigen (CRAG) by lateral flow assay and fungal culture positive for *Cryptococcus gattii* (MALDI-TOF).
- EBUS guided paratracheal lymph node biopsy showed granulomatous inflammation with cryptococci.
- Fluconazole MIC was 16 µg/ml (Fig 3).
- He was treated with liposomal Amphotericin B with Flucytosine for 2 weeks.
- After good clinical recovery and negative fungal culture, high dose (1200 mg) Fluconazole was started.
- He is asymptomatic with weight gain at 6 months follow up.

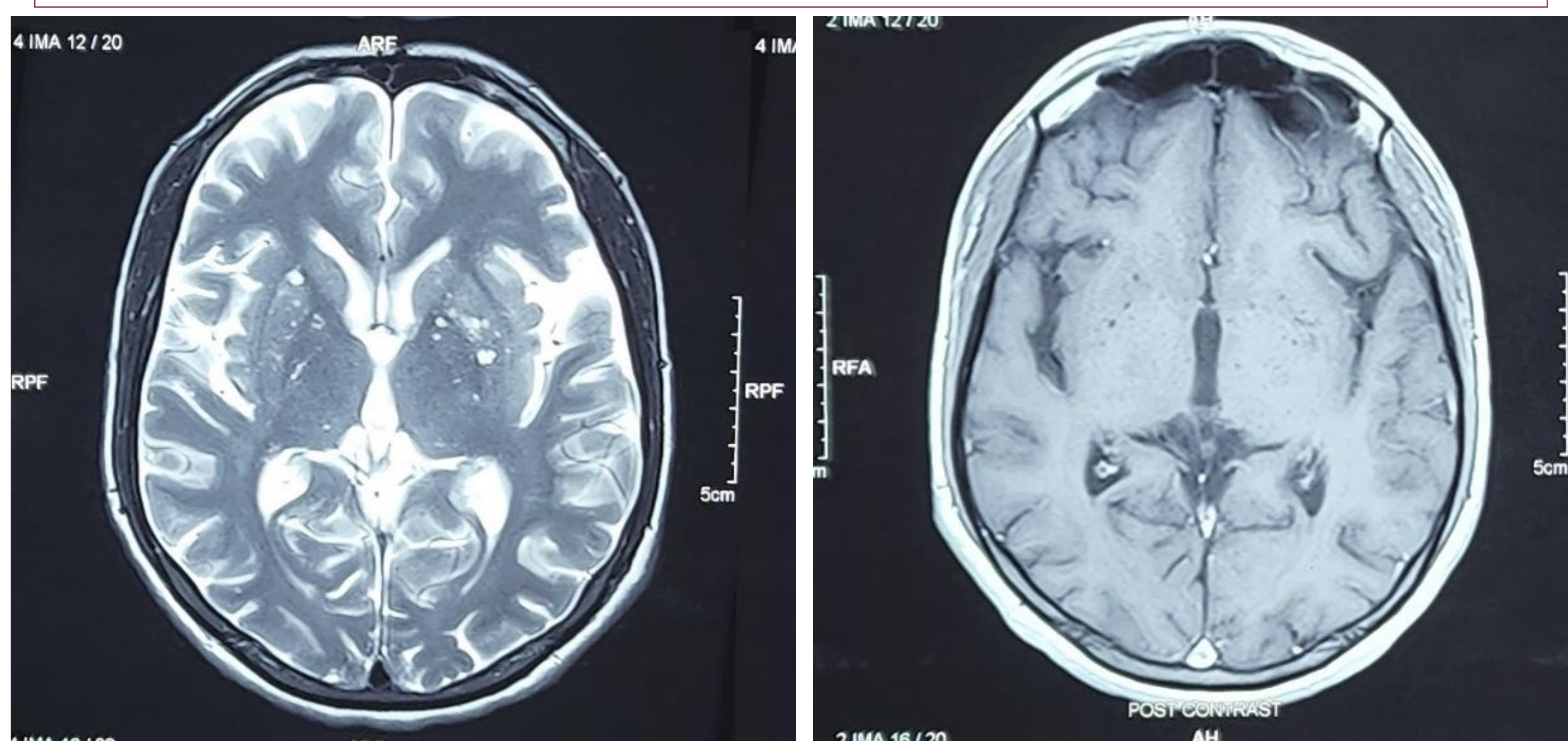


Fig 1 : MR Brain : Multiple small non – enhancing foci S/O prominent perivascular space lesions

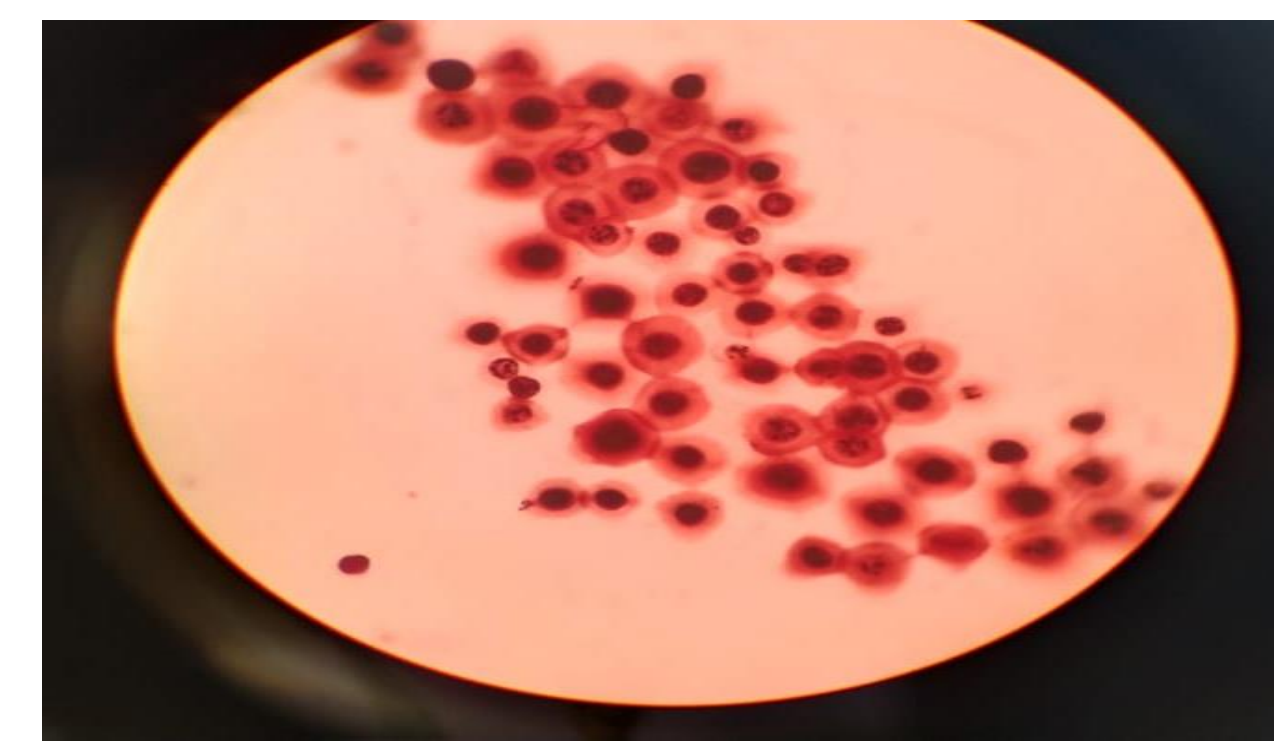


Fig 2 : Cryptococci on gram stain

Specimen	Pure growth on Sabouraud agar plate received CSF)
Organism	<i>Cryptococcus neoformans</i> var <i>gattii</i>
Fungus MIC	
Anidulafungin	R (8)
Micafungin	R (8)
Caspofungin (0.008 - 16 µg/ml)	R (8)
Flucytosine (0.03 - 64 µg/ml)	S (1)
Posaconazole (0.008 - 8 µg/ml)	S (0.12)
Voriconazole (0.008 - 16 µg/ml)	S (0.12)
Itraconazole (0.008 - 16 µg/ml)	S (0.12)
Fluconazole (0.125 - 256 µg/ml)	R (16)
Amphotericin-B (0.008 - 16 µg/ml)	S (0.5)

Fig 3 : Antifungal susceptibility of *Cryptococcus gattii*

## Case 2

- A 37 year-old patient from Rajasthan, on ART (TDF/3TC/DTV) for HIV-1 diagnosed a month earlier elsewhere, presented with cough, weight loss and fever for 2 months with severe chest pain on drinking and eating.
- He was diagnosed to have cytomegalovirus (CMV) esophagitis based on the CMV inclusion bodies in biopsy from the esophageal ulcers (Fig 4) 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 forms 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 Inj Liposomal Amphotericin B, Flucytosine and Ganciclovir, along with ART.
- He improved on treatment, however, was lost to follow up after a month.

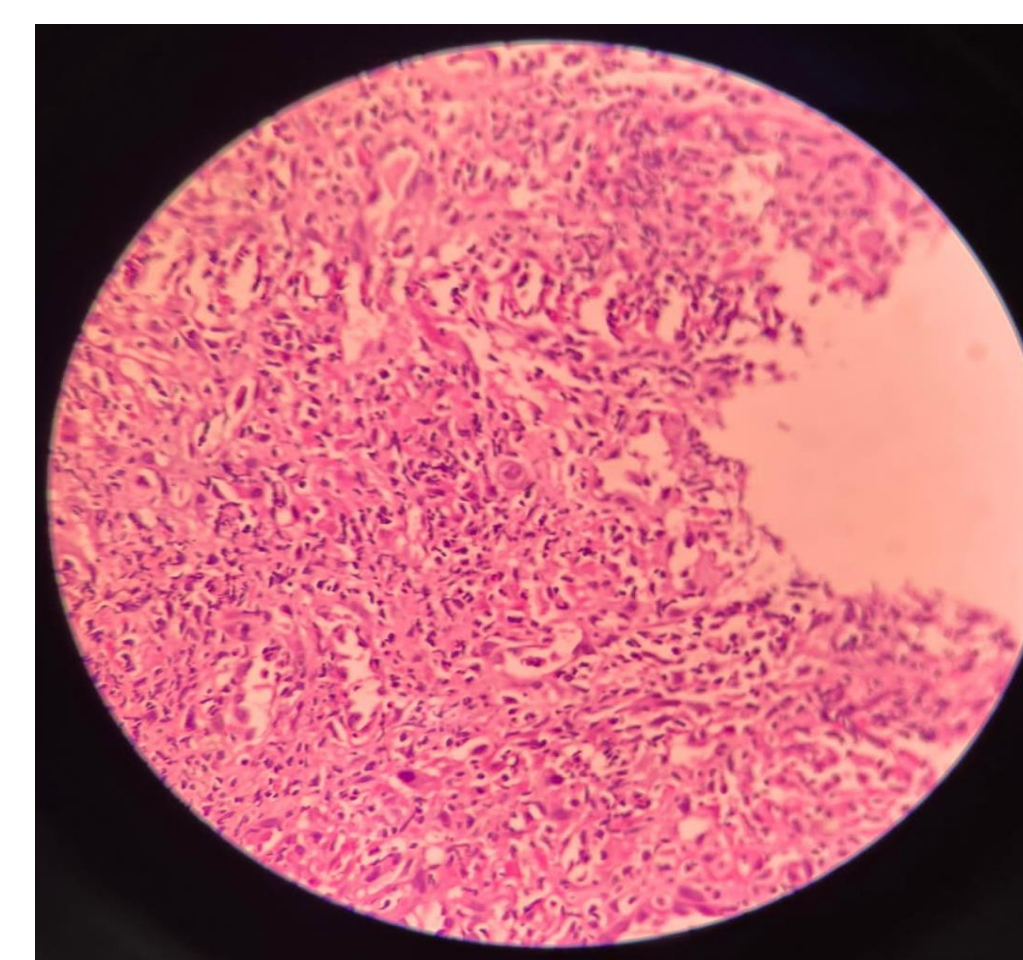


Figure 4 : Esophageal ulcer histopathology

## Discussion

- Although the widespread use of HAART has lowered the incidence of cryptococcosis in medically developed countries, the incidence and mortality of this infection are still extremely high in areas with uncontrolled HIV disease and limited access to health care resources.
- Though there are changes in the management of cryptococcal disease with short duration AmB, the 'standard' treatment comprises of Induction, consolidation and a prolonged maintenance phase.

## 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.

## References :

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