



## CASE REPORT: CRYPTOCOCCAL MENINGITIS WITH CRYPTOCOCCEMIA IN AN IMMUNOCOMPROMISED HOST

### Microbiology

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### KEYWORDS

Cryptococcus, cryptococcus neoformans, meningitis, meningoencephalitis, AIDS, HIV

### INTRODUCTION:

The emergence and spread of Human immunodeficiency virus (HIV) has posed a great public health challenge in modern times. HIV infection can lead to Acquired immunodeficiency syndrome (AIDS) and patients can suffer from many kinds of opportunistic infections. Here we report a unique case of extrapulmonary cryptococcosis in an AIDS patient with dissemination in blood.

### CASE REPORT:

**Presenting concerns:** A 40yr male patient, from Jharkhand, came to our E.R. with c/o headache since 25days and low grade fever since last 4 days. Each episode of headache lasted from 10min to 1hour with no premonitory symptoms and not associated with nausea/vomitting.

**History and Clinical findings:** He was admitted previously in another hospital due to intermittent fever. There he was diagnosed clinically as tubercular meningitis and started on anti-tubercular drugs, steroids and anti-convulsants. MRI brain was done during this time which only showed acute infarction in left posterior limb of internal capsule. He had no relief, took discharge and presented to our E.R.

**On examination:** Patient was conscious, alert. His blood pressure was 130/80mmHg, pulse was 84/min, respiratory rate was 10/min. He had fever and headache but no neck rigidity or kernig's sign. No other significant findings.

**Interventions started:** He was advised to continue ATD. C.S.F. routine examination, gram stain, ZN stain, india ink preparation, cryptococcal antigen, ADA and GeneXpert was ordered along with HIV antibody and MRI brain. Expert opinion was sought for any choroidal involvement.

### Initial investigation reports:

HIV antibody (+)

On CSF routine examination it was hazy, colourless, no clots/ coagulum seen.

Total cell count 20, – 10%, L- 90%,

RBC's (+)

Protein - 47.10mg/dl

Sugar - 18 mg/dl

Budding yeast cells with clear surrounding halo in CSF india ink seen.

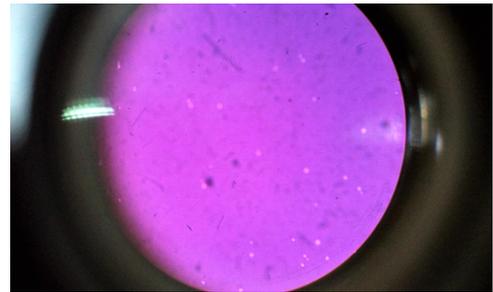
CSF gram stain also showed budding gram positive yeast cells.

CSF cryptococcal antigen (+)

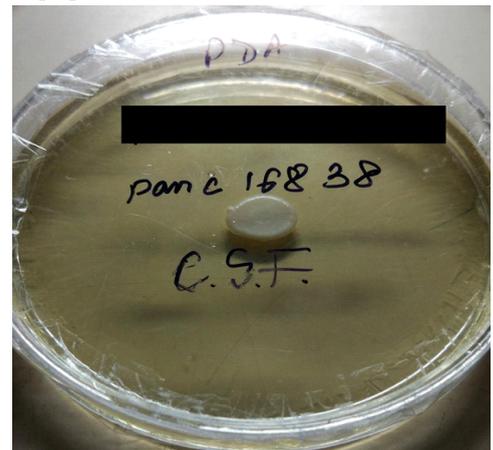
CSF MTB geneXpert (-)

Culture of CSF showed mucoid creamy colonies after 48hrs and confirmed as *Cryptococcus neoformans* by Vitek2 compact.

One eye examination by ophthalmologist, no choroidal involvement was noted. CD4 count revealed a count of 164cells/ul.



India ink preparation of C.S.F.

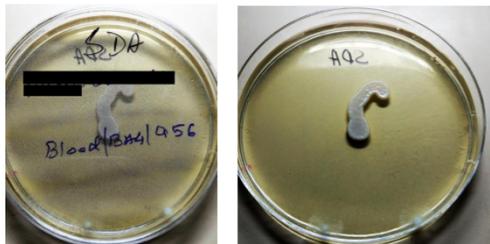


C.S.F. culture

The Calcutta Medical Research Institute Microbiology, Chand Bagh		Patient No. 4017/18/02/01	Patient ID: 4017/18/02/01
Lab/Ref Name	Microbiology, Chand Bagh	Order No. 4017/18/02/01	Order Date: 02/12/2018
Requester Name		Ref. No. 4017/18/02/01	Ref. Date: 02/12/2018
Requester Designation		Ref. Dept. Microbiology, Chand Bagh	Ref. Doctor: Dr. Saikat Pal
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**Blood culture fluid direct gram stain**



#### DISCUSSION:

Cryptococcus is an encapsulated yeast, causing opportunistic infection in immunocompromised pts.

Cryptococcus is classified into various genotypes:

1. Cryptococcus neoformans var. grubii (serotype A)
2. Cryptococcus neoformans var. neoformans (serotype D)
3. Cryptococcus gatii (serotype B and C)

Cryptococcus neoformans var. grubii (serotype A) cause ~95% infections among 98% AIDS pts. [2]

C. gatii is less frequent but has potential to infect immunocompetent persons.

Other encapsulated yeasts which can mimic cryptococcal infection is Rhodotorula.

Incidence is highest in Africa followed by Asia. [1,2] In east, south and south east Asia, prevalence of cryptococcal meningitis is 120/1000 HIV infected individuals/year. [2] In Eastern India, incidence is 4% among HIV patients. [1,2] Randhawa et al from India identified that C. neoformans var. grubii and C. gatii prevail all through the year in environment with highest prevalence in autumn months. Lowest prevalence for C. neoformans var. grubii was in rainy season and for C. gatii its winter. C. neoformans is found in pigeon excreta while C. gatii is found in leaves, bark and surrounding soil.

Risk factors, apart from HIV, for Cryptococcal infection include DM, end-stage renal disease, TB, liver cirrhosis, SLE, malignancy and steroid therapy.

There is paucity of data on cryptococcal infection from India and so this case is quite unique and rare.

CNS is most commonly affected (67-83%) followed by lung (8.4%). Rarely infections of eye, granulomas in brain, cryptococcomas in ventricles, prosthetic valve endocarditis and genitourinary involvement have been reported from India. Extra-neural involvement and bloodstream infection occur less frequently in immunocompetent patients. Meningitis or meningoencephalitis is most common presentation of Cryptococcosis followed by pulmonary infection. Presenting features are fever (86%), headache (67%), stiff neck (37%), change in mental status (29%) and cranial nerve deficit (20%). [2]

Early and accurate diagnosis is essential as mortality is high. India ink, gram stain, antigen detection and culture are easily available and economical for early diagnosis.

Cryptococcal antigen detection by latex agglutination has highest sensitivity followed by C.S.F. India Ink preparation. [2] Sensitivity of India ink is usually high in HIV cases. [2]

Complications: Initiation of HAART leads to development of Immune reconstitution inflammatory syndrome (IRIS) in 10-32% of HIV infected pts. [3] In 6-45% pts with meningitis this happens after 1-2 months of HAART. [4] Amp-B can cause toxicity as well.

AmB-d (0.5–1 mg/kg) plus flucytosine (100 mg/kg) daily for 2 weeks and then with fluconazole (400 mg/d) for at least 10 weeks is the recommended therapy. Maintenance with fluconazole (200 mg/d) till CD4 cell count >200/cu.mm is advised. Initiation of HAART according to *Infectious Diseases Society of America (IDSA)* should be done after 2-10 weeks of antifungal treatment.

Flucytosine being unavailable in our country, we had to manage initially with fluconazole 800 mg along with Amph-B.

For CNS cryptococcosis, poor prognostic markers are a CSF assay positive for yeast cells on initial India ink examination (evidence of a heavy fungal burden), high CSF pressure, low CSF glucose levels, low CSF pleocytosis (<2/μL), recovery of yeast cells from extraneural sites, absence of antibody to capsular polysaccharide, a CSF or serum cryptococcal antigen level of ≥1:32, and concomitant glucocorticoid therapy or hematologic malignancy.

Our patient was initially diagnosed by India ink, had low CSF glucose, Cryptococcus was also isolated from extra-neural site i.e. blood and had exposure to steroids during previous admission which all point towards poor outcome.

#### Outcome:

Discharge on 10<sup>th</sup> day was taken against our medical advice due to persistence of headache. He was subsequently lost to follow-up.

#### REFERENCES:

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