

## Disseminated cryptococcosis in an immune competent patient: an unusual case

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### ABSTRACT

*Cryptococcus neoformans* is an encapsulated yeast-like fungus. *Cryptococcus* infection is common among immunocompetent individual and *Cryptococcal* disease is more common in presence of impaired immunity. Most cases of disseminated cryptococcosis are known to be associated with acquired immunodeficiency syndrome (AIDS). We are reporting a case of 70-year-old male presented with fever, headache and seizure followed by altered sensorium who was finally diagnosed as a case of disseminated cryptococcosis. It was interesting in our case that he was neither HIV-positive nor associated with any condition leading to impaired immunity. He was managed with antifungal therapy and broad spectrum antibiotics but unfortunately patient could not be saved despite our best effort.

**Keywords:** Cryptococcosis, Immunocompetent, Meningoencephalitis, Impaired immunity

### 1. INTRODUCTION

*Cryptococcus neoformans* is an encapsulated yeast-like fungus. The *Cryptococcosis* usually causes meningoencephalitis and pneumonia, while skin and soft tissue involvement are less common. Even though *Cryptococcus* infection is common among immunocompetent individual, *Cryptococcal* disease commonly occurs in presence of impaired immunity. High risk for cryptococcosis are haematological malignancies,

Dinkar et al.

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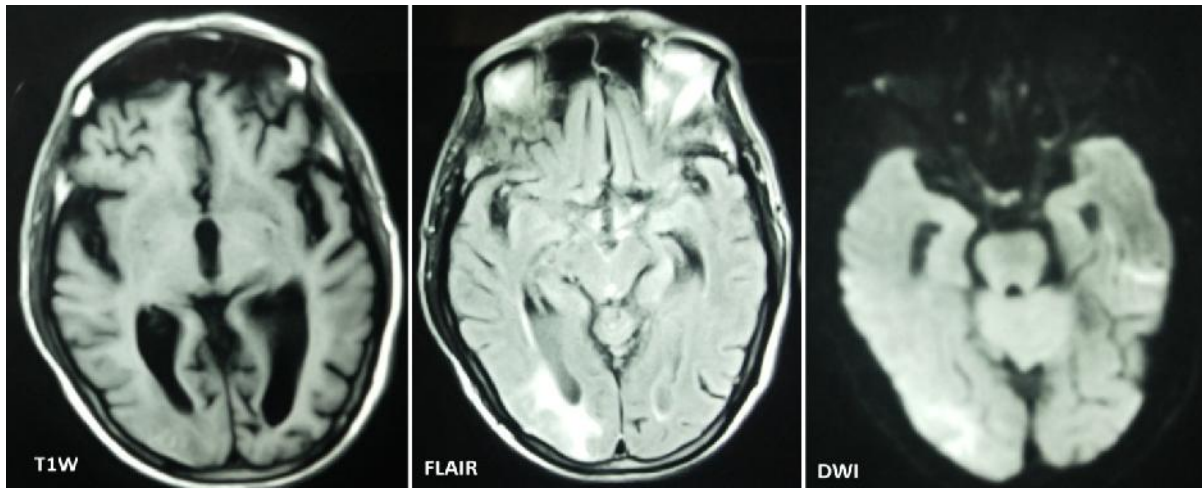
recipient of solid organ transplants on immunosuppressive therapy, medical conditions necessitating glucocorticoid therapy and advanced HIV infection (Casadevall A., 2012). Most cases of disseminated cryptococcosis are known to be associated with acquired immunodeficiency syndrome (AIDS), and less commonly in other immunocompromised conditions (Diamond RD and Bennett JE., 1974) Only few studies have reported cryptococcosis in HIV negative patients (Mithal M et al., 2010, Yehia BR et al., 2009).

## 2. CASE REPORT

A 70-year-old male farmer was referred to our emergency department in stuporous state. He had fever with headache for 14 days, one episode of seizure 4 days back followed by altered sensorium. At the time of admission patient was in stuporous state with a Glasgow coma score (GCS) of 8 (E2M4V2) without any focal deficit. The patient had signs of meningeal irritation. He had no history of hypertension, diabetes mellitus, malignancy, cardiovascular disease, atherosclerosis, trauma, seizure, drug abuses, alcoholism, or any similar episodes of altered sensorium in past. On general examination patient had no pallor or icterus. He was febrile (101°F). His pulse rate-96/ min, B.P-130/70 mmHg and respiratory rate was-18/min. Chest examination revealed occasionally basal crepts on right side. Cardiovascular and abdominal examinations did not reveal any abnormality. Investigations showed haemoglobin of 11.6 gm/dl, total leukocyte count 14500/mm<sup>3</sup> with 76% polymorphs, platelet count 1,98,000/mm<sup>3</sup>. His liver function tests, renal function tests, random blood sugar, serum electrolytes were normal. Serology for enteric fever and smear examination of malaria parasite were negative. Australia antigen for Hepatitis B, Antibody against Hepatitis C virus and Enzyme-linked immunosorbent assay for human immunodeficiency virus were negative. Urine examination was normal. Cerebrospinal fluid (CSF) examination revealed total leucocytes 106 cells/mm<sup>3</sup> with polymorphs-64%, protein 88mg/dl and sugar 34mg/dl with corresponding blood sugar 113mg/dl. Cryptococcus India ink preparation [Fig. 1] and cryptococcal antigen test for CSF were positive. His blood culture in biphasic media was positive for Cryptococcus. Mycobacterium tuberculosis and DNA PCR for Herpes Simplex virus were not detected in CSF. Chest X-ray and ECG were normal. Magnetic Resonance imaging (MRI) of brain was suggestive of encephalitis. [Fig. 2] On the basis of clinical and investigational parameters, patient was diagnosed as a case of disseminated cryptococcosis. The patient was managed with intravenous fluid, antifungal therapy and broad spectrum antibiotic therapy. Intense vital monitoring and supportive care were done during hospitalization. Despite our best effort, patient could not be saved and succumbed to his illness over 5 days.



**Figure 1**  
Microphotograph of India ink preparation showing Cryptococcus



**Figure 2**

Diffuse cerebral atrophy with ischemic demyelinating changes and ill defined area of signal intensity alteration with diffusion restricted in right occipital region suggestive of Encephalitis.

### 3. DISCUSSION

The clinical profile of cryptococcosis depends on the site of fungal infection. Though infection can involve any tissue or organ but majority of the cases of cryptococcosis usually present with CNS or lung infection or both. The clinical features of Cryptococcosis of CNS are headache, fever, lethargy, sensorium deficits, memory deficits, cranial nerve paresis, vision deficits and meningismus while lung cryptococcosis presents with cough with expectoration and chest pain (Casadevall A., 2012). When two or more systems are involved with positive cultures or a positive blood culture, then it is called Disseminated Cryptococcosis (Chuang YM et al., 2008). Meningoencephalitis and pulmonary infiltrates are the two most common manifestations of cryptococcal disease (Chuang YM et al., 2008, Albert-Braun S et al., 2005, Kokturk N et al., 2005). Some previous studies have reported a positive blood culture of *C. neoformans* from blood, CSF, sputum, ascites, urine, bone marrow and skin (Chuang YM et al., 2008, Kokturk N et al., 2005). The imaging of CNS cryptococcosis is usually unremarkable so cerebrospinal fluid analysis is necessary for diagnosis. The typical findings of CSF are lymphocytic pleocytosis, elevated protein and low sugar. *C. neoformans* in CSF, identified by India ink staining is observed more than 90% in HIV infected patient while greater than 50% in patients without HIV infection (Satishchandra P et al., 2000). The cryptococcal antigen in CSF of CNS infected patient is almost universally positive (Satishchandra P et al., 2000, Johns Hopkins HIV guide., visited on 27<sup>th</sup> Dec 2014 ). We ruled out HIV status and other immunocompromised states or risk factors by history and examinations. Patient was finally diagnosed as a case of disseminated Cryptococcus and intravenous amphotericin B was added to treatment. Treatment regimens are determined by anatomic site of infection and host immune status. Immunocompetent patients with cryptococcal meningitis should be treated with amphotericin B and flucytosine for 6-10 weeks, or amphotericin B and flucytosine for 2 weeks followed by fluconazole (400 mg/d) for a minimum of 10 weeks (Saag MS et al., 2000).

Though tuberculosis infection of central nervous system is common in our population but the treating physician must evaluate a patient for all other atypical presentation too, if patient is undiagnosed or deteriorating. Many previous studies have been also demonstrated the risk factors associated with cryptococcosis in HIV-negative patients such as Cushing's syndrome, lymphoma, chronic leukemia, cirrhosis, chronic kidney disease and diabetes (Mitchell TG and Perfect JR., 1995, Pappas PG et al., 2001, Shih CC et al., 2000). Our case highlights the protean manifestations of cryptococcosis in immunocompetent patient.

### 4. CONCLUSION

Cryptococcosis has high rates of morbidity and mortality even with antifungal therapy because the prognosis of disease depends on extent and duration of underlying immunologic deficits. This case was diagnosed late because of lack of consideration towards cryptococcosis in immunocompetent patient. Therefore treating physician must be aware of Cryptococcosis associated with HIV-negative patient. Early diagnosis and management with appropriate antifungal therapy may improve clinical outcomes in these patients.

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