Infect Dis Trop Med 2022; 8: e786

Non-meningeal, non-pulmonary disseminated intra-abdominal cryptococcosis in immunocompromised host: case report and approach to therapy

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ABSTRACT:

The most common presentation of Acquired Immuno-Deficiency Syndrome (AIDS) associated cryptococcosis is meningitis. Non-meningeal and non-pulmonary Cryptococcosis is very rare. We present a case of 16-year-old boy who presented to the Emergency Department with chief complaints of fever and pain abdomen involving left hypochondrium for 2 months. On evaluation, he was found to be HIV positive with very low CD4 count and had splenic abscess along with mesenteric lymphadenopathy. Fine needle aspiration cytology from the splenic abscess showed scattered multinucleated giant cells containing many rounded capsulated organisms within the cytoplasm. Alcian Blue-Periodic Acid Schiff stain (AB-PAS) highlighted the capsulated organisms as *Cryptococcus neoformans.* The patient was treated successfully with liposomal amphotericin B and flucytosine, followed by fluconazole along with antiretroviral therapy.

Keywords: *Cryptococcosis, Splenic abscess, Human immunodeficiency virus, Acquired immunodeficiency syndrome, Opportunistic infections.*

INTRODUCTION

Cryptococcosis is an invasive fungal infection caused by *Cryptococcus neoformans* or *Cryptococcus gattii*. Most patients with cryptococcosis are immunocompromised either due to Acquired Immuno-Deficiency Syndrome (AIDS), prolonged treatment with glucocorticoids, organ transplantation, malignancy, liver disease or sarcoidosis. Non-meningeal and non-pulmonary Cryptococcosis is very rare[1,2]. We present a case report of non-meningeal and non-pulmonary, disseminated abdominal cryptococcosis.

CASE PRESENTATION

A 16-year-old boy of Indian nationality, resident of Uttar Pradesh, presented to the Emergency Department with chief complaints of fever and history of pain abdomen involving left hypochondrium for 2 months. Pain was moderate in intensity and had no correlation with meals. There was also history of significant weight loss for last 3 months. On examination he was conscious, cachectic and had severe pallor. He had tachycardia with pulse rate of 110 per minute and his blood pressure was 100/70 mmHg. On per abdomen examination spleen was palpable 4 cm below left costal margin and there was no other organomegaly. Investigations revealed anemia (hemoglobin 7.5 g/dL), TLC was 3500 µL and platelets were adequate. Renal function was normal and liver function showed hypoalbuminemia (2.5 g/dL). Chest x-ray was normal. Serology for human immunodeficiency virus was positive by enzyme-linked immunosorbent assay (ELISA) and confirmed with Western blot method. CD4 count was found to be very low (21/mm^3). Ultrasound abdomen showed subtle ill-defined areas in upper pole of spleen. Contrast computed tomographic

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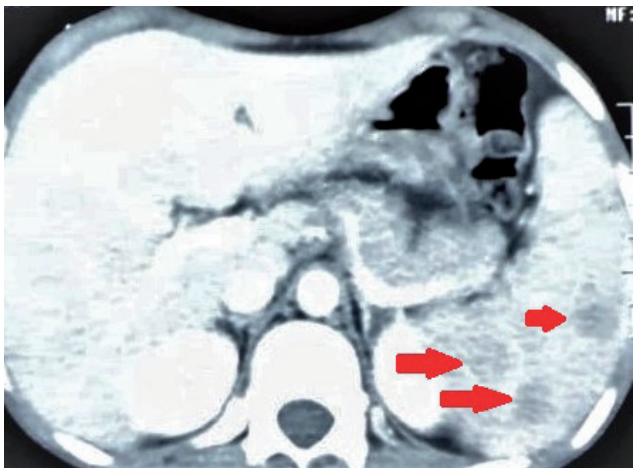

Figure 1. Contrast enhanced CT scan of abdomen showing multiple splenic abscess.
*Arrows-Hypodense lesions in spleen representing splenic abscesses.

scan abdomen (Figure 1) revealed multiple hypodense lesions in spleen with mesenteric lymphadenopathy. Fine needle aspiration and cytology from splenic tissue showed scattered multinucleated giant cells containing many rounded capsulated organisms within the cytoplasm morphologically consistent with *Cryptococcus neoformans*, few budding forms were also noted, few scattered lympho-histiocytic tangles were also seen. Alcian Blue-Periodic Acid Schiff (AB-PAS) stain highlighted the capsulated organisms as *cryptococcus*. Ziehl-Neelsen stain for Acid Fast *Bacilli* was negative. Diagnosis of disseminated abdominal Cryptococcosis was made. The patient had no history or clinical features suggestive of meningitis, and his cerebrospinal fluid (CSF) examination showed 5 cells (all lymphocytes) with protein of 10 mg/dL and sugar 88 mg/dL and cryptococcal antigen was negative.

Patient was started on liposomal amphotericin B 3 mg/kg body weight along with flucytosine 25 m/kg body weight qid for 2 weeks. He tolerated the therapy well and later shifted to fluconazole 400 mg once daily. Anti-Retroviral therapy (tenofovir, emtricitabine and efavirenz) was also initiated 15 days after initiation of antifungal therapy. On follow-up the patient was symptomatically better and afebrile his repeat ultrasound showed that lymphadenopathy had regressed and lesions in spleen had reduced in size. Plan was to give fluconazole 400 mg till 8 weeks, and after 8 weeks decrease the dose to 200 mg till his CD4 count improves above 200 for 3 consecutive months.

DISCUSSION

Cryptococcus is a species of an invasive fungus. It causes cryptococcosis, an infection conventionally associated with immunosuppressed individuals, while being uncommon in healthy immuno-competent individuals. The two species of *Cryptococcus* that are frequently associated with infections in humans are *Cryptococcus neoformans* and *Cryptococcus gattii*. The organism is extensively present in certain regions of the world. However, the most common forms of exposure include a history of exposure to droppings of birds or from soil. Globally, about 1 million cases of cryptococcosis are reported each year causing 625,000 deaths approximately[3]. In the United States of America, the incidence of cryptococcosis is estimated to be about 0.4-1.3 cases per 100,000 persons and about 2-7 cases per 100,000 in patients affected with AIDS with a case fatality rate of about 12 %[4]. There are no data from India about the prevalence and incidence of cryptococcosis. *Cryptococcus neoformans* usually causes infections in immunocompromised patients while *Cryptococcus gattii* is associated with infections in immunocompetent persons. The most frequent presentation of cryptococcosis is meningitis where patient presents with fever, headache and altered sensorium and signs of raised intracranial pressure. It can be diagnosed by CSF examination where protein is raised along with low sugars, and cells predominantly lymphocytes. India ink staining and latex *Cryptococcal neoformans* polysaccharide antigen test are useful for diagnosis. Apart from CNS, the other most common site of infection is respiratory tract. Manifestations of pulmonary cryptococcosis range from asymptomatic colonization of the airways or a simple pulmonary nodule on a chest x-ray to life-threatening pneumonia and acute respiratory distress syndrome[5,6]. Apart from CNS and respiratory tract, other documented sites of infection are skin, prostate, eye, and osteomyelitis. Skin is the third most common site of infection after CNS and pulmonary infections. Lesions often mimic other skin infections, therefore a skin biopsy with culture and histopathology are necessary for definitive diagnosis. Primary cutaneous cryptococcosis is very rare and is mostly associated with injury to dermis and direct inoculation of the yeasts; thus, the appearance of cutaneous lesions usually heralds the presence of disseminated infection. Solid organ transplant recipients on tacrolimus seem to be more likely to develop skin, soft tissue, and osteoarticular infections owing to *Cryptococcus*[7]. Tacrolimus acts on the temperature signaling molecule calcineurin in *Cryptococcus* and has anticryptococcal activity at high temperatures, but it loses this direct antifungal activity as environmental temperatures decrease; this may in part explain the increased frequency of cutaneous lesions in patients receiving calcineurin inhibitors[8]. The prostate is not an uncommon site for cryptococcal infection, but prostatic infections are usually asymptomatic. *C. neoformans* infection has been recognized to disseminate in the bloodstream during urologic surgery on the prostate for other indications[9]. Urine and seminal fluid culture may remain positive for *Cryptococcus* even after initial antifungal treatment in poorly controlled AIDS patients.

There are no studies evaluating treatment of cryptococcal infection involving sites apart from lungs and CNS. In general, infection at a single site in the absence of CNS disease, fungemia or risk factors for immunosuppression may be treated with fluconazole (6 mg/kg

orally once daily) for 6-12 months[10,11]. Since the index patient had disseminated disease involving lymph nodes and splenic abscess, and there is no literature available on treatment of such conditions, he was treated with liposomal amphotericin B along with flucytosine and fluconazole. On follow-up, he demonstrated resolution of symptoms and fever with this empirical approach.

CONCLUSIONS

Although the most common cryptococcal infection is of CNS followed by pulmonary infection, it can rarely cause disseminated abdominal infections in AIDS patients including abscess formation, which can be treated with combination of liposomal amphotericin and flucytosine along with aspiration of abscess or pigtail drainage, followed by course of fluconazole and antiretroviral therapy.

Author contributions:
Dr. Mandip S. Bhatia and Dr. Ritu Attri wrote the first draft; Dr. Saurabh C. Sharda, Dr. Mandip S. Bhatia and Dr. Ritu Attri critically reviewed and edited the manuscript. MSB takes responsibility for the paper.

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Acknowledgements:
We acknowledge Professor Navneet Sharma for his guidance and support.

Consent for Publication:
Given by the patient and submitted to journal.

Availability of Data and Material:
It is available and submitted to the journal and available on genuine request addressed to bhatiamandip@gmail.com

Conflict of Interest:
The authors declare that they have no conflict of interests.

Funding:
None.

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