

## **Histoplasmosis Presenting as an Adrenal Mass in Immuno competent Patient: a Case Report**

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**Abstract:** Histoplasmosis is an important systemic fungal infection in endemic areas. The disease is not very frequently reported from India except for the north-eastern Indian states like West Bengal, which is considered as the endemic region for histoplasmosis. In the last two decades, histoplasmosis has been reported with increased frequency from other regions as well, but most of the cases are associated with AIDS. Here we report a case of progressive disseminated histoplasmosis presenting as bilateral adrenal mass with pain abdomen and altered sensorium in an immuno competent patient from the state of Andhra Pradesh.

**Keywords:** Histoplasmosis, Progressive Disseminated Histoplasmosis, immuno competent host, Adrenal mass

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### **INTRODUCTION**

Histoplasmosis is a cosmopolitan systemic mycosis caused by the fungus *Histoplasma capsulatum*. Although histoplasmosis can affect healthy individuals, the disease has been frequently related to immunocompromised patients [1]. Severe manifestations are common with rapid progression being in many cases lethal. Facing that, a precise and quick diagnosis is needed to ensure efficient treatment [2]. Approximately 10% of individuals infected with histoplasmosis may develop progressive disseminated histoplasmosis which usually presents with fever, malaise, hepato splenomegaly and lymphadenopathy. Other manifestations of PDH include pancytopenia, renal failure, disseminated intravascular coagulation (DIC), skin lesions, gastrointestinal manifestations like diarrhea, and vomiting, neurologic manifestations like encephalopathy, focal parenchymal lesions and sometimes adrenal insufficiency [3]. The infection occurs after initial exposure to *H. capsulatum* by inhaling the spores present in the environment. Once inhaled into the alveoli, the organism readily spreads in macrophages throughout the reticulo endothelial system [4]. At the same time, the conidia transform into yeast-like cells, characterizing the dimorphism of this species. Many foci were observed after accidental exposure to great amount of bird and bat feces on endemic and non-endemic areas [5]. There are some case reports describing infections caused by *H. capsulatum* after tourism trips [6].

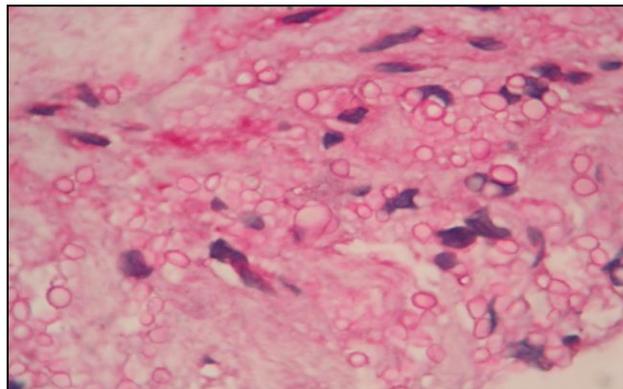
### **CASE REPORT**

A male ex-army man aged 57 years old, married, resident of Cumbum, Draga village, Andhra Pradesh was admitted on day 0 to a tertiary care hospital in Hyderabad with complaints of pain abdomen and altered sensorium for last 15 days. He complained of nausea, though there was no history of vomiting and fever. His appetite was decreased and bowels were irregular, micturation was normal. He was non smoker, takes alcohol occasionally.

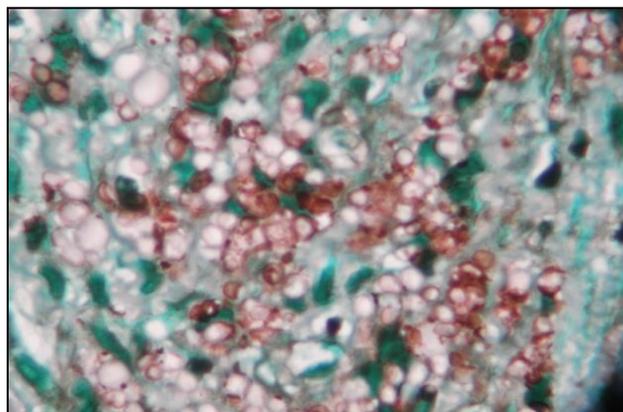
At admission on day 0, on examination patient was conscious but with altered sensorium. Physical examination revealed tenderness in lower abdomen without any radiation. Laboratory workup done on day +1 revealed haemoglobin 14 gm/dl; total leukocyte count of 12,000/mm<sup>3</sup>, with differential count of neutrophils 64%, lymphocytes 33%, monocytes 2% and eosinophils 1%. Platelet count was 2.5 lakh. Serum electrolytes and ESR were in normal limits. Random blood sugar, glycosylated haemoglobin, coagulation profile, liver function test were all within normal limits. ELISAs for anti-nuclear antibodies, HIV antibody and HIV antigen were all negative. Mantoux test was also negative. Complete urine examination showed +1 proteinuria, granular cast and 80 – 90 pus cells. Serum creatinine was 3.8 mg/dl. Urine was sent for culture sensitivity on +2 day, which showed significant growth of *Escherichia coli*.

In view of altered sensorium and pain abdomen, a CT head and CT abdomen without contrast was done on day +3. CT head showed age related atrophy and no other abnormalities. CT abdomen showed heterogenous mass lesions on both adrenal glands with minimal perilesional fat with no evidence of internal calcification. On day +4 serum cortisol levels were investigated and it was 0.93 mcg/dl at 8:00 am and was 0.61 mcg/dl at 4:00 pm. Serum cortisone was 61.71. In view of adrenal mass, ultrasound guided FNAC of right adrenal mass was done and 20cc pus

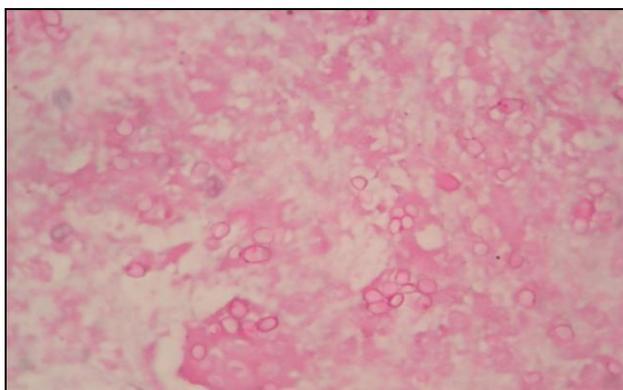
was aspirated which was sent for cytological and microbiological studies. Cytological features were consistent with acute suppurative inflammation. Histopathological examination showed necrosis of the tissue along with the sheets of foamy histiocytes embedded within were small round to ovoid budding yeast cells (Fig 1). Special stains like Periodic acid schiff (PAS) and Gömöri methanamine silver (GMS) stains confirmed the presence of fungal yeast cells (Fig 2).



**Fig -1: Heamatoxylin and Eosin stain of pus showing foamy histiocytes and ovoid budding yeast cells**



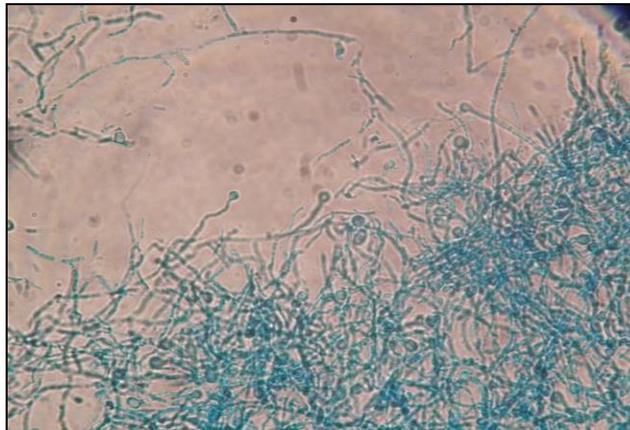
**Fig -2: GMS stain showing budding yeast cells stained brownish black in colour**



**Fig -3: Gram stain of pus showing clear unstained spaces of budding yeast cells**



**Fig -4: Growth on SDA slant after 10 days of incubation**



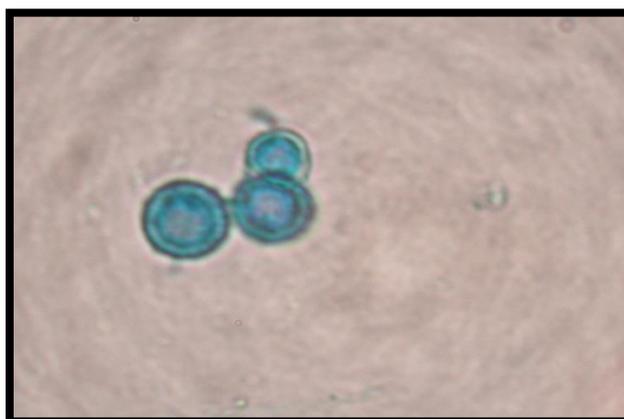
**Fig -5: LCB mount showing hyaline branched septate hyphae with terminal microconidia**



**Fig -6: Growth on SDA slant after 17 days of Incubation**



**Fig -7: LCB mount showing numerous double walled macroconidia**



**Fig -8: LCB mount of double walled macroconidia with tuberculate projections**

Microbiological examination of pus showed yeast cells in KOH mount and unstained clear spaces of budding yeast cells in Gram stain (Fig 3). Pus was cultured on sabourauds dextrose agar slant with chloramphenicol and incubated at 25°C and 37°C for fungal growth. There was off-white cottony mycelial growth on SDA slant kept at 25°C after 10 days of incubation i.e. day +14 (Fig 4). Lactophenol cotton blue mount (LCB) of growth showed hyaline branched septate hyphae with smooth walled terminal microconidia (Fig 5). Further incubation for one week, on + 21 day showed numerous double walled macroconidia with tuberculate projections along with microconidia on LCB mount (Fig 6,7,8). As the macroscopic and microscopic features were consistent with histoplasma it was provisionally identified as *Histoplasma capsulatum*.

#### **Treatment**

In view of pus cells in urine patient was started on antibiotics on day +2 with injection Ciprofloxacin 500 mg i.v. twice daily for 7 days i.e., till +9 days when again urine was sent for complete urine examination which showed no pus cells. In view of abnormal renal parameters and adrenal crisis, patient was treated accordingly with diuretics and corticosteroids

Dexamethasone from day +3, to which he responded well and showed improvement in his altered sensorium.

On day +6 after histopathological reports and microbiological report showing budding yeast cells in pus, he was started on antifungal treatment with injection Amphotericin B deoxycholate i.v. at a daily dose of 1mg/kg b.wt. Pain abdomen gradually subsided and the patient's appetite improved. He was continued on this for 14 days, then shifted on oral Itraconazole 200mg twice daily on day +20 and was planned to continue for 6 months. Patient was discharged on day +21 in conscious and coherent state with no symptoms and was called for follow up after 1 month.

#### **Follow up**

Patient reported to general medicine outpatient department for follow up on day +51. Patient was asymptomatic and was feeling good. A repeat ct abdomen was done which showed regression of mass in both adrenal glands present earlier. Patient's renal and liver functions were within normal limits. Patient was asked to continue with oral Itraconazole and to come for follow up again after 1 month but the patient did not turn up.

## DISCUSSION

"Histoplasmosis capsulatum" is found throughout the world. Histoplasmosis has been reported in immuno competent and immunocompromised individuals with the disseminated forms being more common in the latter group. PDH develops mostly in patients who are immunocompromised and are unable to mount an effective CMI response to the organism. This includes patients with AIDS [3, 7] transplant recipients [3, 7, 8], those with hematologic malignancies [3, 7], and those on corticosteroids [3, 7].

In the present case, the patient had no major identifiable underlying immuno compromising condition. The risk factors for acquiring the infection include, occupations involving disruption of soil rich in bird and bat guano like, agriculture, outdoor construction and rehabilitation of buildings inhabited by birds [9]. The present patient was an army man by occupation and could have been exposed to contaminated soil during the course of his work.

The disease is not very frequently reported from India except for the north-eastern Indian states like West Bengal, which is considered as the endemic region for histoplasmosis [12, 13]. In the last two decades, histoplasmosis has been reported with increased frequency from other regions as well and most of the cases are associated with AIDS. S Subramanian et al in 2005 in their study found that 60% of patients were from South India and 40% were from West Bengal [7]. This seems to indicate that histoplasmosis has no particular predilection to East India as was hitherto believed. There have been sporadic reports of histoplasmosis in patients from Andhra Pradesh [7, 8].

Another notable feature in the present case was the presence of adrenal mass in the patient. There has been few case reports of Histoplasmosis in India isolated from unusual sites like oral histoplasmosis [14], semen [15], eye-lids [16]. The present case could be the first case report of isolation of *Histoplasma capsulatum* directly from the adrenal mass in a patient from Andhra Pradesh. Despite a high proportion (80%) of adrenal gland affection detected via imaging studies and autopsy findings, clinical manifestation of adrenal insufficiency is uncommon, and occurs in only about 7-20% [17]. The adrenal gland affection may be silent or may present as unilateral or bilateral adrenal masses [18]. Gopalkrishnan *et al.*; 2012 retrospectively analysed the medical records of Apollo hospital of which 24 patients were diagnosed to have histoplasmosis of whom 23 were male. Bilateral adrenal enlargement was detected by imaging in 15 patients and adrenal insufficiency was noted in 4 patients [19].

## CONCLUSION

In the present case, histoplasma was successfully cultured from the adrenal mass pus. However, in most of the other reports from India, diagnosis of adrenal involvement in histoplasmosis is based on histopathology and imaging alone and only few are culture proven. Although, in many patients with PDH, spontaneous remission is known to occur, antifungal therapy initiation is mandatory with amphotericin B and itraconazole being the preferred antifungal and fluconazole, a second line antifungal [3]. In the present case, treatment with Itrconazole at the appropriate dose, proved effective; the lesion healed completely within a few weeks of starting treatment.

PDH should always be considered in the differential diagnosis of adrenal mass, irrespective of the patient's immune status and endemicity of the disease in the region. Recognition of the varied and confounding clinical presentations of histoplasmosis, good diagnostic laboratory facilities and extensive population based studies to know the endemicity of the disease in different regions are all necessary for improved understanding of the epidemiology of histoplasmosis.

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