

Case Report

Progressive disseminated histoplasmosis presenting like chronic parenchymal liver disease with ascites: a rare case report and discussion

Arnab Banerjee*

Department of Internal Medicine, IPGMER, Kolkata, West Bengal, India

Received: 16 July 2014

Accepted: 9 August 2014

***Correspondence:**

Dr. Arnab Banerjee,

E-mail: milu_ban@yahoo.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

A 82 year old diabetic and hypertensive Muslim man presented with ascites along with features of portal hypertension. Though it initially seemed to be a primary case of chronic parenchymal liver disease, investigations revealed it to be a case of Progressive Disseminated Histoplasmosis (PDH) with bilateral adrenomegaly, hepatosplenomegaly and ascites. The ascites was high SAAG in nature and no evidence of malignancy or tuberculosis could be found. The patient was treated with liposomal amphotericin B and was subsequently discharged on oral itraconazole therapy. On follow-up he was found to be significantly better at 3 months.

Keywords: Progressive disseminated histoplasmosis, Adrenomegaly, Ascites, Chronic parenchymal liver disease

INTRODUCTION

Histoplasma capsulatum, a thermal dimorphic fungi is the etiopathological agent of histoplasmosis. It can be of 2 types: pulmonary & extrapulmonary. The extrapulmonary form is also known as disseminated histoplasmosis and it can affect virtually any organ of the body, with or without organ failure. The infection is primarily by the inhalation of microconidial spores of *H. capsulatum*.

It can present in different ways but ascites is very uncommon in these patients. We describe a patient who presents with ascites and is ultimately diagnosed to be a case of PDH.

CASE REPORT

A 82 year old Muslim man from a district named Murshidabad of West Bengal, India presented on 1st Nov, 2013 with gradual swelling of the abdomen for the last 6 months followed by slowly progressive respiratory distress for the last three months. He was a wood-cutter

by profession but has been enjoying retired life for the last 10 years. A known hypertensive and diabetic for the last 15 years, the patient did not have any history of other major ailments throughout his life. There was no history of tuberculosis in him or his family members. No other significant symptoms like black stool, bloody vomiting, fever, abdominal pain or chest pain could be elicited. There wasn't any background history of smoking, alcoholism or unprotected sexual intercourse. Patient was on oral anti-diabetics and anti-hypertensives (metformin, glimepiride & ramipril) for the last 10 years.

On examination, the BP was 146/86 mm Hg, pulse rate - 88/min.....mild bilateral pitting edema and jaundice were present. Systemic examination revealed presence of tense ascites along with hepatosplenomegaly. No other significant abnormality was noted in spite of a thorough clinical examination.

Blood reports revealed the following results: Urea - 36 mg/dl, creatinine - 1.1 mg/dl, normal sodium & potassium, total bilirubin - 1.8 mg/dl, conjugated - 1.1

mg/dl, ALP - 1114 U/L, ALT - 36 U/L, AST - 87 U/L, albumin - 2.4 g/dl, globulin - 3.6 g/dl, GGT- 542 U/L. Hemoglobin, total and differential count were within normal limits but ESR was 73 mm/hr. Eosinophilia was absent (2%, absolute count 106/mm³). PT, APTT, INR were normal, serum AFP- WNL. Ascitic fluid albumin - 1.0 g/dl (SAAG - 1.4 g/dl.....high), ascitic fluid cell count was 200/mm³ (N₃L₉₇), ascitic fluid gram stain, fungal stain, AFB stain and culture were all negative. Ascitic fluid for M cells was also negative twice. Serum ammonia was normal. HbA_{1C} - 7.2%, Mantoux test - negative, sputum for AFB - negative, HIV I/II - negative, HBsAg/anti-HCV - negative. CXR was normal...USG revealed ascites with hepatosplenomegaly with some sub-centimeter periportal lymph nodes with bilateral adrenomegaly. CECT abdomen also gave us similar features (Figure 1 & 2). An 8 AM serum cortisol was found to be normal - 18.34 microgram/dl (normal: 4.3-22.40) (ACTH stimulation test could not be done due to non-availability of the drug during that time in this area). We went for a CT guided FNAC from the adrenal gland (Figure 2) which subsequently showed us spores of *Histoplasma capsulatum* on a background of necrotising inflammation with a few macrophages and acute inflammatory cells on histopathological examination followed by fungal staining (Figure 3).

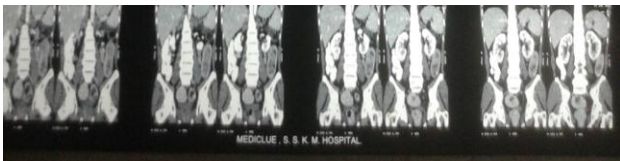


Figure 1: Bilateral adrenomegaly with hepatosplenomegaly in CECT abdomen.

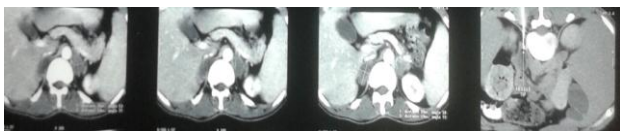


Figure 2: CT guide FNAC from adrenal gland in the same patient.

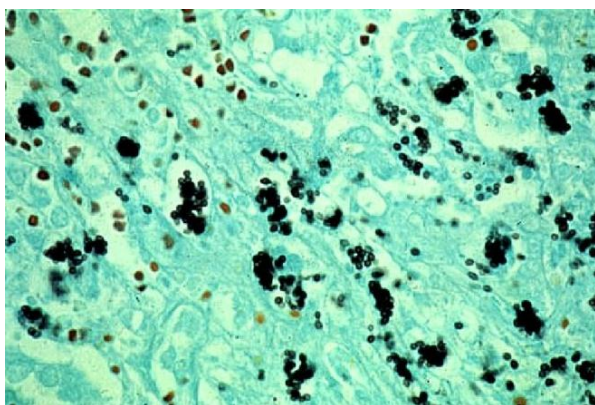


Figure 3: HPE of adrenal FNAC showing spores of *H. capsulatum* (Grocott's stain).

A provisional diagnosis of progressive disseminated histoplasmosis with reactive ascites was made and the patient was started on liposomal amphotericin B. Therapeutic abdominal paracentesis was done to provide symptomatic relief to the patient. Other supportive management was also given. But after 7 days of therapy, the patient eventually refused to stay any more in the hospital and for this reason he was discharged with oral itraconazole therapy (200 mg bid*1 year).

The patient came for follow-up after three months....he was doing fine on itraconazole therapy....his ascites has reduced considerably from before....and he was also taking his regular anti-hypertensive & anti-diabetic medications.

DISCUSSION

Histoplasma capsulatum, a thermal dimorphic fungus, is the causative organism of histoplasmosis. Histoplasmosis can be of two types: pulmonary & extrapulmonary or disseminated. Histoplasmosis is the most prevalent endemic fungal infection in North America. Although this fungal disease has been reported throughout the world, its endemicity is particularly notable in certain parts of North, Central, and South America; Africa; and Asia. This is due to the humid and acidic nature of the soil in these areas. Soil enriched with bird or bat droppings provides a congenial environment for the growth and sporulation of *Histoplasma*. Disruption of soil containing the organism leads to aerosolization of the microconidia and exposure of human beings who are close enough. Activities associated with high-grade exposure include spelunking, excavation, cleaning of chicken coops, demolition and remodeling of old buildings, and cutting of dead trees. After inhalation of the microconidia, they are phagocytosed by the alveolar macrophages....here; the microconidia are transformed into budding yeasts. The persistence of these organisms is dependent on the iron and calcium concentration in the phagosomes.¹ From the alveoli, the yeasts are transported by the phagosomes to the local draining lymph nodes...and from there hematogenous spread of these yeast infected phagosomes distribute them to the various organs of the body...resulting in disseminated histoplasmosis. Progressive disseminated histoplasmosis (PDH) can involve multiple organs, most commonly the bone marrow, spleen, liver, adrenal glands, and mucocutaneous membranes. In the immunocompetent host, macrophages, lymphocytes, and epithelial cells attack the site of infection & form granulomas that contain the organisms. But in immunocompromised individuals with conditions like AIDS (CD4+ T cell count, <200/L), extremes of age, use of immunosuppressive drugs like steroids, methotrexate, or anti-TNF agents and diabetes, these containment is deficient leading to dissemination of the organism.²

Most *Histoplasma* infections are either asymptomatic or mild and self-limited. Heavy exposure can lead to a

flulike illness with fever, chills, sweats, headache, myalgia, anorexia, cough, dyspnea, and chest pain. CXR show signs of pneumonitis with hilar or mediastinal lymphadenopathy.³ The spectrum of PDH may range from an acute, rapidly fatal course - reticulonodular or diffuse interstitial lung involvement leading to respiratory failure, shock, DIC (disseminated intravascular coagulopathy), and multiorgan failure - to a more sub-acute course with a focal organ involvement. Common manifestations include fever, weight loss, hepatosplenomegaly. Meningitis or focal brain lesions, oral mucosal & gastrointestinal ulcers, adrenal insufficiency can also be there.⁴ Fibrosing mediastinitis is an unusual but serious complication of histoplasmosis. It can lead to superior vena cava syndrome, obstruction of pulmonary vessels and airway, recurrent pneumonia, hemoptysis, or respiratory failure.⁵ This condition is fatal in up to one-third of cases. Pericarditis can be there but ascites is very, very uncommon.⁶

It is generally diagnosed by tissue samples (biopsy, FNAC, BAL fluid etc.) by histopathological exam followed by fungal staining or by fungal cultures. Detection of antigen in body fluids (like CSF) can be extremely helpful, as is a skin allergy testing. A number of antigen & antibody detection methods (precipitating and complement-fixing antibody) have been developed. A fourfold or greater rise in titre over a 1 month period is necessary for the diagnosis of histoplasmosis.

In our patient, diabetes mediated immunosuppression led to a disseminated histoplasmosis involving the adrenals, liver, spleen and lymph nodes. Obstruction by the periportal lymph nodes led to an obstructive jaundice. The high SAAG ascites may be a result of an occult chronic parenchymal liver disease from before leading to portal hypertension or may be reactive in nature resulting from PDH. It may also be due to histoplasma induced liver disease. A liver biopsy could have diagnosed chronic liver disease but since ascites was present, a liver biopsy could not be done. However, we must bear in mind that ascites can be associated with PDH. Though further studies are necessary to draw any conclusion, we must be careful about the possibility of PDH in a patient presenting like chronic liver disease.

CONCLUSION

Though histoplasmosis is quite a common disease in the endemic region, still it can present in different ways. As seen in this patient, it can also present like chronic parenchymal liver disease along with ascites...so any patient with such picture from an endemic region must be evaluated thoroughly before jumping into any diagnosis. To end with "Truth is stranger than fiction".

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

REFERENCES

1. Goswami RP, Pramanik N, Banerjee D, Raza MM, Guha SK, Maiti PK. Histoplasmosis in eastern India: the tip of the iceberg? *Trans R Soc Trop Med Hyg.* 1999;93:540-2.
2. Kauffman CA. Histoplasmosis: a clinical and laboratory update. *Clin Microbiol Rev.* 2007;20:115.
3. Hage CA, Bowyer S, Tarvin SE, Helper D, Kleiman MB, Wheat LJ. Recognition, diagnosis, and treatment of histoplasmosis complicating tumor necrosis factor blocker therapy. *Clin Infect Dis.* 2010;50:85-92.
4. Vyas S, Kalra N, Das PJ, Lal A, Radhika S, Bhansali A, et al. Adrenal histoplasmosis: an unusual cause of adrenomegaly. *Indian J Nephrol.* 2011 Oct-Dec;21(4):283-5.
5. Faisal A. Khasawneh, Subhan Ahmed, Ruba A. Halloush. Progressive disseminated histoplasmosis presenting with cachexia and hypercalcemia. *Int J Gen Med.* 2013;6:79-83.
6. Dan Longo, Anthony Fauci, Dennis Kasper, Stephen Hauser, J. Jameson, Joseph Loscalzo. Histoplasmosis. In: Chadi A. Hage, L. Joseph Wheat, eds. *Harrison's Principles of Internal Medicine.* 18th ed. New York: McGraw-Hill Professional; 2011: Chapter 199.

DOI: 10.5455/2320-6012.ijrms20141186

Cite this article as: Banerjee A. Progressive disseminated histoplasmosis presenting like chronic parenchymal liver disease with ascites: a rare case report and discussion. *Int J Res Med Sci* 2014;2:1699-701.