CASE REPORT

Chronic Progressive Disseminated Histoplasmosis in an Immunocompetent Host – A Case Report

ABSTRACT

An elderly male patient presented with fever, breathlessness, and weight loss for 4 months. He was pale and had mild hepatosplenomegaly. His blood counts revealed anemia and thrombocytopenia. His bone marrow aspirate showed macrophages loaded with yeast-like cells, on Giemsa stain, suggestive of *Histoplasma capsulatum*. There was growth of *H. capsulatum* (mycelial form) in the bone marrow culture. He was treated initially with amphotericin B and then with oral itraconazole. However, the patient expired due to disseminated disease and late referral to tertiary care center.

Key words: Chronic progressive disseminated histoplasmosis, *Histoplasma capsulatum*, Immunocompetent

INTRODUCTION

Histoplasmosis, a disease caused by a dimorphic fungus *Histoplasma capsulatum*, occurs worldwide. This disease is till now, sporadic in India.[1] Histoplasmosis has three main types of clinical presentations-acute primary, chronic cavitatory, and progressive disseminated.[1] Immunocompetent middle aged to older adults typically present with chronic progressive course of disseminated histoplasmosis. This form of histoplasmosis is more common in males than females. Usual presentation is low-grade fever, malaise, and oropharyngeal ulcers. Chest X-ray may show patchy infiltration in one or more lobes along with lymphadenopathy.[2] This is a case report of a non-immunocompromised patient who presented with the chronic progressive disease, probably because of prolonged exposure and late diagnosis.

Asmita Sagar Sakle

Department of Microbiology, Bombay Hospital and Medical Research Center Mumbai, Mumbai, Maharashtra, India

Corresponding Author:
Asmita Sagar Sakle,
Department of Microbiology, Bombay Hospital and Medical Research Center Mumbai, Mumbai, Maharashtra, India.
E-mail: asmiband@gmail.com

CASE REPORT

A 63-year-old male patient presented with complaints of fever with chills, headache, and weight loss for 4 months. He was having breathlessness for 4 months which got exaggerated since a week. On general examination, the patient was pale, febrile. Systemic examination revealed hepatosplenomegaly and lymphadenopathy. Computed tomography scan showed pulmonary fibrosis. A differential diagnosis of malaria/typhoid was thought of due to the presence of fever and hepatosplenomegaly. He was given antimalarials, steroids, and antibiotics ofloxacin and cefpodoxime.

Blood counts showed anemia and thrombocytopenia. Malarial antigen test as well as peripheral smear for malarial parasite (thick and thin) was negative. Widal test was negative. HIV 1 and 2 antibody test was negative. Bone marrow aspirate stained by Giemsa stain showed oval globose yeast-like cells measuring 2–4 μm in size, suggestive of *H. capsulatum* [Figure 1]. Yeast-like cells with bright eosinophilic nuclei and clear halo round them highly suggestive of *H. capsulatum* were seen on periodic acid–Schiff stained bone marrow biopsy slides. Bone marrow aspirate culture on Sabouraud's agar showed white cottony mycelial growth of *H. capsulatum* after 10 days of incubation at 25°C. Lactophenol cotton blue (LPCB) mount prepared from the growth on Sabouraud's agar showed large (8–10 μ) thick-walled spherical spores with tubercles or finger-like projections [Figure 2]. The mycelial form was converted to yeast form by repeated subcultures in brain heart infusion broth at 37°C, thereby confirming the diagnosis.

DISCUSSION

A dimorphic fungus *H. capsulatum* is found in the temperate regions of the world. It is endemic in the Ohio and Mississippi river valleys of the United States of America.[3] The soil and bird or bat droppings contaminated areas possess mycelial form of *H. capsulatum* as such places provide added nutrients for the mycelia growth of this fungus.[3] In endemic areas, infections are typically caused by wind-borne spores arising from point sources such as bird roosts, old houses or barns, or activities where there is disruption of the soil such as farming

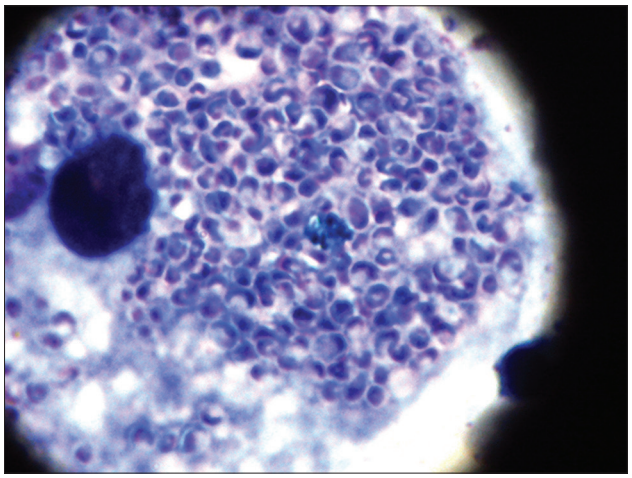

Figure 1: Bone marrow giemsa stain

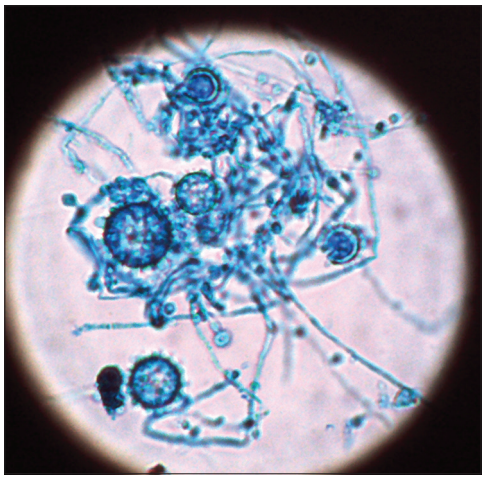

Figure 2: LPCB mount of *H.capsulatum*

and excavation.[3] Histoplasmosis is also known as Darling's disease because in 1905, Darling discovered this organism during an autopsy and named it *H. capsulatum* considering it to be an encapsulated plasmodium.[4] It was DeMonbreum, who, in 1934, recovered it from a fatal case and proved it to be a fungus and not a protozoan.[4] In 1954, the first case of histoplasmosis in India was reported.[5] Subsequently, several cases have been reported from different regions of India.[1]

The patient was a resident in part of Ramgarh village in Rajasthan commonly inhabited by pigeons. Pigeon droppings might have served as the potential source of infection in this case.

In 95% of cases, infection with *H. capsulatum* is asymptomatic. In immunocompetent individuals, it usually presents as respiratory infection comprising fever, malaise, cough, and chest pain that are self-limiting. Chest X-ray may show focal infiltrates and hilar or mediastinal lymphadenopathy.[6] There may be systemic dissemination of initial pulmonary infection with hematogenous spread, leading to extrapulmonary manifestations. The lymphatics or the liver and spleen may lead to hematogenous spread to regional lymph nodes.[7] The slowly progressive and generally fatal infection due to *H. capsulatum* is known as chronic progressive disseminated histoplasmosis (PDH) and this form of the disease mostly occurs in older adults that are not evidently immunosuppressed. Although such patients do not have obvious immunosuppression, their macrophages cannot effectively kill *H. capsulatum*.[7] In the present case, the patient is a 63-year-old individual who is immunocompetent, yet showed significant hepatosplenomegaly with bone marrow involvement.

Although fungal staining of tissue and blood is a rapid test for laboratory diagnosis of histoplasmosis, it has a significantly lower sensitivity than culture or antigen detection.[3] Fungal staining of bone marrow has the highest yield, staining positive in as many as 75% of cases of disseminated disease.[3] Yet, fungus culture is the gold standard test for diagnosis of histoplasmosis. However, culture test is slow and results may not be ready for up to 1 month.[8] In about 75% of cases of PDH, cultures are found to be positive.[8] In PDH, culture yield is highest from bronchoalveolar lavage fluid, bone marrow aspirate, and blood.[9] The present case was diagnosed as chronic PDH on the basis of fungal staining of bone marrow and involvement of liver and spleen. Furthermore, we could isolate *H. capsulatum* from bone marrow aspirate within 10 days. Subramanian *et al*.[9] stated that diagnosis of histoplasmosis by histopathology and/or culture from bone marrow, adrenal gland, lymph node, etc., is confirmatory.

The severity of the clinical syndrome decides the treatment of histoplasmosis. Symptomatic treatment is sufficient in mild cases, but in cases of chronic or disseminated disease and in severe or prolonged acute pulmonary infection, antifungal therapy is indicated.[3] Liposomal amphotericin B for 1–2 weeks is considered the treatment of choice in severe or disseminated disease. This is followed by oral itraconazole for at least 12 months.[8] In the present case, the patient was given amphotericin B but he could not survive, may be because of severe disseminated histoplasmosis and late initiation of treatment.

The PDH occurs in 1 case per 2000 cases in adults who are immunocompetent.[10] Death occurs within 2–24 months in untreated cases of subacute form and within weeks in untreated cases of acute form.[10] Histoplasmosis is as yet a sporadic disease in India. There have been few reports of histoplasmosis in patients from Andhra Pradesh,[11] Maharashtra, and other parts of the country.[1] In Asia Pacific region, lack of adequate laboratory facilities, limited experience with fungal infections, and few epidemiological surveys may give inaccurate epidemiological picture of endemic fungal infections.[12]

CONCLUSION

Though histoplasmosis is uncommon in immunocompetent individuals, it should be considered as a differential diagnosis in patients with chronic fever and hepatosplenomegaly.

Early diagnosis and timely antifungal treatment can help in preventing lethal complications.

REFERENCES

1. Sane SY, Patel MG, Patel BM, Kokal KK. Disseminated histoplasmosis (a case report). J Postgrad Med 1983;29:270-3.
2. Gray ND, Grossman C, Brath LK. Endobronchial and progressive disseminated histoplasmosis masquerading as metastatic cancer. Infectious disease cases by American College of Chest Physicians. Case reports. CHEST.2007;132:698.
3. Kurowski R. Ostapchuk M. Overview of histoplasmosis. Am Fam Physician 2002;66:2247-52.
4. Deepe Jr GS. Histoplasma capsulatum. In: Mandell GL, Benett JE, Dolin R (eds) Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. Philadelphia: Churchill Livingstone, 2000;2:2718-32.
5. Panja G, Sen S. A unique case of histoplasmosis. J Indian Med Assoc 1954;6:257-8.
6. Dutta AK, Sood R, Karak AK. Disseminated histoplasmosis-fulminant presentation in an AIDS patient. A case report. JIACM 2005;6:327-30.
7. Mukharjee A, Tangri R, Verma N, Gautam D. Chronic disseminated histoplasmosis bone marrow involvement in an immunocompetent patient. Indian J Hematol Blood Transfus 2010;26:65-7.
8. Hage CA, Wheat LJ. Histoplasmosis. In: Harrison's Principles of Internal Medicine. 17th ed., Vol. 1. New York: McGraw Hill Education; 2008. p. 1244-6.
9. Subramanian S, Abraham OC, Priscilla R, Zachariah A, Mathews MS, Mathai D. Disseminated histoplasmosis. J Assoc Physicians India 2005;53:185-9.
10. Kauffman CA. Histoplasmosis: A clinical and laboratory update. Clin Microbiol Rev 2007;20:115-32.
11. Subbalaxmi MV, Umabala P, Paul R, Chandra N, Raju YS, Shivaprakash M, *et al.* A rare presentation of progressive disseminated histoplasmosis in an immunocompetent patient from a non-endemic region. Med Mycol Case Rep 2013;2:103-7.
12. Chakrabarti A, Slavin MA. Endemic fungal infections in the Asia pacific region. Med Mycol 2011;49:337-44.

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