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Disseminated Histoplasmosis in an Immunocompetent Patient - A Case Report

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ABSTRACT

Histoplasmosis is a fungal infection is caused by the dimorphic fungus Histoplasma capsulatum. In the immunocompromised host, a disseminated form of the disease can be frequent. We provide a case of disseminated histoplasmosis in an immunocompetent young person, emphasising the significance of maintaining a high index of suspicion even in immunocompetent people, particularly in developing countries like India. (1)

Keywords- *Histoplamsa, fungal infection, immunocompetent.*

INTRODUCTION

Darling's disease, also known as histoplasmosis, is a systemic fungal illness caused by the dimorphic fungus Histoplasma capsulatum, which can take the shape of mycelia or yeast. In India, the disease is predominantly seen in the eastern half of the country, particularly West Bengal *2* ,*3.* Histoplasmosis is typically seen in immunocompromised patients, but here we discuss an immunocompetant patient acquiring the disease, the clinical presentation , the treatment and outcome of the patient.

CASE REPORT

For a period of six months, this patient, a 31-year-old building contractor from Bihar, India, who had recently been diagnosed with Type 2 diabetes mellitus, complained of dyspnea, dry cough, and constitutional symptoms including gradual weight loss, loss of appetite, and fever.

He had been the subject of a number of Tuberculosis investigations in his hometown. They were all negative, but he was started on empirical treatment in view of high clinical suspicion. However he continued to have progressive symptoms with persistent cough , fever and weight loss and was admitted with hemodynamic instability at a local hospital in his hometown. He was found to have miliary lesions on both lung fields , bilateral hilar lymphadenopathy and bilateral enlargement of adrenal glands on CT chest and USG abdomen imaging respectively. He was continued on ATT and was started standard dose regimen of HRZES and steroids (Wysolone 30mg) in suspicion of adrenal insufficiency with military TB.

He was admitted at our hospital for further evaluation as his symptoms began to worsen. On examination he was dehydrated, hypoxic with SPO2 - 90% at room air and hypotensive with BP of 90/60mm Hg. He was started on inotropes and oxygen supplementation (6 litres of O2 via face mask).

General examination revealed oral thrush and generalized lymphadenopathy involving the cervical, axillary and inguinal lymph nodes. The largest being the left axillary lymph node of size-2*3 cm. The nodes were non tender, firm in consistency and mobile. Systemic examination revealed splenomegaly and coarse crepts on both lung fields. He was admitted in the ICU for intensive monitoring and further evaluation.
His initial investigations revealed pancytopenia, cholestasis as mentioned below. Serological tests for HIV, Hepatitis B, C were negative.

Investigations (first 24hrs)	
Hb	10.2gm/dl
Total count	2,900 cells/mm3
Differential count	Neutrophils- 94% , Lymphocytes- 2%, monocytes –2%
Platelet count	45,000cells/mm3
Creatinine	1.2
Total bilirubin	1.0mg/dl
Direct bilirubin	0.4mg/dl
Indirect bilirubin	0.6mg/dl
SGOT	95IU
SGPT	7IU
ALP	393IU
GGTP	149IU

Radiological investigations –X -ray chest revealed diffuse mottling with military infiltrates. CT chest revealed mottling, nodular septal thickening with bilateral hilar lymphadenopathy (as shown in the picture below).

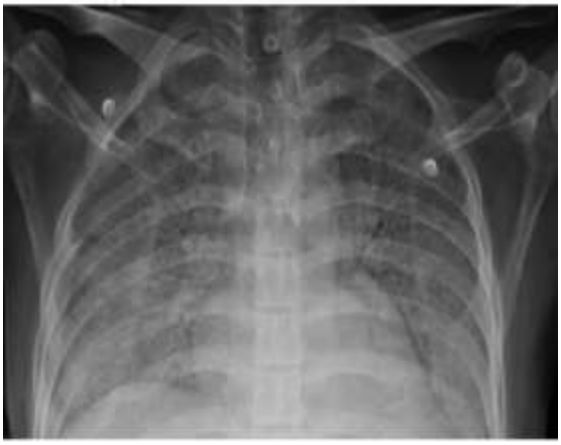

Figure 1.X-RAY CHEST - BILATERAL DIFFUSE MILIARY INFILTRATES

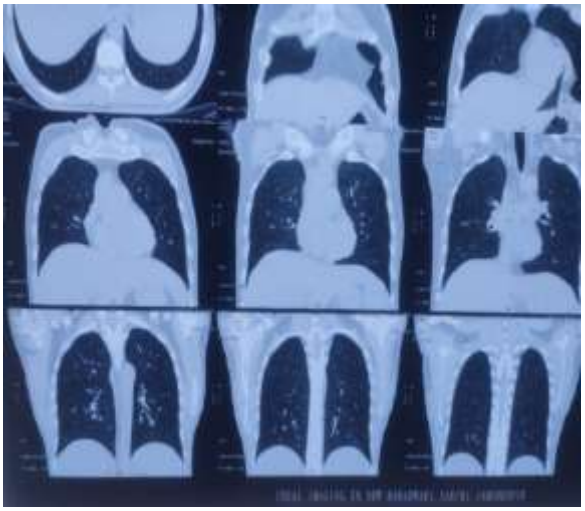

Figure 2 CT chest revealed diffuse GGOS with nodular septal thickening and mottling in bilateral lung fields.

He tested negative for COVID19 RTPCR . He underwent Bronchiovalevoalr lavage and sputum was also tested for X-PERT MTB and AFB stain , which were negative. BAL was also negative for Gram staining and fungal staining.
His hypoxia continued to worsen and he was intubated due to severe respiratory distress. Considering his clinical history with progressive deterioration despite being on ATT, generalized lymphadenopathy, negative work up for Tuberculosis, bilateral bulky adrenals with adrenal insufficiency Progressive disseminated form of Histoplasmosis was suspected.
Urine histoplasma antigen was therefore sent and turned out to be positive. Left axillary lymph node biopsy was performed. It was negative for XPERT-MTB, Gram and fungal staining, however axillary lymph node biopsy HPE revealed cores of lymphoid tissue with many histiocytes enclosing tiny dot like organism positive for PAS stain suggestive of histoplasmosis. He was started on IV amphotericin B at a dose of 3mg/Kg/day. He was supported with mechanical ventilation, inotropes and intravenous steroids.

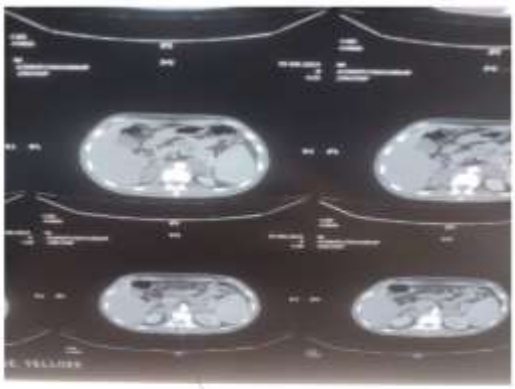

Figure 3. CT abdomen showing -Diffuse enlargement of bilateral adrenal glands (right gland- 6.1*3.3; left gland 6.3*2.9cm)

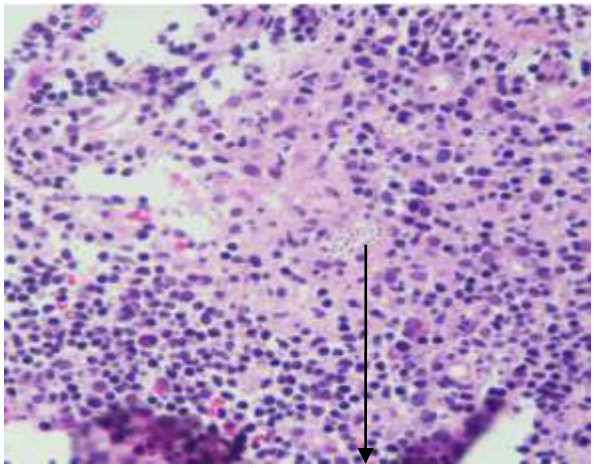

Figure 4. Histopathology of axillary lymph node Showing histiocytes with tiny PAS positive organisms.

Another major problem was his progressive cytopenias. He required support with multiple blood product transfusion –platelet and PRBCS. Hemophagocytic lymphohistiocytosis was contemplated as it well known to occur secondary disseminated forms of Histoplamosis. Bone marrow aspiration and biopsy was performed. Bone marrow aspirate revealed hypercellularity with significant hemophagocytosis .

He fulfilled the criteria for Hemophagocytic lymphohistiocytosis. Bone marrow biopsy revealed linear cores of lymphoid tissue with many histiocytes forming granulomas enclosing spherical organisms confirming Histoplasma Capsulatum by PAS staining (as shown below). He was continued on IV Amphotericin B , as treatment of the disseminated infection would likely suffice. Cytopenias was likely due to secondary hemophagocytic syndrome and would likely respond with anti-fungal therapy.

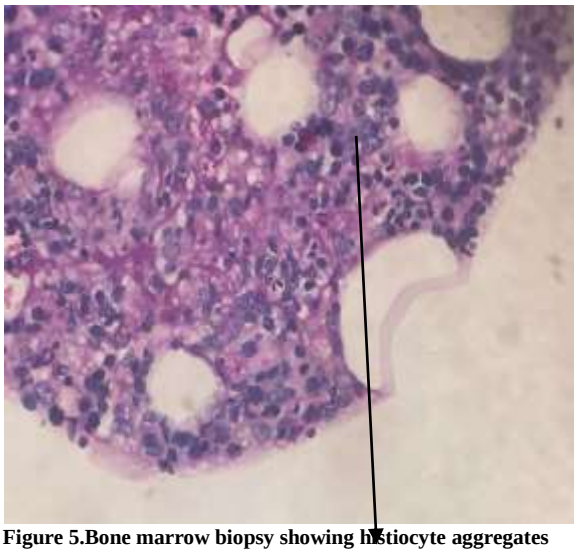

Figure 5.Bone marrow biopsy showing histiocyte aggregates And granulomas with PAS positive organisms.

Despite treatment with IV amphotericin B his hemdynamics remained unstable and he continued to require inotropes. Steroids were continued for support of his adrenal insufficiency, Serum cortisol and ACTH were measured . Both of which were low confirming adrenal insufficiency . He significantly improved with Amphotericin B and steroids. He was extubated and weaned off inotropes on (day 11). He completed the course of IV Amphotericin B for 2 weeks . He was discharged home with oral Posaconazole and oral hydrocortisone .

DISCUSSION

Darling's disease, also known as histoplasmosis, is a systemic fungal illness caused by the dimorphic fungus Histoplasma capsulatum, which can take the shape of mycelia or yeast. In India, the disease is predominantly seen in the eastern half of the country, particularly West Bengal *2* ,*3*

Infection is spread mostly through inhalation of infectious microconidia during activities such as cleaning chicken coops, visiting bat-infested caves, excavation, destruction of old structures, and cutting down dead trees, all of which result in soil

disruption and microconidia aerosolization. *3*

Histoplasmosis has three major clinical manifestations: pulmonary, progressive disseminated (PDH), and primary cutaneous . *4* Cutaneous manifestations are those that appear on the skin. Papules, plaques, pustules, and nodules, as well as erythematous papules and keratotic plaques, are examples of skin lesions. The face, trunk, and extremities are the most commonly affected areas *5* . PDH, on the other hand, is a reticuloendothelial system disease that affects the liver, spleen, lymph nodes, bone marrow, and adrenal glands, among other organs. In immunocompetent people, adrenal involvement is common *6* . The immunological status of the host determines the severity of the disease. The majority of infections in immunocompetent hosts (50–90%) result in self-limiting flu-like disease *3*. PDH manifests as chronic disease in immunocompetent hosts or acute progressive disease in immunocompromised persons who are unable to establish an efficient cell-mediated immune response against the pathogen *7*, as seen in tuberculosis*8* immunocompetent individuals may experience endogenous reactivation of the disease, which may manifest at a later stage of life.

Despite its limited sensitivity, histopathology remains a useful diagnostic tool because a positive result allows for the start of particular antifungal therapy. Cryptococcus neoformans, Blastomyces dermatitidis, Candida glabrata, Pneumocystis jirovecii, Coccidioides spp., Talaromyces marneffei, Leishmania spp., Trypanosoma cruzi, and Toxoplasma gondii are other pathogens to consider when developing a histopathologic diagnosis of histoplasmosis *9*. Differentiation of these infections is aided by the use of particular histochemical stains such as GMS and PAS. Urinary antigen detection is a valuable indication of therapy response since it is quick, non-invasive, and extremely sensitive. Because of cross-reactivity with antigens of other fungi that cause endemic mycoses, even modest positive (quantitative) and false positive test results have clinical importance [15]. Furthermore, this test is inexpensive and can be performed in standard laboratories in nations with limited resources *10* Serological tests such as complement fixation, immunodiffusion, and enzyme immunoassays can also used in the evaluation. Healing granulomas in the lungs, spleen, or liver may be seen on imaging. The affected lymph node or skin lesions can also be biopsied and histopathologically examined.

In terms of treatment, IV amphotericin B for two weeks should be followed by Itraconazole 200 mg twice daily for patients with severe disseminated histoplasmosis *11*. Patients with PDH usually require amphotericin-B induction therapy for two to four weeks, followed by a year of itraconazole treatment. There is evidence that liposomal amphotericin B produces superior results than other amphotericin B formulations *12*. IDSA currently does not suggest any other antifungal agents, but there have been cases of patients being treated with posaconazole and as salvage therapy in the maintenance phase instead of itraconazole and in the induction phase instead of amphotericin B*14*

Disseminated histoplasmosis is more common in immunocompromised patients; nevertheless, our patient was neither HIV positive nor on immunosuppressive drugs when he acquired histoplasmosis. It's unclear if this was due to a high fungus burden inhaled or a particularly aggressive strain of Histoplasma capsulatum.

CONCLUSION

On a number of levels, this situation is debatable.

To raise physician knowledge that though disseminated histoplasmosis is uncommon in immunocompetent people, it should be evaluated and counted as a differential diagnosis since DH can mirror many other disorders, particularly tuberculosis, it is often overlooked, particularly in countries

where tuberculosis is more prevalent, such as India.

It's often difficult to tell it apart from pulmonary tuberculosis because the symptoms and radiology are so similar. In places like India, where both of these diseases are widespread, a correct diagnosis is totally dependent on a high degree of suspicion and laboratory results.

Declaration by Authors

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