Progressive Disseminated Histoplasmosis with Coomb’s Positive Hemolytic Anemia in an Immunocompetent Host

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Abstract
Progressive Disseminated Histoplasmosis (PDH) is mainly described in immuno-compromised individuals and rare in immuno-competent subjects. Here we report a case of progressive disseminated histoplasmosis with Coomb’s positive hemolytic anemia, which is infrequently reported from a country like India where histoplasmosis is not an endemic mycosis.

Introduction
Histoplasma capsulatum, a thermal dimorphic fungus, is the etiologic agent of histoplasmosis. It is the most prevalent endemic mycosis in North America. Human infection is acquired by inhalation of mycelial forms. Clinically it manifests as three main types- acute pulmonary, chronic pulmonary/cavitatory and progressive disseminated histoplasmosis.¹ It can present as fever of unknown origin (FUO) in immuno-deficient as well as immuno-competent and non-neutropenic subjects. Although uncommon in Indian subcontinent, high index of suspicion is necessary for early diagnosis and treatment.

Case Report
A 30-year-old male patient was admitted in our hospital with complaints of high-grade fever with chills and rigors associated with profuse sweating since two months. He developed cough since last 20 days, that was non-productive in nature and had no diurnal variation. He complained of fatigue and exertional dyspnoea for last 8 days.

On general examination, the positive findings were fever (103°F) and pallor. Systemic examination revealed a tender palpable liver (4 cms below costal margin) and a non-tender palpable spleen (4 cms below costal margin). Rest of the systemic examination was normal.

Laboratory investigations revealed pancytopenia. Hemoglobin was 4.5 gm/dl, total leucocytes count was 1.66 × 10³/µl (differential leucocyte count showed N-60%, L- 37%, E-02%, B- 01%), platelet count was 56 ×10³/µl. Peripheral blood film examination was normochromic normocytic RBCs with thrombocytopenia and no atypical cells. Malarial antigen by card test and peripheral smears (thick and thin) were negative. Widal test and dengue profile were normal. Serum electrolytes and renal function tests were normal.

Chest x-ray had mild hilar prominence. HRCT thorax showed multiple enlarged lymph nodes in the pre and paratracheal region with confluent patches of ground glass haziness in bilateral lower lung fields suggestive of interstitial pattern of pneumonitis. Ultrasonography revealed hepatosplenomegaly.

Sputum for AFB, gram stain and KOH mount was negative. Blood and urine culture yielded no growth. Autoimmune workup showed positive CRP, negative ANA and positive direct coombs test suggesting autoimmune hemolytic anemia. Reticulocyte count was 6.8%. BM aspiration and biopsy showed erythroid hyperplasia with decreased megakaryocytes.

Discussion
Histoplasmosis is not an endemic mycosis in India. Majority of progressive disseminated histoplasmosis cases are diagnosed on immune-compromised hosts who cannot mount effective cell mediated immunity. There are few case reports in immuno-competent subjects from various parts of our country.² ⁴ Present case is probably first of its kind, diagnosed in an immuno-competent subject in our institution.

Bone marrow abnormalities in the form of cytopenias are reported due to diffuse marrow infiltration. Isolated thrombocytopenia is rare but reported.² In our case all three cell lineages were

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Received: 20.05.2015; Revised: 20.07.2015; Accepted: 17.08.2015
affected and there was pancytopenia. Despite bone marrow involvement, the bone marrow examination didn’t report conclusive pathology and we had to think of alternative diagnosis. Further we performed liver biopsy, keeping auto-immune hepatitis in our mind and asked pathologist to comment upon some infiltrative disorder with fungal stains. Here he identified the intracellular PAS positive and methylamine silver stained intracellular and extracellular pathogen as Histoplasma species.

Comb’s positive hemolytic anemia is rarely reported elsewhere as in our case with histoplasmosis. Acquired hemolytic anemia may be due to immune mediated as well as non immune mediated mechanisms.

For the management of moderately severe to severe histoplasmosis, liposomal amphotericin B is recommended for 1–2 weeks followed by oral Itraconazole 200 mg twice daily for at least 12 months. The deoxycholate formulation of amphotericin B is recommended as an alternative to the lipid formulation in patients who cannot afford or are at a low risk for nephrotoxicity. In our patient we started conventional amphotericin B for two weeks and then Itraconazole 200 mg twice daily. The patient is improving well and he is under close follow-up in medical OPD.

In conclusion, progressive disseminated histoplasmosis with hemolytic anemia is rarely reported in immuno-competent subjects from the Indian subcontinent. We as clinicians should keep this uncommon cause of fever of unknown origin (FUO), as differential diagnosis for early detection and management of this treatable illness.

References