Case Report

Progressive Disseminated Histoplasmosis in an Immunocompetent Host with Reversible CD4 Lymphocytopenia

Abstract

We report an 18-year-old male patient presented to us with complaints of fever and progressive weight loss for past 4 months. On examination, he also had multiple umbilicated papular to nodular lesions over his chin and forehead region. Blood count revealed anemia with leukopenia. An excisional biopsy of the skin lesion was suggestive of cutaneous histoplasmosis. On further investigations for anemia and leukopenia, he was found to have bone marrow histoplasmosis on trephine biopsy. Patient’s serology for HIV I and II was negative but his CD4 counts were low. Patient received amphotericin B and itraconazole. He showed remarkable improvement in his general condition and blood counts. A repeat CD4 count done at 4 months of treatment was also normal. Progressive disseminated histoplasmosis (PDH) presenting as cutaneous lesions in an immunocompetent host is very rare and has been reported in a few cases only.

Keywords: Progressive disseminated histoplasmosis, reversible CD4 depletion.

Background

Histoplasmosis is a fungal infection and prevalent worldwide, in which Ohio and Mississippi river valleys of North America have the highest prevalence. There are a few case reports of this fungal infection from non-endemic regions too. In India, histoplasmosis has been reported in large numbers from eastern states like West Bengal and a few cases from southern states as well. Other regions of the country rarely see any cases of histoplasmosis. Histoplasmosis is most commonly seen in immunosuppressed patients but there are a few case reports in immunocompetent hosts as well.

Case Presentation

An 18-year-old, unmarried male patient, resident of Delhi (central India), presented to our hospital with complaints of low-grade prolonged fever, loss of appetite and weight loss of 10 kg in last 4 months. No history of high-risk behavior, promiscuous sexual activities or blood transfusion in the past. He was a non-smoker and non-alcoholic. There was also no history of exposure to bird’s dropping or recent travel to endemic parts of the country. There was no past history of tuberculosis, diabetes mellitus or any other chronic systemic illness.

On examination, the patient was of thin-built male with stable vitals. There were multiple umbilicated papular to nodular lesions over forehead and chin, without any erythema or tenderness (Fig. 1).

He had pallor, but no icterus, clubbing, cyanosis, or peripheral lymphadenopathy. The abdominal examination revealed mild, non-tender hepatosplenomegaly, but no free fluid. The chest and cardiovascular examination did not reveal any abnormality.
Investigations

The blood count revealed bicytopenia (hemoglobin 7.2 gm/dL, total leucocyte count 3200/mm$^3$ with polymorph 75%, lymphocyte 20%, eosinophil 3% and monocyte 2%. Platelet count was 2.5 lac/mm$^3$ and erythrocyte sedimentation rate (ESR) was 38 mm in first hour. The anemia was normocytic normochromic on peripheral smear examination. The biochemical tests revealed a total protein of 7.5 gm/dL, albumin 2.5 gm/dL, globulin 5.0 gm/dL with reversal of albumin-globulin ratio. The serum LDH level was 308 IU/L. Other routine biochemical tests, like bilirubin, transaminases, alkaline phosphatase, urea, and creatinine were normal. The blood culture and urine culture were sterile after 48 hours of incubation. Sputum examination did not reveal any organism by Gram’s or acid-fast staining. Chest X-ray was normal; however, the contrast enhanced CT chest revealed left hilar and pre-tracheal lymphadenopathy with foci of calcification but no necrosis. Ultrasound abdomen revealed hepatosplenomegaly. CECT abdomen ruled out involvement of adrenal glands. Serum protein electrophoresis revealed hypergammaglobulinemia. Skin biopsy showed ill-defined non-caseating granulomas with macrophages showing yeast forms of histoplasma capsulatum (Fig. 2). Fungal stain was also positive. Bone marrow aspiration and biopsy showed normal hematopoiesis with presence of yeast forms of histoplasma capsulatum (Figs. 3, 4).

The patient was thus diagnosed as a case of progressive disseminated histoplasmosis (PDH). He underwent further investigations to look for any underlying immune dysfunction. Serology for HIV I and II was negative on two occasions while the CD4 count was low at 161/µL (normal 500-1200 cells/mm$^3$). The bone marrow aspirate cultures were also positive for histoplasma capsulatum at 1 month.
Differential Diagnosis

Patient presenting with longstanding fever, loss of appetite, significant weight loss, bicytopenia and hepatosplenomegaly in India, the first provisional diagnosis that was considered was disseminated tuberculosis. Other differential would include visceral leishmaniasis, lymphoma, leukemia, and HIV-AIDS. Once we got a report of skin and bone marrow biopsy little was of doubt that we were dealing with progressive disseminated histoplasmosis. The HIV report came out to be negative, but the CD4 count was low. Due to lack of sufficient funds, we could not investigate further to rule out primary immunodeficiency.

Treatment

Patient was started on intravenous amphotericin B at a dose of 0.5 mg/kg/day with gradual escalation to 1 mg/kg/day for 4 weeks and then oral Itraconazole at a dose of 200 mg daily which was continued for 6 months. There was marked improvement of his symptoms and he was discharged on oral Itraconazole. He visited again 3 weeks later with fading skin lesions and was on regular follow up. At fourth month, the CD4 count was also repeated to exclude the possibility of idiopathic CD4 cell lymphocytopenia which was normal at 584 cells/mm³. An extensive workup for primary immunodeficiency states could not be done due to the non-availability of the same at our hospital and also because the patient belongs to a poor social strata and could not afford expensive tests.

Outcome and Follow-Up

The patient responded very well to the treatment and, till today, has not shown any new or recurrent infection on follow up.

Discussion

Histoplasmosis is a fungal infection caused by histoplasma capsulatum var capsulatum and histoplasma capsulatum varduboisii. Our patient
presented with skin lesion, the biopsy of which confirmed histoplasma. Similar skin-colored, papulonodular lesions have been seen in literature. However the lesions were present on head, trunk and extremity. It was also associated with nodulo-ulcerative growth in hard palate. Patient living with HIV and AIDS may present with reddish papules and pustules in the skin of the scalp, face, back, thighs, abdomen, palms, and soles. Our patient also had biciphenia and hepatosplenomegaly, which is a feature of infection of reticuloendothelial system and bone marrow involvement. Our patient was negative for HIV and had low CD4 lymphocyte count at presentation. There have been a few case reports, from various parts of the world, of immunocompetent patients presenting with infections which are normally seen in HIV-AIDS patients or in patients with immunosuppression. These infections are, however, associated with idiopathic low CD4 lymphocytopenia or dysfunction of T helper cells. In our patient, we suspected this condition but the repeat count after 3 weeks came out to be normal; hence, this condition was ruled out.

Learning Points
Progressive disseminated histoplasmosis should be considered in a immunocompetent host. It may be seen in HIV-AIDS negative individuals with low CD4 count. Low CD4 count is reversible on treatment of histoplasmosis with anti-fungal therapy.

Conflict of Interest: None

References