CASE REPORTS

DISSEMINATED HISTOPLASMOSIS AS PRESENTING FEATURE OF ACQUIRED IMMUNODEFICIENCY SYNDROME: A CASE REPORT

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Abstract

Histoplasmosis is a mild self-limiting respiratory illness in immune-competent individuals. It disseminates in immune-suppressed states like patients with human immunodeficiency virus (HIV) infection, haematological malignancies, post transplant states and patients receiving immune-suppressive therapy. Here we report a case of disseminated histoplasmosis in a 45 year old diabetic, returning worker who presented with fever, cough, rash, oro-genital ulcer and weight loss. He was anaemic, there was crepitation on lung auscultation and hepatomegaly. Diagnostic workup revealed HIV infection with disseminated histoplasmosis. Intravenous amphotericin B was started along with other supportive therapy and for anti-retroviral therapy he was sent to a referral center. Being an uncommon condition in our perspective, we are reporting the case.

Key words: *Disseminated histoplasmosis, AIDS, immunocompromized.*

Introduction

Histoplasmosis is a fungal infection caused by *Histoplasma capsulatum*, which is a dimorphic, saprophytic, soil-based fungus endemic throughout the Ohio and Mississippi river valleys. [1] Inspite of being non-endemic area, sporadic cases have been described in Bangladesh mostly in immunocompetent patients. [2-5] Spores are found in contaminated soil and their growth is facilitated by excreta of birds and bats. In human, spores enter into the body through inhalation and then germinate into yeast form. In immune-competent individuals, infections are usually asymptomatic or mild flu-like illness can occur. But in immune-compromised hosts, it can manifest as disseminated infection. When disseminated, it can involve liver, spleen, bone marrow, lympho-reticular and gastro-intestinal systems. Skin involvement can occur in up to 10% cases with HIV infection.[6] Diagnosis depends on clinical manifestation and demonstration of fungus in biopsy specimen or culture or by serological tests.

Case Report

A 45-year-old diabetic patient presented with intermittent fever reaching upto 101°F, cough with scanty mucoid sputum production without haemoptysis and 6 kg weight loss over 1 month. He developed painful, multiple oral and genital ulcers which initially appeared as blisters and then ruptured. He had generalized rash. There was no history of joint pain, photosensitivity, drug intake or limb swelling. He had history of extra-marital unprotected sexual exposure while residing abroad 12 years back but he denied any homosexuality or anal intercourse in his lifetime. He was generally well before and there was nothing indicative of congenital immunodeficiency.

He was moderately anaemic and there was generalized maculo-papular rash involving extensor and flexor surfaces of limbs, trunk, palm and sole (Figure 1 and 2) and multiple tender round to oval ulcers involving lips, tongue, gum, palate, glans penis having regular margin, erythematous base and slough in the center. He did not have any lymphadenopathy. He had few bilateral crepitation scattered over whole

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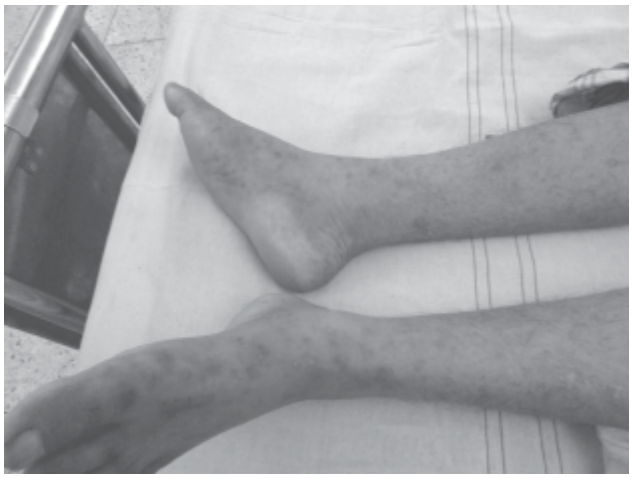

Fig.-1: *Maculo-papular rash in legs, feet and sole*

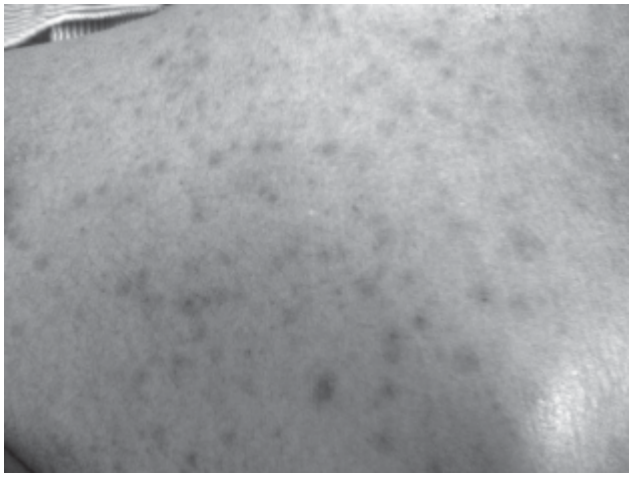

Fig.-2: *Maculo*-papular rash in trunk

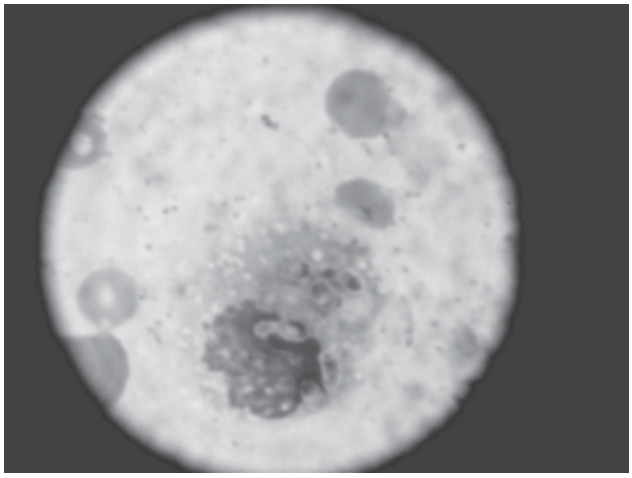

Fig.-3: *Bone marrow showing intracellular Histoplasma capsulatum.*

lung field. He had 6 cm smooth, non-tender hepatomegaly without any other organomegaly or ascites. His vital signs and other examination findings were unremarkable.

His diabetes was uncontrolled, fasting blood glucose was 9.2 mmol/L and HbA1c 8.8%. Haematological examination revealed pancytopenia; Hb 8.2 gm/ dl, TC of WBC 3600/ cmm with normal differentials, platelet count 103000/ cmm, ESR 115 mm in 1st hour, chest X-ray was normal, sputum Gram stain, silver stain and AFB (3 samples) were negative. Urine RME was normal. Sputum, blood and urine culture revealed no growth. Triple antigen was insignificant, MT 5 mm at 72 hours. ICT for kala-azar and malaria were negative. Bilirubin was 0.4 mg/ dl, SGPT 146 IU/ l, SGOT 537 IU/ l, alkaline phosphatase 407 U/L, serum total protein 69 g/ L, albumin 21.2 g/ L, lactate dehydrogenase (LDH) 826 U/L, viral markers for hepatitis B and C were negative. Abdominal ultrasonography revealed mild hepatomegaly with bright parenchyma. VDRL was non-reactive as was TPHA. Bone marrow aspirate revealed hypoplastic marrow showing proliferation of macrophages containing *H. capsulatum* (Figure 3), consistent with systemic histoplasmosis. Anti HIV (1+2) were positive, Western blot confirmed HIV infection. His CD4 count was 04/ µL. HIV screen for his wife and sons were negative.

So, the patient was finally diagnosed as a case of acquired immunodeficiency syndrome (AIDS) with disseminated histoplasmosis and type 2 diabetes mellitus. He was treated with insulin, paracetamol and blood transfusion. Intravenous amphotericin B was started and for specific anti-retriviral therapy he was referred to ICDDR,B but the patient expired there on the day of admission.

Discussion

Samuel Darling reported the first case of histoplasmosis in human in December 1905 in Panama.[7] Disseminated histoplasmosis (DH) was first reported in AIDS in 1982 [8] and was added to the United States Centers for Disease Control and Prevention (CDC) AIDS defining condition in 1987.[9] Histoplasmosis is diagnosed in up to 10% of cases with AIDS in endemic areas.[10]

Manifestation depends on patients' immune-status and organ involvement. The majority of AIDS patients with disseminated disease have CD4 counts <150 cells/ µL, with a median CD4 count of 50 cells/ µL.[11]Common features are fever, weight loss and malaise. In 50% cases, vague respiratory symptoms are reported.[11] In a review of 3 reported case series, fever, hepatomegaly, splenomegaly and generalized lymphadenopathy were the most common features (19-81%, 19-26%, 12.5-31% and 6-19% respectively).[11,12] Skin manifestations range from

papules to ulcers to erythema multiforme. Skin involvement is more common and more severe in Brazilian cases.[13] In our case, many typical features of DH were present except lymphadenopathy and splenomegaly. CD4 count in our patient was only 4/ μL.

Haematological findings are mostly nonspecific. Leukopaenia, anaemia and thrombocytopaenia suggest infiltration of marrow. In our case, there was pancytopaenia and bone marrow examination revealed intracellular H. capsulatum. Elevated alkaline phosphatase may suggest hepatic infiltration and markedly elevated LDH may indicate DH in AIDS patients.[14] Both enzymes were elevated in our case.

In AIDS patients, *H.capsulatum* can be isolated from blood and bone marrow (sensitivity 91% and 90% respectively).[11] It can be isolated from respiratory secretions, lymph nodes, localized lessions and CSF. Culture may take upto 4 weeks, treatment should not be delayed if suspected in appropriate circumstances. Fungal stains of tissue specimens are positive in less than half of DH cases.[15] Antigen can be detected in urine and serum (in 95% and 85% cases respectively)[15], antibodies develop in 4-6 weeks but may be negative in immune-suppressive states. In countries where HIV is prevalent, identification of histoplasma infection is relatively easier. In our case, we suspected the patient as having HIV infection, but DH in this case was an incidental finding during work up for pancytopaenia. Chest radiograph may show multiple small, diffuse, nodular opacities and it should be noted that in up to 50% cases of DH chest x-ray are normal.[16] CXR was normal in our patient as well.

Treatment of DH include 12 weeks induction phase with amphotericin B. Liposomal amphotericin B seems to be better than conventional amphotericin B in induction therapy (success rate 88% vs 64%).[17]Maintenance therapy with ictraconazole is directed at preventing relapse. Without maintenance therapy relapse is common. In the era of potent anti-retroviral therapy, a total of 12 month anti-fungal treatment appear to be safe in patients with sustained immunologic improvement.[18]We started induction phase of treatment with liposomal amphotericin B. There is no general recommendation for prophylaxis, but ictraconazole prophylaxis might be considered for those at risk for such infection.

Mortality of DH is 80% if untreated. Antifungal therapy reduces it to 25%.[19] Our patient expired 1 day after starting amphotericin B, which might be possibly due to delay in diagnosing the case, initiationg treatment or arrhythmia as an adverse effect of systemic antifungals.

Conclusion

In an area where prevalence of HIV infection is low like Bangladesh, DH is a rare entity. Here most of the rural people keep poultry in their home and birds excreta facilitates growth of *H. Capsulatum*. If immunity is compromised, histoplasma infection can dissaminate. So, a high index of suspicion is necessary for early detection of cases.

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