Cutaneous manifestations leading to a diagnosis of a case of severe disseminated histoplasmosis in a human immunodeficiency virus-positive child

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Abstract

This 9-year-old boy who was human immunodeficiency virus positive since birth presented with raised skin lesions, breathlessness, and cough and was treated as a case of disseminated tuberculosis. When no improvement was seen, he was referred to

the dermatologist whose examination revealed papulonodular lesions with crusting over the face and extremities. Based on clinical suspicion of histoplasmosis, investigations done revealed a CD4 count of 3 cells/μL and histopathological features of histoplasmosis along with the disseminated disease. Cutaneous manifestations thus led to an early diagnosis of the case and a good prognostic outcome.

Key words: Cutaneous, disseminated, histoplasmosis, human immunodeficiency virus

Introduction

Disseminated histoplasmosis is an opportunistic infection more commonly occurring in the immunocompromised. In human immunodeficiency virus (HIV)-positive patients, 95% of histoplasmosis occurs as disseminated infection,[1] and is typically seen with a CD4+ cell count of >150/μL.[2] However, >10% of these patients have cutaneous manifestations.[3] We herein present a case of disseminated histoplasmosis with cutaneous manifestations in a 9-year-old boy with HIV infection since birth, who was initially diagnosed as disseminated tuberculosis and later based on the clinical suspicion on dermatological examination and histopathology confirmation was diagnosed as disseminated histoplasmosis. The timely diagnosis was a lifesaver for the child and this article highlights the early diagnosis based on dermatological examination.

Case Report

A 9-year-old male child, infected with HIV since birth (acquired through vertical transmission from mother) presented with complaints of multiple small brownish to black colored, raised, mildly painful lesions over face, upper and lower limbs of 3 weeks' duration. He gave a history of bouts of intermittent dry cough and weight loss for the past 1 month. Associated headache, intermittent fever with chills, generalized weakness, and excessive irritability were present. The patient had been on antiretroviral therapy (ART) since the age of 2 years (abacavir, lamivudine, and efavirenz). His father, mother, and sister were also HIV positive and on ART without any complications.

Sputum acid-fast bacilli was negative and the chest radiograph was normal. Although no evidence of tuberculosis was found during investigations, the patient was empirically started on antitubercular therapy (ATT) by the chest physician, suspecting disseminated tuberculosis based on his fever, cough, breathlessness, skin lesions, and immunocompromised status. However, the patient showed no improvement after 2 weeks of ATT. His fever was unabated and the skin lesions worsened. He was then referred to the dermatologist.

On clinical examination by the dermatologist, the patient was found to have pallor, moderate grade fever, and significant axillary and inguinal lymphadenopathy. Dermatological examination revealed multiple erythematous to hyperpigmented, mildly tender papules and nodules, a few verrucous and some of which had central necrotic areas, distributed symmetrically over face, neck, and upper and lower limbs, with sparing of the trunk [Figures 1 and 2]. Abdominal examination revealed hepatomegaly while chest examination was unremarkable. Clinical diagnosis of histoplasmosis was suspected based on the skin findings and investigations were ordered.

The patient was found to have severe anemia hemoglobin (Hb 4.9 mg/dl), thrombocytopenia (96,000/μL), raised liver enzymes (serum glutamic-oxaloacetic transaminase – 92 units/L, serum glutamic-pyruvic transaminase – 86 units/L), raised alkaline phosphatase – 945 units/L, and raised lactate dehydrogenase (1106 units/L). The patient was found to have a CD4 count of only 3 cells/μl.

Chest radiograph and pulmonary function tests were normal. Contrast-enhanced computerized tomography (CECT) chest showed a 7.3 mm × 4.0 mm, subpleural soft-tissue density nodule seen in the posterior segment of the right upper lobe, and a 6 mm calcified granuloma in the left lower lobe. CECT abdomen showed hepatomegaly, enlarged kidneys, and retroperitoneal lymphadenopathy. Fine-needle aspiration cytology from lymph nodes showed nonspecific inflammatory infiltrate.

Histopathology from the skin nodules showed circumscribed necrotic foci in the dermis with occasional histiocytes in the periphery [Figure 3]. Hematoxylin and Eosin stain showed 2–4 μm rounded yeast forms in the necrotic area with a halo around them suggestive of *Histoplasma capsulatum* and periodic acid–Schiff (PAS) stain showed these yeast forms to be PAS positive [Figure 4]. Fungal culture from the tissue sample confirmed the diagnosis of histoplasmosis [Figure 5].

The patient was started on injection of liposomal amphotericin B at a dose of 100 mg IV daily for 2 weeks along with the continuation of ART. Thereafter, the patient has shifted to oral itraconazole 100 mg twice daily. The patient was also given a blood transfusion once weekly for 2 weeks with a rise in Hb

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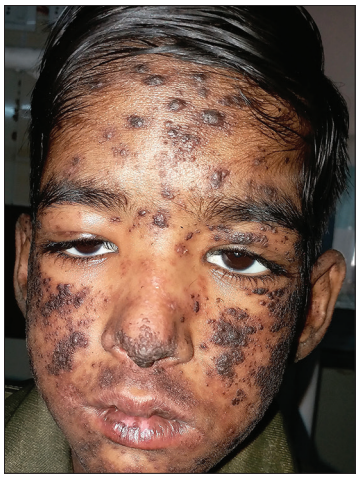

Figure 1: Clinical image of patient showing the papulonodular and crusted lesions on the face

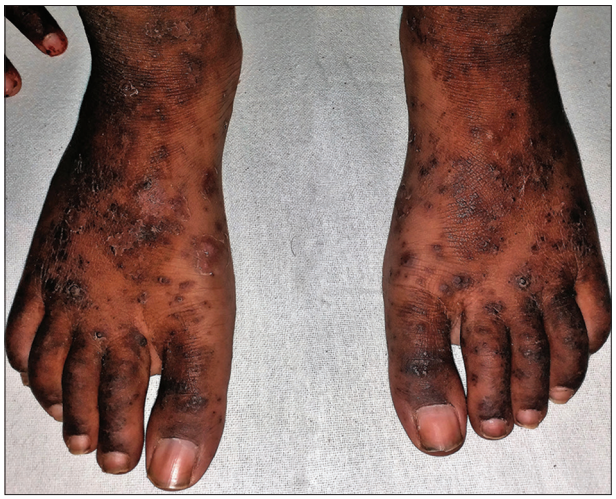

Figure 2: Papulonodular lesions on both legs

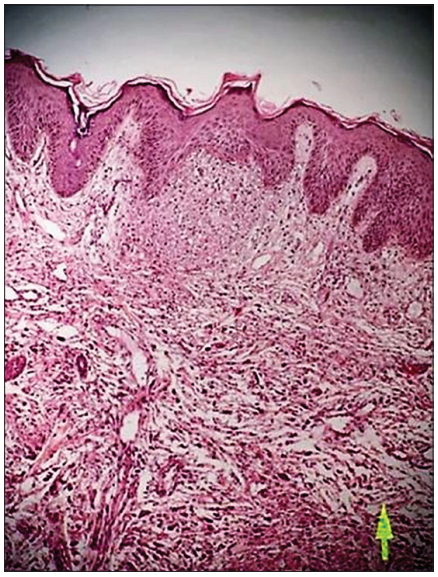

Figure 3: Histopathology revealing huge granulomatous infiltrate in the dermis with areas of necrosis (H and E, ×100)

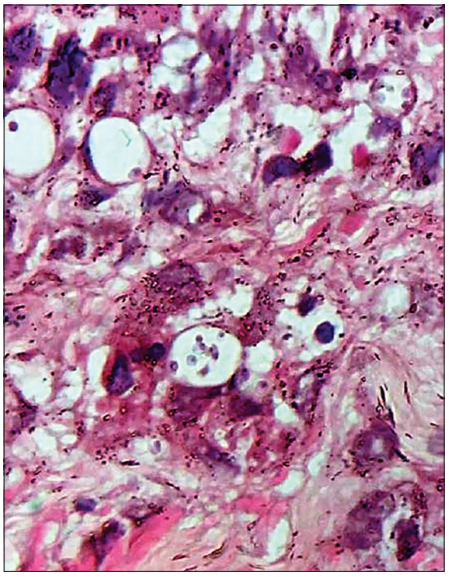

Figure 4: Periodic acid–Schiff stain confirming the presence of *Histoplasma capsulatum* (PAS STAIN × 400). PAS = Periodic acid–Schiff

Figure 5: Culture showing the growth of *Histoplasma* at 37°C

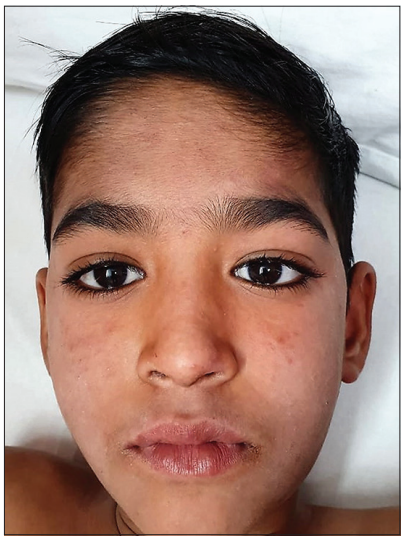

Figure 6: Clinical images of the patient 6 months after therapy

to 7.1 mg/dl. After 2 weeks of therapy, the patient's skin lesions started to resolve and his fever and cough subsided. Liver enzymes and lactate dehydrogenase levels normalized. Repeat CD4 count after a month, however, showed only a mild rise to 8 cells/µl. The patient was discharged on second-line ART and oral itraconazole. A follow-up after 6 months showed that all his skin lesions had completely resolved [Figure 6]. He had no systemic abnormalities and the CD4 count had improved to 300 cells/µL.

H. capsulatum is a dimorphic fungus that remains in a mycelial form at ambient temperatures and grows as yeast at body temperature in mammals causing histoplasmosis. Although Panja and Sen first reported histoplasmosis from India in 1959,[4] reported cases are few and far between.[5,6] Progressive disseminated histoplasmosis occurs in 1 per 2000 cases in adults who are immunocompetent and in 4%–27% of infected children, older individuals, and persons who are immunosuppressed.[7]

After initial exposure, the infection is self-limiting and restricted to the lungs in 99% of cases while the remaining 1% progress to either disseminated or chronic disease involving the lungs, liver, spleen, lymph nodes, bone marrow, and less commonly the skin and mucous membranes.[8] Cutaneous lesions may be seen rarely with all forms of histoplasmosis or, rarely, as primary cutaneous histoplasmosis. Cutaneous lesions occur in up to 17% of patients with disseminated histoplasmosis manifesting as papules, pustules, plaques, ulcers, molluscum or wart-like lesions, and rarely erythema nodosum.[9] Cutaneous lesions may be an initial presentation of disseminated histoplasmosis in about 10% of cases and may serve as a marker for acquired immunodeficiency syndrome (AIDS) in endemic areas.[10]

The various drugs used in the treatment of histoplasmosis are amphotericin, itraconazole, ketoconazole, and terbinafine, of which amphotericin B is preferred in severe cases.[11] Suppressive therapy at least for a year must be administered to prevent relapse, especially in immunosuppressed patients. Disseminated histoplasmosis in an immunocompromised host carries a poor prognosis with the untreated acute forms resulting in death within weeks.[12]

This case is unique, due to the florid cutaneous manifestation as an initial manifestation, which has rarely been reported. Even though our patient was symptomatic with fever, cough, and breathlessness, yet there was no evidence of heavy pulmonary infiltration on imaging, and pulmonary function tests and bronchoalveolar lavage evaluation were normal. However, there was heavy cutaneous infiltration as seen in the skin histopathology and this along with the florid cutaneous manifestations could be an early marker for disseminated disease.

This case is being reported to reiterate the need to maintain a high index of suspicion for opportunistic infections such as histoplasmosis in AIDS patients even in nonendemic areas and that a good dermatological examination can help in giving a lead to early diagnosis of this condition which can rapidly become fatal.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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