Disseminated histoplasmosis as a presenting manifestation in an HIV patient – A case report from South India

G. Anu Kiruba Devi, Remya Raj Rajamohanan[1], Vinupriya Sakkaravarthi, Pampa Ch Toi[2], Malathi Munisamy

Departments of Dermatology and [2]Pathology, Jawaharlal Institute of Postgraduate Medical Education and Research, [1]Department of Dermatology, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry, India

Address for correspondence:
Dr. Remya Raj Rajamohanan, Department of Dermatology, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry - 605 014, India.
E-mail: drremyarajr@outlook.com

Abstract

Histoplasmosis has heterogenous clinical presentation ranging from mild and self-limiting respiratory disease to disseminated forms with high mortality. In progressive disseminated histoplasmosis (PDH), patient presents with fever, lymphadenopathy, hepatosplenomegaly, adrenal enlargement, hemophagocytic lymphohistiocytosis and non-specific mucocutaneous lesions, usually in late stage of HIV. Cutaneous involvement is upto 25% in PDH which are papules, plaques, nodules and ulcers. Forty-two year old male, recently diagnosed as HIV positive presented with complaints of multiple painful ulcerated lesions over face, neck, tongue, arms, trunk & genitalia. Skin Biopsy was suggestive of histoplasmosis. Patient showed excellent response with amphotericin B and itraconazole. Since histoplasmosis is relatively uncommon, there should be a high-index of suspicion when an HIV patient presents with disseminated skin lesions.

Key words: Disseminated histoplasmosis, HIV, intracellular yeast, periodic acid–Schiff

Introduction

Histoplasmosis is an endemic mycosis common in immunocompromised individuals and is considered as an acquired immunodeficiency syndrome (AIDS) defining illness. Histoplasmosis has heterogeneous clinical manifestations ranging from mild and self-limiting respiratory disease to disseminated forms with high mortality. In AIDS patients, it usually occurs as acute progressive disseminated histoplasmosis (PDH).[1] However, cutaneous involvement is not very common, especially in South India.[2] Even then it is extremely rare to have disseminated mucocutaneous histoplasmosis as the initial manifestation prompting testing in HIV since it is usually associated with advanced immunosuppression with CD4 counts <150 cells/µl.[3] In addition, it can be challenging to suspect the diagnosis of histoplasmosis because the morphological spectrum of mucocutaneous lesions in histoplasmosis is shared by a large number of infectious and noninfectious diseases that are common in patients with AIDS. Here, we report a case of disseminated mucocutaneous histoplasmosis as a presenting manifestation of HIV.

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Case Report

A 42-year-old male from Tamil Nadu presented to dermatology outpatient department with complaints of multiple painful ulcerated lesions over the face, neck, tongue, arms, trunk, and genitalia for 8 months. Initially, lesions started over the chest, abdomen, and face as flat raised lesions followed by central ulceration, gradually progressive with the development of multiple new plaques associated with pain and mild itching. He also had hoarseness of voice and pain in swallowing both solids and liquids for the same duration. He had significant weight loss with chronic cough with expectoration for the past 5 months, for which he was evaluated and diagnosed to have HIV infection and was started on antiretroviral drugs (TLE regimen). He was referred to the dermatology clinic in our center as the skin lesions were worsening with new onset of lesions over eyelids and glans penis despite starting anti-retroviral therapy (ART).

Cutaneous examination revealed multiple well-defined skin-colored to erythematous umbilicated papules and

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plaques with central crusting and ulceration of size ranging from 0. 5 cm × 0.5 cm to 4 cm × 2 cm present over the face (including eyelids, nose, and lips), neck, upper chest and abdomen, bilateral upper arms, and buttocks [Figure 1a and b]. These lesions were tender on palpation. Two well-defined mildly indurated ulcerated plaques were present over the glans penis. The oral cavity showed a single well-defined indurated and ulcerated tender plaque of size 1.5 cm × 1.5 cm over the tip of the tongue and multiple erythematous papules over the hard palate. General examination revealed bilateral inguinal lymphadenopathy. We considered the differentials of secondary syphilis, histoplasmosis, cryptococcosis, penicilliosis, papulonecrotic tuberculid, atypical mycobacterial infection, and cutaneous lymphoma.

Routine laboratory investigations, including hemogram, liver, and renal function tests, were normal. His baseline CD4 count was 61. HIV viral load was <50 copies/ml and repeat CD4 count was 86. Chest X-ray did not reveal any abnormality. High-resolution computed tomography of the thorax revealed multiple cavitary lesions in the lower zone of the left lungs [Figure 2a]. There were a few subcentimetric nodules in the left lower lobe with some of them showing tree-in-bud pattern suggestive of the endobronchial spread of infection. Fundus examination was found to be normal. Other serologies, including venereal disease research laboratory, TORCH, and treponema pallidum hemagglutination, were negative. Evaluation for hoarseness of voice with bronchoscopy revealed proliferative lesions in the supraglottic airway [Figure 2b]. Biopsy from one of the plaques over trunk demonstrated a dense infiltrate composed of lymphocytes, plasma cells, and histiocytes with intracellular yeasts surrounded by typical halo of clear space in the dermis highlighted by periodic acid-Schiff (PAS) and Grocott's methenamine silver stain, suggestive of *Histoplasma capsulatum* infection [Figure 3a-d]. Sputum for fungal culture and CBNAAT were negative. The patient was started on systemic antifungal therapy with intravenous amphotericin B at a dose of 1 mg/kg/day for 2 weeks followed by itraconazole 200 mg twice daily in addition to ART. He showed excellent improvement in a few weeks and is currently on the maintenance dose of itraconazole [Figure 1c and d].

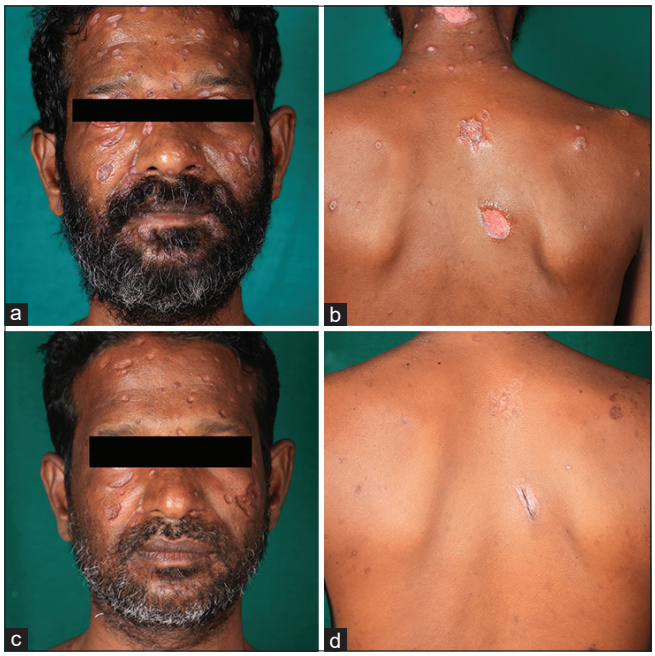

Figure 1: (a) Multiple umbilicated papules and plaques with ulceration and crusting and ulceration overface and neck (b) Papules and ulcerated plaques over upper back (c) Lesions resolved with only postinflammatory changes after 2 months of itraconazole overface and neck (d) Postinflammatory changes over the upper back

Discussion

Histoplasmosis, also known as Darling's disease, is an infection caused by the dimorphic fungus, *H. capsulatum*. It has two variants. *H. capsulatum* var. capsulatum is the more common variant usually found in tropical areas, while *H. capsulatum* var. duboisii is found almost exclusively in Africa. In India, it is thought to be endemic in Eastern States such as West Bengal. It is sometimes found in soil contaminated with chicken droppings or bat guano, and the infection can be acquired via airborne route by inhalation of fungal spores. Once the spores are engulfed by neutrophils and macrophages in the lungs, mycelia are converted to yeast which migrates through lymphatics to other internal organs, mainly those which are rich in mononuclear phagocytes.[4] However, in immunocompetent patients, the infection is usually self-limiting due to the activation of cell-mediated immunity and is extremely rare to progress to disseminated histoplasmosis.[5]

Gupta *et al*. did a literature review of all cases of histoplasmosis reported from India during the period from January 2001 to December 2015.[4] Of 214 cases analyzed (including ten unpublished cases from the authors' institute), 70 patients had underlying immunosuppression, of which the majority were HIV positive, followed by renal transplantation recipients. The mean age of presentation was lower in immunocompromised (37.9 ± 14.0 years) compared to immunocompetent patients (49.2 ± 14.9 years), and the majority of patients were males. Of 57 cases, in which occupational exposure was documented, 17 patients had exposure to soil through agriculture-related work, and nine had a history of exposure to birds. Of 39 patients who were HIV positive, CD4 count was available for 23 patients, and the mean CD4 count was 65/µl ± 53. The geographical distribution of the cases was found to be in accordance with our existing understanding with a definite history of residence in a particular state (27% from North India and 51% from North East India) mentioned in the reports.

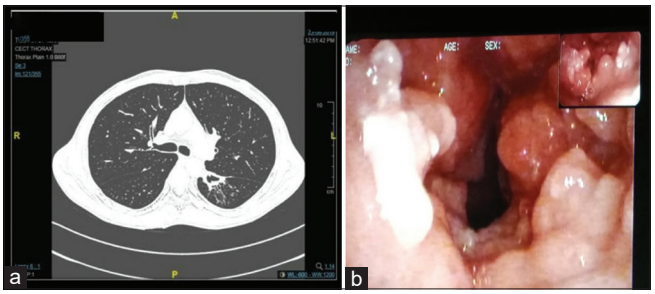

Figure 2: (a) High-resolution computed tomography thorax showing cavitary lesion in the lower zone of the left lung with surrounding bronchiectatic changes (b) Bronchoscopy showing proliferative lesions in supraglottis and both vocal cords

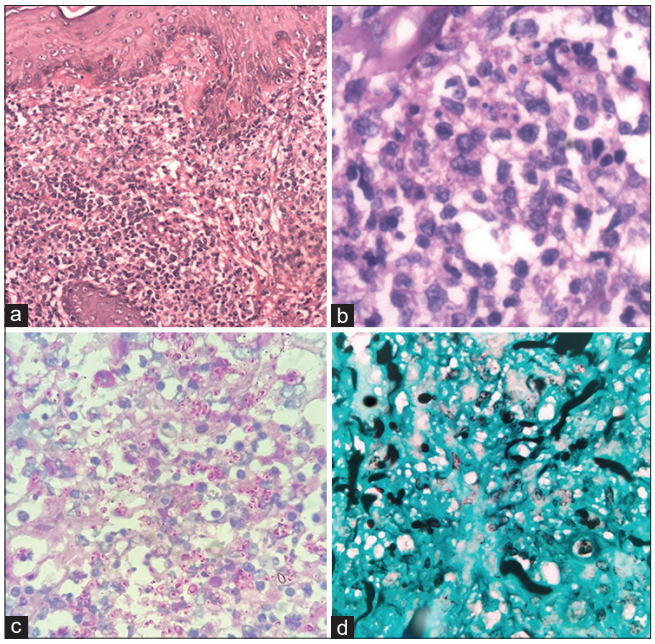

Figure 3: (a) Dense inflammatory infiltrate in the dermis consisting of lymphocytes, histiocytes, and plasma cells (H and E ×100) (b) Numerous round cells surrounded by a halo of clear space (H and E ×400) (c) Periodic acid–Schiff stain highlighting intracellular organisms as bright eosinophilic structures (×200) (d) Grocott's methenamine silver stain showing small grouped yeasts with narrow-based budding in histiocytes (×200)

The infection usually starts in the lungs, but can later involve the liver, spleen, kidney, nervous tissue, etc. Adrenal involvement was noted in 35% of the cases in the review by Gupta *et al*.[4] Cutaneous involvement may be seen in around 10%–25% of PDH. Mucocutaneous histoplasmosis can have varied presentations such as papules, plaques, nodules, ulcers, mucosal erosions, molluscum contagiosum-like lesions, acneiform eruptions, erythema multiforme, or even severe pruritus as the presenting sign before the onset of any skin lesion.[5] Patients with PDH usually have associated hepatosplenomegaly, lymphadenopathy, and hemophagocytic lymphohistiocytosis.[6] Serum lactate dehydrogenase (LDH) is usually elevated in PDH, and LDH levels of more than 600 IU/ml have even been suggested as a diagnostic clue.[2] However, our patient had normal LDH levels.

Of 84 patients treated with itraconazole in the review by Gupta *et al*., 34 recorded improvement/cure while 5 had relapsed. Amphotericin B was the next commonly used drug either alone or in combination with itraconazole. The mortality rate was significantly higher in immunocompromised cases (27.5%) compared to immunocompetent cases (10%).[4] Thus, it is important to consider steps to be taken to prevent the occurrence of this infection which causes significant morbidity and mortality. Center for Disease Control (CDC) recommends the use of wetting agents to reduce aerosolized dust, wearing personal protective equipment (PPE) such as respirators, and expelling birds and bats from sites and buildings where excavation activity is being planned. These measures help in the prevention of inhalational exposure to various organisms such as Histoplasma, Cryptococcus, or *Chlamydia psittaci* which is important for immunocompromised people engaged in farming or constructional activity.

Although histoplasmosis is rarely reported outside of the endemic areas in Indian patients, in the setting of immunodeficiency like HIV, it is a fairly common opportunistic pathogen and has varied morphological presentations with involvement of skin, mucosa, and lungs. There should be a high index of suspicion for histoplasmosis when an HIV patient presents with disseminated skin lesions and painful mucosal ulcers.

Declaration of patient consent

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

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Nil.

Conflicts of interest

There are no conflicts of interest.

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