Case Report

Histoplasmosis in an immunocompetent host: a rare case report

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Received: 04 January 2017
Revised: 06 January 2017
Accepted: 04 February 2017

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ABSTRACT

Histoplasmosis, a systemic mycosis caused by Histoplasma capsulatum manifests clinically in immunocompromised patients as acute or chronic pulmonary infection or as a progressive disseminated disease. In immunocompetent hosts, the disease is usually self-limited or presents as flu-like symptoms. It is endemic in North, Central and South America as well as parts of Europe and Africa. We report a case of a 76-year-old diabetic, HIV negative patient who presented with white nodular patches on the tongue and gingiva which were reported as histoplasmosis on histopathology. He also had idiopathic CD4 lymphocytopenia and thrombocytopenia.

Keywords: Histoplasmosis, Histoplasma capsulatum, Immunocompetent, Idiopathic CD4 lymphocytopenia

INTRODUCTION

Histoplasmosis is an infectious disease caused by a thermal dimorphic fungus Histoplasma capsulatum. In immunocompetent individuals with low level of exposure, the infection is self-limited whereas high level of exposure presents as flu-like illness, fever, chills, headache, myalgia, anorexia, cough and dyspnea.1 Progressive, disseminated form of the disease is seen in immunocompromised individuals.2 However, a few cases of disseminated disease have also been reported in immunocompetent hosts.3,4 We hereby report a case of oral histoplasmosis in an immunocompetent individual from a nonendemic region of India.

CASE REPORT

A 76-year-old male, resident of Mumbai and a known case of type 2 diabetes for over 20 years presented with white nodular patches on the dorsal aspect of the tongue for 20 days. The lesion started as a small patch on the left lateral margin of the tongue which spread to the rest of the tongue and gingiva. He also complained of fever with dry cough, loss of appetite and weakness for one month. He consulted a dental surgeon who suspected malignancy. He came to us for a second opinion. There was no significant past or personal history.

General and systemic examination of the patient was normal. Oral examination revealed white nodular patches on the gingiva and the dorsal aspect of tongue involving one-third of the anterior tongue and the posterior tongue (Figure 1). Routine blood count revealed haemoglobin-11.3 gm/dl, total leucocyte count-4920/cumm, platelets of 9300/cumm. Protein creatinine ratio was 0.32 mg/dl. Enzyme-linked immunosorbent assay (ELISA) for human immunodeficiency virus (HIV) was nonreactive. However, absolute CD4 and CD8 counts were low and reported as 264 (28.95%) and 158 (17.37%) respectively. CD4/CD8 ratio was reported as 1.67. Blood sample which was sent for culture in a fungal bottle and plated on Sabouraud’s dextrose agar showed no growth. Bone marrow studies could not be done as the patient did not consent for it. Sonography of abdomen showed mild hepatosplenomegaly. The tongue lesion was biopsied and submitted for histopathological examination. It revealed a
focally ulcerated hyperplastic squamous mucosa which was replaced by hemorrhagic fibrinous material and sheets of neutrophils. The underlying stroma revealed neutrophils, plasma cells, and multinucleate giant cells with numerous budding oval yeast forms surrounded by a ‘halo’ suggesting a differential diagnosis of Cryptococcus neoformans and Histoplasma capsulatum. The latter was confirmed with GMS and PAS positivity and negative staining for mucicarmine (Figure 2). The patient was started on an induction dose of liposomal Amphotericin B and discharged in stable condition with a maintenance dose of Itraconazole.

Figure 1: White nodular patches on the lateral aspect of tongue.

Figure 2: PAS positivity and negative staining for mucicarmine.

DISCUSSION

Histoplasmosis is an uncommon disease caused by Histoplasma capsulatum var capsulatum and Histoplasma capsulatum var duboisii. Myelia are the naturally infectious forms and have microconidia and macroconidia forms. The mode of infection is by inhalation of the mold microconidia which are small enough to reach the terminal bronchioles and alveoli. Once inside the alveolar spaces, they are engulfed by the macrophages where they transform to budding yeasts and multiply. Yeasts use these phagosomes for translocation to local draining lymph nodes from where they spread hematogenously throughout the reticulo-endothelial system.

In India, histoplasmosis is rare and is endemic only in small regions in West Bengal and Maharashtra. However; sporadic cases from Southern India have been reported. Infection with H. capsulatum is associated with development of cell-mediated immunity, as demonstrated by a positive result of a delayed hypersensitivity skin test to H. capsulatum mycelial antigens. Histoplasmosis is rare in the immunocompetent host. Immunocompromised individuals, particularly those with T-lymphocyte-related defects are unable to stop the growth of the organism. This includes patients with AIDS, transplant recipients, those with hematologic malignancies or cases on corticosteroids. Even though our patient had normal CD4, CD8 counts, he was a chronic diabetic which could have played a role in suppression of immunity. Hence, it was difficult to explain the presence of histoplasma infection in a minimally symptomatic individual. Histoplasmosis infection is often classified as being present in an HIV positive or HIV negative individual, as there are differences in presentation and response to therapy.

Disseminated histoplasmosis with oral involvement in an immunocompetent patient has rarely been described around the world. In immunosuppressed patients, they can manifest in a variety of forms like ulcers, erythematous or vegetative nodules or wart-like growths. Many reports show development of ulcerating, indurated and painful ulcers. The palate, gingiva and oropharynx are the most frequent sites of oral histoplasmosis. In nodular or noduloulcerative oral lesions, the differential diagnosis should include squamous cell carcinoma, lymphoma, and other systemic mycoses, in addition to histoplasmosis, irrespective of the immune status of the patient.

Thrombocytopenia is reported in disseminated histoplasmosis along with other cytopenias whenever there is bone marrow involvement, but reports of patients presenting with isolated thrombocytopenia as in the present case are rare. The yeast form of H. capsulatum activates the platelets resulting in serotonin release reaction and aggregation without the involvement of the complement pathway leading to thrombocytopenia. The plasma cofactors which are involved are Ig G which is necessary for induction of release reaction. Fungal culture remains the gold standard for diagnosis though they can often be negative. Samples of tissue or body fluids are plated onto Sabouraud’s dextrose agar and
incubated at 25°C to allow for growth of the mycelial phase of *H. capsulatum*. After 6 weeks, growth of a white to light tan mold occurs. On histopathological examination with H&E staining, the budding yeast forms are seen predominantly within histiocytes as a clear space or artifactual “halo” due to the retraction of the basophilic fungal cell cytoplasm from the poorly stained cell wall.

GMS and PAS positivity confirms the presence of Histoplasma while negative staining of mucicarmine rules out Cryptococci.19 Confirmatory diagnoses in immunocompetent patients also include detection of Histoplasma antigen in body fluids and serological tests like immunodiffusion and complement fixation.1

**CONCLUSION**

Present case highlights the rare occurrence of oral histoplasmosis in an immunocompetent patient along with idiopathic CD4 lymphocytopenia and thrombocytopenia, in a non-endemic region. Periodic follow up for lymphoma is necessary.

**Funding:** No funding sources

**Conflict of interest:** None declared

**Ethical approval:** Not required

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1. Harrison’s principles of internal medicine, 19th ed, Ch.236:1332.