

Oral histoplasmosis masquerading as acute necrotizing ulcerative gingivitis: A rare case report

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ABSTRACT

Histoplasmosis also called as “Darling’s Disease” is a community-acquired primary pulmonary disease caused by inhalation of dust containing spores of soil-dwelling dimorphic fungi, *Histoplasma capsulatum*. Presentation of fungi in the oral cavity is usually rare and is generally associated with an immunocompromised state. Here, we present a rare case of histoplasmosis in an immunocompetent patient, with discrete oral presentation, that initially mimicked acute necrotizing ulcerative gingivitis. Gingival biopsy confirmed the diagnosis of histoplasmosis, which responded favorably to the initial treatment with intravenous amphotericin and later to oral itraconazole. Thus, a vigilant approach is paramount in reducing the fatality due to disease.

Keywords: Oral histoplasmosis, Darling’s disease, immunocompetent, acute necrotizing ulcerative gingivitis

Introduction

Histoplasmosis also called as “Darling’s Disease” was first described by Samuel Taylor Darling, an U.S physician in Panama in 1906 who considered it an encapsulated protozoa.^[1] Histoplasmosis is a noncontagious community-acquired primary pulmonary disease caused by inhalation spores of *Histoplasma capsulatum* present in dust contaminated from excreta of birds such as pigeon, starling, bat, and blackbird.^[1]

H. capsulatum is found worldwide, but it is more common in North America and Central America particularly along the river valleys.^[1] The first case of histoplasmosis reported in the Indian literature was by Panja and Sen (1954) in Calcutta.^[2]

In this article, we present a rare case of oral histoplasmosis in an HIV-seronegative patient.

Case Report

A 39-year-old man presented to the Department of Periodontology, Government College of Dentistry, Indore, with the chief complaint of severe ulceration in the mouth,

sore throat, and low-grade fever for 4 weeks and skin lesions on his hands and back.

Intraoral examination revealed the presence of chronic ulcerative lesion on the buccal mucosa, gingiva, corner of the mouth, and palatal mucosa with subsequent disruption and necrosis of buccal mucosa and advanced bone loss involving all teeth [Figure 1a-c]. The lesions were indurated, painful to touch, and covered with gray pseudomembrane accompanied by bilateral submandibular lymphadenopathy. Multiple firm, dark pigmented papules (<1 cm) were present on the dorsal surface of hands, forearms, and back [Figure 1h].

The patient gave a history of sore throat and hoarseness in voice for 6 months and chronic low-grade fever for 4 weeks. The patient was tested HIV seronegative.

The initial lesions mimicked necrotizing ulcerative periodontitis, for which he was prescribed amoxicillin (500 mg) and metronidazole (400 mg) thrice daily for 7 days. Lesions were swabbed with cotton pellet dipped in H₂O₂ to remove pseudomembrane; oral hygiene instructions were reinforced, and the patient was recalled after 3 days [Figure 1d-g].

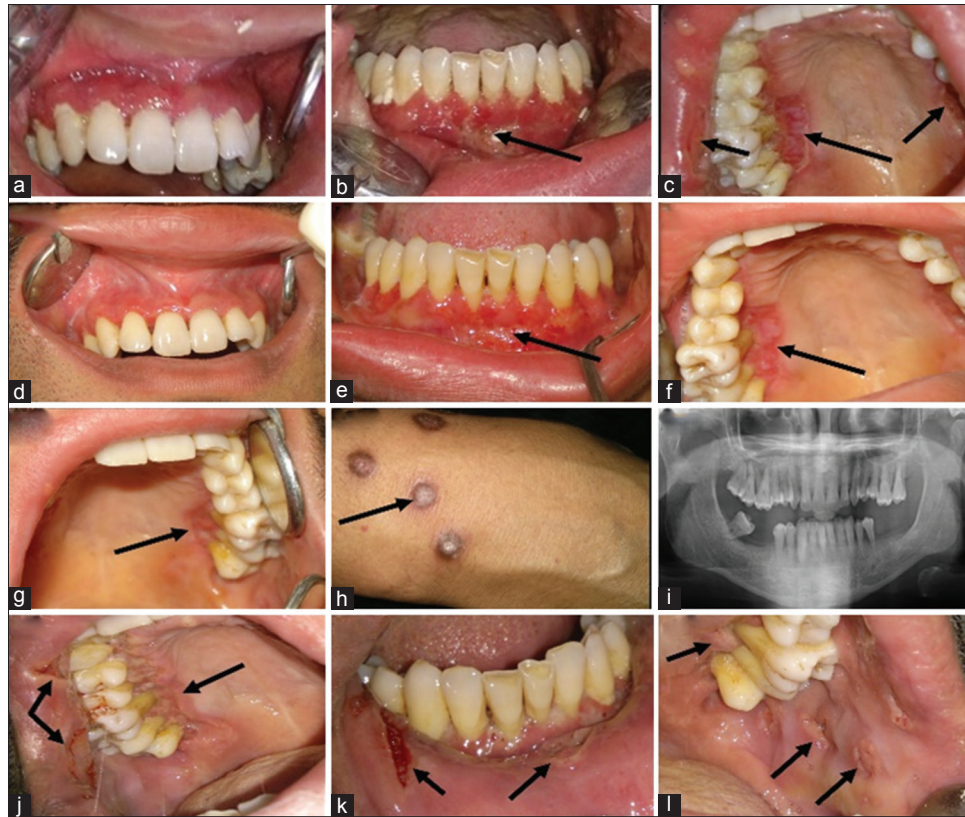


Figure 1: (a-c) Ulcerated lesions with granular surface in the maxillary and mandibular gingiva and the hard palate and corner of the mouth (day zero), (d-g) Initial improvement in lesions 3 days after using H₂O₂ mouthwash and antibiotic regimen, lesions on back of the hand (h), and OPG depicting generalized bone loss (i). (j-l) Photograph showing recurrence of ulcerative lesions involving maxillary and mandibular gingiva, hard palate, buccal mucosa, and corner of the mouth 15 days after initial improvement with antibiotic therapy

The patient presented a significant improvement, following which the patient underwent staged, nonsurgical, quadrant-wise scaling, and root planing over a 2-week period. There was an initial reduction in inflammation during the treatment phase, but the palatal soft tissues in relation to maxillary posterior teeth remained intensely inflamed with bilateral disruption of the buccal mucosa showing no significant improvement [Figure 1g-i].

An incisional biopsy of the affected area was done, which demonstrated the presence of epithelioid cell granulomas in the connective tissue with multiple histiocytes that formed multinucleated giant cells. The cytoplasm of histiocytes demonstrated small round, oval basophilic bodies surrounded by clear halo, which is characteristic of *H. capsulatum* [Figure 2a-c]. The tissue sections were further stained with Grocott Gomori methenamine silver stain [Figure 2d], which is highly specific for *H. capsulatum* and Periodic acid–Schiff (PAS) [Figure 2c].

The response to antifungal therapy with intravenous liposomal amphotericin B at 0.7 mg/kg/day administered for 10 days was good. As the symptoms subsided, the patient was shifted on oral itraconazole (200 mg) twice daily for 6 months. The lesions completely resolved on completion 6-month course

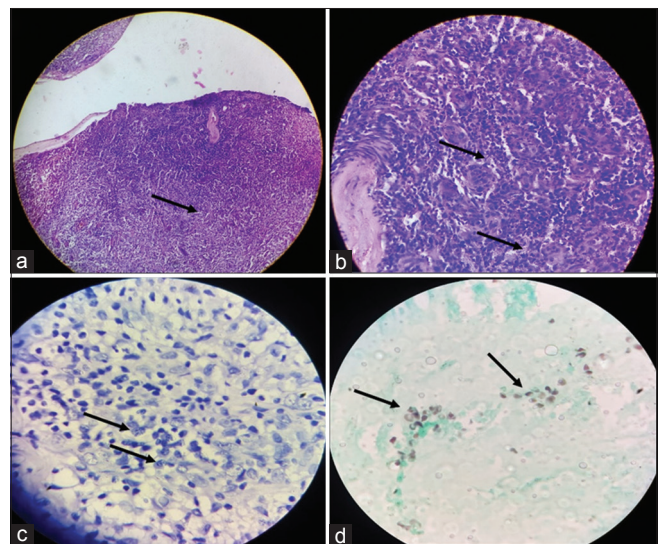


Figure 2: (a) Low-power photomicrograph of specimen shows numerous yeast cells in vacuolated cytoplasm of macrophage (hematoxylin and eosin stain at ×4) (b) High-power photomicrograph of specimen showing macrophages with intracellular microorganisms surrounded by clear halo (arrows) (hematoxylin and eosin stain at ×40) (c) A photomicrograph of specimen showing macrophages with intracellular microorganisms surrounded by clear halo (arrows) (Periodic acid–Schiff stain at ×100 oil immersion) (d) Numerous circular yeast-like cells stained black (arrow) scattered throughout the tissue (Gomori-Grocott's stain at ×1000 oil immersion)

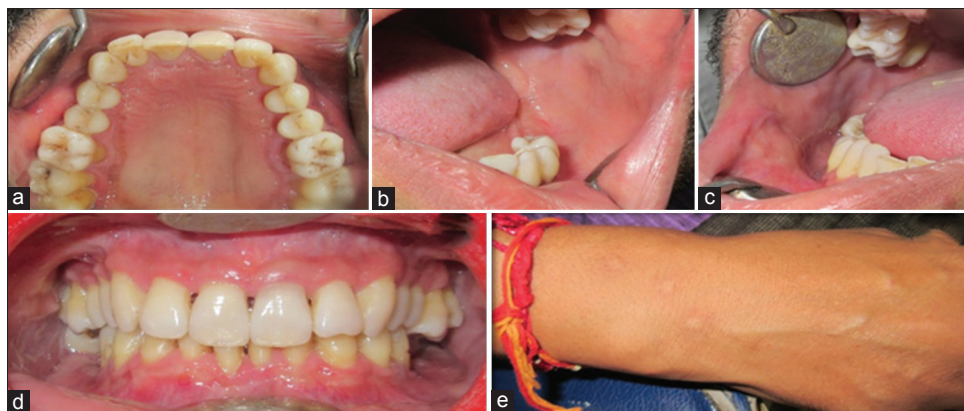


Figure 3: (a-e) One and a half years' follow-up photograph showing the complete healing of ulcerations after antifungal therapy

of medication. The patient is asymptomatic and under regular follow-up for one and half year [Figure 3a-e].

Discussion

Histoplasmosis also called as “cave disease,” “Ohio Valley disease,” or reticuloendotheliosis is caused by inhalation of reproductive cells (spores) of dimorphic fungi *H. capsulatum*, which primarily dwells in the soil in mycelial form and in mammals in yeast form. Its contamination is primarily caused by bird droppings, and the mode of entry is through inhalation of soil contaminated with the fungal spores. The organism is found worldwide, being endemic in Ohio and Mississippi River valley, parts of North and Central America, and has been found to be present in soils of the Gangetic plains of India.^[1]

Important risk factors for histoplasmosis include AIDS with CD4 cells <150/Ml, corticosteroids, and other immunosuppressive agents given for various conditions and solid organ transplantation.^[1] A Study by Padhya *et al.* supported the fact that Indians primarily suffer with extrapulmonary histoplasmosis, manifesting in the oral cavity.^[3] Our HIV-seronegative patient presented with ulcerations on the gingiva, palate, and buccal mucosa. Histopathologic findings supported the diagnosis of histoplasmosis. He gave a negative history for known risk factors for histoplasmosis.

Tissue biopsy for histopathologic identification of fungi is a rapid means for establishing the diagnosis of histoplasmosis in critically ill patients.^[1] The fungus is visible in hematoxylin and eosin staining but is better demonstrated by Gomori's methenamine silver, Gridley, or PAS stain.^[4]

Although pneumonia is an important clinical symptom of histoplasmosis, most patients have either no symptoms or mild respiratory symptoms and thus do not seek medical advice.^[1] Some investigators are of the opinion that oral lesions of histoplasmosis occur as a secondary manifestation of pulmonary or disseminated disease, while others believe that primary lesions of oral histoplasmosis are possible by direct inoculation of spores into the mucosa.^[5] Majority of cases of

oral histoplasmosis occur in immunocompromised patients, and it is estimated that around 3% of HIV-infected individuals have histoplasmosis.^[6] Up to 66% of patients with oral manifestations of histoplasmosis have disseminated disease. A number of conidia that are inhaled and the immune response of the host determine the severity of disease. Majority of individuals are asymptomatic or present with mild symptoms.^[4] The severity and frequency of histoplasmosis are more among HIV-seropositive persons residing in geographic areas that are endemic for *H. capsulatum* and have been reported to occur in up to 5% of patients with AIDS living in these areas.^[7] HIV-seropositive individuals demonstrated lesions of oral histoplasmosis 43 times more frequently compared to individuals with HIV-seronegative status.^[8] We have not identified any source of immunodeficiency in our patient till now.

The Infectious Diseases Society of America and American Thoracic Society have studied and evaluated the efficacy of oral itraconazole and liposomal amphotericin B and found them to be an effective antifungal agent against histoplasmosis^[9,10] supporting the treatment given in the present case.

Conclusions

Histoplasmosis is a potentially fatal disease which if not diagnosed and treated at an early stage could result in serious complications. The diagnosis of histoplasmosis is primarily based on the presence of organism in tissue and culture, so biopsy should be considered in a patient with chronic mucosal ulceration not responding to routine therapy and presenting with systemic symptoms.

Patient's consent

Written informed consent has been taken from the studied subject.

Conflicts of interest

None.

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