Histoplasmosis masquerading as solitary oral ulcer: An unusual case report

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Introduction
Ulcers in the oral cavity are one of the common problems of a dental patient. Three pieces of information in particular help the clinician to rapidly come to a diagnosis of the patient's disease; time duration since occurrence of the lesion (acute or chronic); history of recurrent lesions; and number of lesions present (solitary or multiple). However, some ulcers occurring at unusual sites and varied forms should alert the clinician to a broader outlook and initiate appropriate investigations to help diagnose the lesions. Oral presentation of histoplasmosis as the only entity is a very rare manifestation. This case report of a 60-year-old male with isolated oral histoplasmosis emphasizes the need for clinicians to be aware of uncommon conditions presenting orally or as the only manifestations of a disease. Early diagnosis and identification of the underlying disease is the duty of an alert clinician, which helps to reduce morbidity and mortality to a greater extent. We present a case of a 60-year-old male who reported with a painful ulcer in his left cheek since about 5 months, which finally came to be diagnosed as isolated oral histoplasmosis. Opportunistic fungal infection occurring in acquired immunodeficiency syndrome accounts to significant morbidity. Early diagnosis and identification of the underlying disease is the duty of an alert clinician.

Keywords: Acquired immunodeficiency syndrome, histoplasmosis, itraconazole

Case Report
A 60-year-old male patient reported to the outpatient Department of Oral Medicine and Radiology, Coorg Institute of Dental Sciences, Virajpet, with a painful ulcer in his left cheek since about 5 months. The ulcer had begun as a raised lesion, which ulcerated. The ulcer gradually grew in size after which he visited a nearby dentist who treated him symptomatically. Patient had a habit of smoking cigarettes since 42 years. He had undergone extensive dental treatment over the last 2 years for missing teeth. Patient did not report of any discharge or paresthesia from the ulcer. Patient reported of lassitude, weight loss, and lethargy since 2 months.

On examination, there was a well-defined, tender, indurated ulcer of size 2 cm × 1 cm on the left buccal mucosa above the line of occlusion [Figure 1]. There were no local etiologic factors like a sharp tooth or overhanging restoration that could have caused the ulcer. The base of the ulcer was white and was not fixed to the underlying tissues. The ulcer did not bleed and showed no discharge. The palate was diffusely reddish-pink. The lymph nodes in the left submandibular group were enlarged, tender, and mobile.

Routine blood investigations showed the patient to be diabetic with a fasting blood sugar level of 260 g%. Sputum sample was negative for acid fast bacilli. A venereal disease research laboratory test performed with serum for syphilis turned out to be non-reactive. A chest radiograph showed the lung spaces to be normal. An ultrasonography of the abdomen ruled out hepatosplenomegaly.
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Smears from the ulcer were sent for histopathology. Hematoxylin and eosin stained slides reported of hyphae and spores of *Candida albicans*, Gram-positive cocci, Gram-negative diplococcic, and few small intracellular fungal spores (Figures 2 and 3). The presence of intracellular spores warranted further investigation to identify the organism. Special staining with Gomori’s Methenamine silver (GMS) stain was performed which showed fungal spores with a peripheral halo within the macrophages and giant cells suggestive of *Histoplasma capsulatum*, the causative of histoplasmosis. The diagnosis of histoplasmosis prompted us to check the HIV status of the patient. The patient turned out HIV positive by enzyme-linked immunosorbent assay and was confirmed with the Western Blot test.

The patient was diagnosed with isolated oral histoplasmosis and was referred to the infectious disease center for the treatment of HIV. The patient was treated with tablet itraconazole 400 mg twice a day for 3 days followed by tablet itraconazole 200 mg once daily for the following 2 weeks. The oral ulcer had healed up satisfactorily after 3 weeks follow-up.

**Discussion**

Histoplasmosis, also commonly known as Darling’s disease was first discovered and reported by Dr. Darling in 1905 and was demonstrated by isolation and culture by Demonbreun under varying environmental conditions. Histoplasmosis is a highly infectious mycoses, caused by a dimorphic fungus *H. capsulatum* and affecting primarily the lungs where it is asymptomatic. The course of the disease is influenced by the host immune status and by their exposure to infective propagules and has a wide spectrum of clinical manifestations, ranging from asymptomatic infection to severe disseminated disease depending on the size of the inoculums, immune status of the affected individual, and the virulence of the fungal strain.

In 1982, histoplasmosis was first reported in patients with acquired immune deficiency syndrome (AIDS) and, since 1987 extra-pulmonary histoplasmosis in an individual with a positive serologic test for HIV is a case definition of AIDS according to the centers for disease control. Immune compromised individuals have a generalized form of the disease involving multiple organs and less frequently oral lesions may be the only manifestation of the disease.

Oral lesions of histoplasmosis can occur as ulcerative, nodular, verrucous, vegetative, granulomatous, and plaque-like lesions involving the lips, gingiva, tongue, and palate. Our case had presented with an ulcer in the left buccal mucosa. Most investigators believe that human infection occurs via inhalation of the spores. On the contrary, some investigators claim that primary oral lesions can occur by direct inoculation of the fungus in the mucosa. For differential diagnosis, the lesions...
caused by herpes simplex, major aphthae, traumatic ulcers, acute necrotizing ulcerative gingivitis, tuberculosis, syphilis, epidermoid carcinomas, and lymphomas must be considered. [6]

Diagnosis of the disease includes a thorough clinical examination supplemented by adequate radiological and laboratory examinations. [5] The gold standard for the diagnosis is the isolation of the *H. capsulatum* in culture with observation of the conidia, as well as its conversion to yeast forms at 37°C. Special stains such as GMS and Periodic acid-Schiff are the ones commonly used to study mycotic diseases histopathologically. [5,6,7,9]

An accurate and rapid early diagnosis can also be achieved through immunofluorescent methods to differentiate between viral or other granulomatous diseases. [6] The CD4 count in this patient was 298 cells/μl, which is well below the normal range of 500-1600 cells/μl showing a relation to the appearance of oral manifestations as compared by other authors. [8]

Serological testing by immune-diffusion and complement fixation tests can be done although it can detect only cases with a recent infection where host anti – *H. capsulatum* antibodies are detected. A much more specific test is the Western Blot Assay that can identify early infection before seroconversion can be detected by immune-diffusion or complement fixation, with a high degree of specificity. [5]

Amphotericin B has been the mainstay drug for treatment of disseminated histoplasmosis in patients with AIDS. Itraconazole, a triazole derivative has emerged as the newer drug of choice with a better patient tolerance, better absorption, and lesser toxic effects systemically even when administered for a period of 6 months and also helps to prevent relapse. [5,6,7] Our patient responded to itraconazole very promptly and the lesions healed by the 3rd week.

In conclusion, awareness of the various oral manifestations of histoplasmosis may enable an earlier diagnosis and prompt initiation of therapy. The presence of an unexplained lesion should prompt a biopsy, and a positive identification of histoplasmosis should search for concurrent HIV status or other underlying debilitating disease.

**References**