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Oral Histoplasmosis Presenting as a Solitary Ulcer on Tongue in an Immunocompetent Adult

To the Editor:

Histoplasmosis or Darling disease is caused by the opportunistic dimorphic fungi *Histoplasma capsulatum*, which is ubiquitous in soil contaminated by bird or bat excreta. Humans get infected by inhaling spores of the organism. The organism mainly affects the aerodigestive tracts of susceptible individuals, but it can also involve other organs and occur in disseminated and localized forms. Most cases have been associated with immunosuppression particularly in individuals with HIV in whom disseminated disease is more common, but immunocompetent patients with underlying risk factors may rarely develop histoplasmosis. Oral lesions have been reported in 30%-50 % cases, mainly affecting the palate, buccal mucosa, and tongue.[1] Few localized oral histoplasmosis cases have been reported.

A 71-year-old male, without any known comorbidities and addiction presented with a nonbleeding ulcerative lesion on his tongue of 4 months' duration. On examination, a single ulcer measuring about 3 × 2.5 cm was found on the left lateral border of his tongue with rolled out margins, granular base, and cheesy exudates (Figure). Systemic examination was unremarkable. Routine laboratory investigations and viral serology markers were noncontributory. Abdominal and chest imaging were within normal limits. CD4/CD8 profile of the patient was normal. An incisional biopsy of the lesion revealed ulcerated epithelium at places, with base of ulcer showing inflammatory exudates. The submucosa showed epithelioid granulomas with foreign body giant cells. Fungal organisms resembling *Histoplasma* sp. were demonstrable in hematoxylin and eosin stain (H&E) as well on special fungal stains like periodic acid-Schiff-diastase (PAS-D) and Giemsa stain. The patient was treated with liposomal amphotericin B dosed at 3 mg/kg/d for 2 weeks followed by oral itraconazole (200 mg/d) for 6 weeks. A marked recovery was noted after 2 weeks.

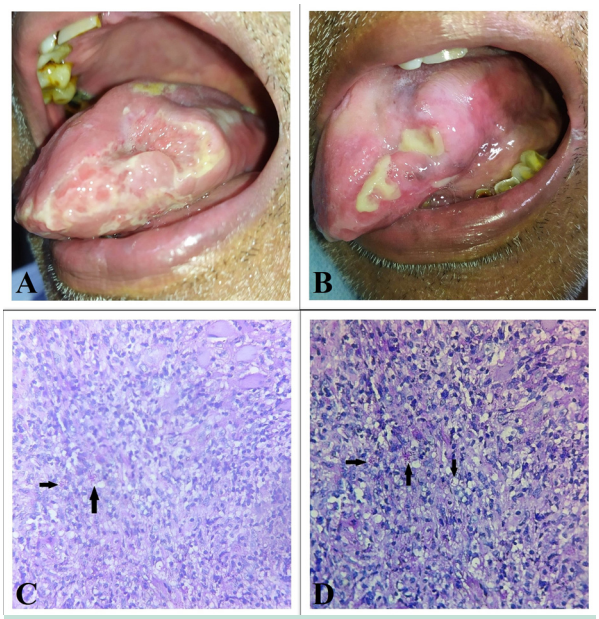

Figure **(A)** A solitary ulcer measuring about 3 cm × 2.5 cm on the left lateral border of tongue with everted rolled out margins, granular base, and cheesy exudates; **(B)** healing ulcer after 14 days of therapy; **(C)** hematoxylin and eosin (H&E) stain showing presence of intracytoplasmic histoplasma inclusion (arrow) with background showing characteristic lymphohistiocytic infiltration. Magnification (×400); **(D)** periodic acid-Schiff (PAS) stain highlights characteristic magenta-colored intracytoplasmic histoplasma bodies (arrow). Magnification (×400)

Histoplasma is an opportunistic pathogen known to affect both immunocompromised and immunocompetent patients. The 2 pathogenic subspecies of histoplasma are *Histoplasma capsulatum* and *Histoplasma duboisii*, which are prevalent in the United States, Brazil, Africa, and Indonesia but rarely detected in India, where only a handful of cases have been reported from West Bengal, Maharashtra, Uttar Pradesh.[2] Apart from immunosuppression as a result of HIV or AIDS, several risk factors have been identified for development of histoplasmosis, such as patients with chronic illness, diabetes mellitus, travel to countries endemic to histoplasma, extremes of ages, long-term intake of immunosuppressants, and organ transplant. After inhalation of spores, most patients may have cough, sore throat, fever, and fatigue that subside without treatment but few

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patients with the aforementioned risk factors may develop disseminated disease with multisystem involvement that might become potentially fatal.[3] Oral histoplasmosis may occur anywhere on the gums, palate, tongue, buccal mucosa, or pharynx in the form of painful ulcers, granular ulcerative growths, vegetative or nodular lesions, or deep ulcers with erythematous and whitish raised edges. These lesions may often mimic malignancies of the oral cavities, mycobacterial and deep fungal infections, or ulcers associated with systemic diseases like Crohn disease.[4]

Diagnosis of histoplasmosis can be easily confirmed by biopsy and special fungal stains. Amphotericin B is usually the treatment of choice, which is later replaced by systemic antifungals like itraconazole for long-term management.[5] Itraconazole, voriconazole, and posaconazole are preferred in cases of amphotericin intolerance.

Oral lesions are quite common with severe systemic disease, but localized histoplasmosis with only oral lesion is a rare presentation. In our case, the immunocompetency and localized disease-mimicking squamous cell carcinoma of tongue was a diagnostic dilemma. Moreover, no particular risk factor except for the age and residence in an endemic zone was contributory, which made the situation unique and challenging. The high degree of suspicion and subsequent investigation helped to establish the case as histoplasmosis, enabling proper management of the case.

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