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Case Report

Histoplasmosis masquerading as tongue carcinoma: a rare case report in an immunocompetent male

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ABSTRACT

Darling's disease, another name for oral histoplasmosis, is an uncommon but important form of Histoplasma capsulatum infection that can appear as oral cavity lesions that frequently mimic cancers like squamous cell carcinoma. Immunocompromised people, notably those with HIV, are most vulnerable to this fungal infection, while immunocompetent patients can still get it. Because of their appearance and chronic nature, the clinical presentation usually consists of painful, ulcerative lesions that could be mistakenly diagnosed as cancer. In the uncommon instance described in this analysis, an 80-years-old man who had no known addictions or comorbidities showed up with a non-bleeding ulcero-proliferative lesion on his tongue that had been there for two months. The lesion was eventually determined to be oral histoplasmosis after being misdiagnosed as mouth cancer. The diagnostic difficulties associated with this illness were highlighted by the histopathological investigation, which showed granulomatous inflammation and the distinctive yeast forms of Histoplasma. Inappropriate treatment plans and delays in efficient management can result from misdiagnosis. This example emphasizes how crucial it is to take oral histoplasmosis into account when making a differential diagnosis for oral lesions, especially in areas where it is endemic. To get positive results and avoid consequences from misdiagnosis, early detection and adequate antifungal medication are essential.

Keywords: Fungal lesion in oral cavity, Mimicking malignancy, Oral histoplasmosis, Oral cancer

INTRODUCTION

Histoplasmosis or Darling's disease, is a systemic infection caused by the dimorphic fungus *Histoplasma capsulatum*. This organism exists as a mycelial form in soil, particularly in environments enriched with bird or bat droppings and transforms into a yeast form at the human body temperature of 37°C.[1,2] The disease was first identified by Samuel Taylor Darling in Panama in 1906, who described it as an encapsulated protozoan. Histoplasmosis is highly prevalent in the Mississippi and Ohio river valleys of the southern United States, but cases have since been reported in temperate regions worldwide.[3] In Indian medical literature, Panja and Sen (1954) reported the earliest known case of histoplasmosis (HP) in Calcutta.[2] The primary route of infection occurs when spores are inhaled from dust in soil contaminated with bat or bird droppings. HP manifests in three clinical forms: the acute pulmonary type, characterized by spores infiltrating the tiny bronchioles or alveoli and a variant in which *Histoplasma capsulatum* colonizes pre-existing compromised lung tissue and a disseminated form, which typically affects individuals with weakened immune systems and can be particularly severe or even fatal.[4] The condition has been at risk of spreading among immunocompromised people with a history of organ transplantation, long-term corticosteroid use, systemic lupus erythematosus, Hodgkin's lymphoma or HIV infection. The most frequent sites of involvement have been identified as the tongue and buccal mucosa. India has reported less than 50 cases of histoplasmosis.[5]

CASE REPORT

This 80 years old immunocompetent male patient reported with chief complaints of painful ulcer on left side of tongue for two months. There is no history of trauma prior to the onset of the ulcer. The ulcer was also associated with severe sharp stabbing pain which led to odynophagia. There was no evidence of systemic symptoms. Patient had no exposure to bird or animal droplets.

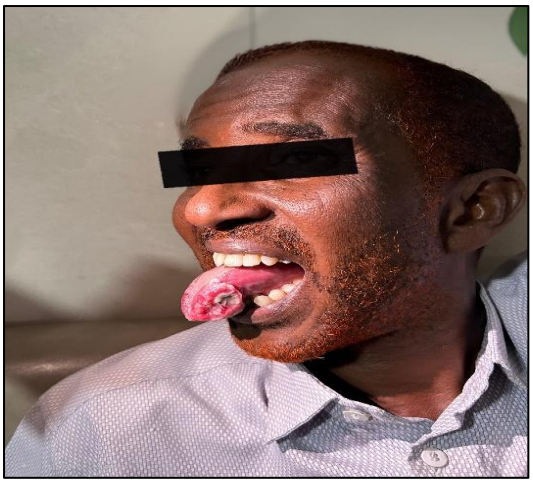

Figure 1: Image showing non healing ulcer over left lateral boarder of tongue.

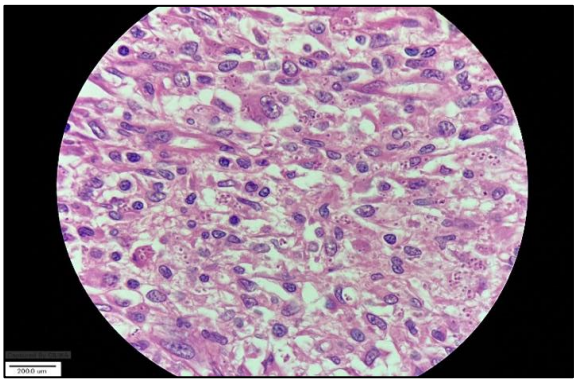

Figure 2: H&E stain showing histoplasmosis (40X).

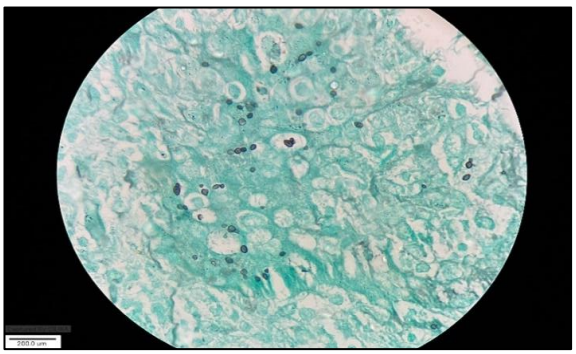

Figure 3: GMS stain showing yeast forms of histoplasmosis (100X).

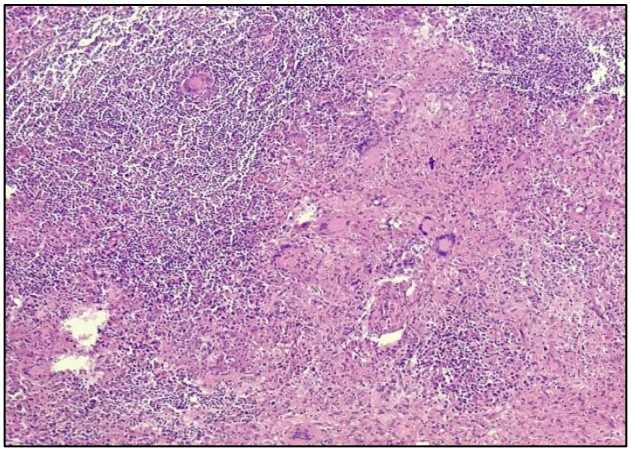

Figure 4: H&E stain, lymph node section showing granulomatous lymphadenitis and histoplasmosis (10X).

On examination: a solid ulcero-proliferative lesion on left lateral border of tongue measuring 2×1.5 cm, which was elliptical, granular, tender and indurated on palpation. Evidence of mild enlargement of lymph nodes in level I, II of left neck noted. An edge biopsy was carried out for histopathological analysis and routine hematological examinations. All the hematological parameters were within normal limits. The patient tested seronegative for HIV.

Patient underwent wide local glossectomy and intra-op frozen section, which showed sheets of lympho-histiocytic cells beneath the squamous epithelium and involving the lingular muscle fibers, scattered giant cells seen in deeper tissue. Mild to moderate nuclear atypia seen in histiocytes. So, patient also underwent supra-omohyoid neck dissection. Final deeper section biopsy report revealed scattered capsulated yeast like fungal organisms in the inflammation and giant cells. GMS stain on additional sections showed capsulated fungi. So, the final diagnosis amended to inflammatory pseudotumor of fungal etiology. Post recovery patient was kept on antifungals for 6 weeks and on follow up patient recovered completely.

DISCUSSION

Soil is the ecological reservoir for histoplasmosis, which is mostly a lung illness.[6] Two human-pathogenic strains of *H. capsulatum* are endemic in Central America and North America (*H. capsulatum* var. capsulatum) and West Africa (*H. capsulatum* var. duboisii). A third strain, *H. capsulatum* var. farciminosum, is an equine pathogen that is found in Africa.[6,8] A small number of cases have been documented from the Gangetic plains, Maharashtra, West Bengal and Uttar Pradesh in India, while this virus is prevalent in several parts of the USA, Brazil, Indonesia, Australia and Malaysia.[7] The fungus infects the mucosa directly or through a hematogenous pathway.

According to reports, there are around 3.4 instances of HP for every 100,000 people aged 65 and over.[9] Its severe form typically affects older people due to a decrease in cell-mediated immunity and newborns with documented immune process immaturity.

In Indians, HP primarily affects the extrapulmonary areas, especially in the oral cavity, according to Padhye et al.[10] Rarely, direct inoculation of *H. capsulatum* into the oral mucosa might cause localized HP.[7] A clinical differential diagnosis of squamous cell carcinoma, oral involvement of tuberculosis, syphilitic chancre, granulomatosis with polyangiitis or major aphthous ulcer is suggested by oral lesions present with constitutional symptoms such as dysphagia, weight loss, appetite loss and irregular low-grade fever. According to research by De and Nath, DH is a major contributor to pyrexia in individuals who are immunocompetent. The majority of those impacted are male and from rural areas (85%), highlighting the importance of occupation and soil exposure as indicators of DH diagnosis.[8]

H. capsulatum must be isolated on specific culture media, such as Sabouraud agar and cultured for six to twelve weeks at 25°C in order to provide a definitive diagnosis. The fungal colonies are smooth at first, but they soon become cottony, filamentous and brownish. Nonetheless, most asymptomatic individuals have negative cultures. In addition to cultures, skin scrapings, secretions, should be analysed using Parker ink or calcofluor white mounts and 10% potassium hydroxide (KOH). Gram stain, GMS or PAS should be used to stain tissue slices. [11]

There are three methods for employing serology as a marker to find antibodies to *H. capsulatum*: enzyme immunoassay (EIA), complement fixation (CF) and immunodiffusion (ID). A CF test antibody titre of 1:32 or above indicates an acute infection. The ID test measures the precipitating (H and M precipitin bands) antibodies qualitatively. The M band is less accurate, while the H band always indicates an active infection. Despite being the most sensitive test, the EIA has a significant false-positive rate. To assess therapy response, serum and urine levels of Histoplasma antigen and antibody can be tested repeatedly.[12] Based on the amplification of fungal gene sequences, polymerase chain reaction diagnostics is an effective technique for detecting invasive mycoses.[11]

The best course of therapy is antifungal medication, which is contingent upon the patient's health and the extent of the illness. Intravenous liposomal amphotericin B is the preferred treatment for immunocompromised individuals, such as those with HIV, who present with limited or disseminated disease. This is because the conventional form, amphotericin B deoxycholate, is less frequently used because of negative side effects. However, because itraconazole is less toxic than amphotericin and is safe, it is the recommended treatment option for immunocompetent patients and those with limited illness.[13,14] Immunocompetent patients with mild to severe infections typically have a favourable prognosis. Patients with severe diseases, immunocompromised individuals and those suffering from meningitis, fibrosing mediastinitis or chronic cavitary pneumonia, however, have a dismal prognosis.

Treatment

Itraconazole is the recommended treatment option for immunocompetent patients and those with limited disease since it is less harmful than amphotericin and is safe. Immunocompetent patients with mild to severe infections typically have a favourable prognosis. Nevertheless, the outlook is inadequate for individuals with serious illnesses, immunocompromised people or those suffering from meningitis, fibrosing mediastinitis or chronic cavitary pneumonia.[15]

CONCLUSION

A high index of suspicion and appropriate diagnostic measures are essential for differentiating between oral fungal lesions and oral malignancy ulcers to ensure effective treatment and management. Early diagnosis and management of such a deep fungal disease are crucial to preventing it from getting disseminated throughout the body. On review of the literature, oral HP is most found in elderly males, with the tongue being the most common intraoral site. Such lesions can be frequently mistaken for malignant ulcers, which should always be ruled out before performing any treatment.

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