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LOCALIZED MUCOCUTANEOUS HISTOPLASMOSIS OF TONGUE IN AN IMMUNOCOMPETENT PATIENT: A RARE ENTITY FROM A NON-ENDEMIC SUB-HIMALAYAN REGION.

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ABSTRACT A 46-year-old male presented to Department of Dermatology with complaints of multiple plaque like lesions on his tongue which were present since last 9 months. The systemic investigations were normal which included. hemogram, Liver and kidney blood chemistries, blood sugar, electrolytes, serum cortisol, urine and stool microscopy, electrocardiograph were all normal. HIV test was negative. CBNAAT for tuberculosis (TB) was also negative. Biopsy, on mycological staining revealed multiple yeast cells, intracellularly as well as extracellularly. A diagnosis of deep fungal infection as histoplasmosis was made and confirmed on culture.

KEYWORDS : Histoplasmosis, immunocompetent, giemsa staining, tuberculate conidia, itraconazole, oral lesion.

INTRODUCTION

Histoplasmosis also known as Darling's disease in the honour of Samuel Taylor Darling, is a systemic granulomatous fungal infection caused by *Histoplasma capsulatum*. It is a dimorphic fungus that grows on soil with high nitrogen content like soil which is contaminated with bird droppings. There are three varieties or var of *H.capsulatum: capsulatum, duboisii and farciminosum*. *H.capsulatum: capsulatum and duboisii* infect humans where a *farciminosum* is an equine pathogen. *H.capsulatum* is endemic in countries like USA, South America, Malaysia and Indonesia.[1,2] It is rare in India but is endemic in small regions of West Bengal, the Gangetic Plains and Western India.[1,2]

Histoplasmosis is clinically classified into four presentations: Mucocutaneous form, primary acute pulmonary, chronic pulmonary and disseminated. Oral manifestations of histoplasmosis are usually associated with chronic disseminated form of the disease, though it may occur as an isolated superficial infection in immunocompetent individuals without underlying clinical disorders. The oral lesions are frequently located on the tongue, palate, or lips.[4]

We report herein a case of histoplasmosis in an immunocompetent patient with lesions exclusively in the oral cavity.

Case report:

A 46-year-old male, labourer, resident of Kangra, Himachal Pradesh North India, with a history of working with poultry in last one year, presented with complaints of multiple plaque like lesions on his tongue which were present since last 9 months in the department of Dermatology. He was a chronic smoker. There was no history of diabetes or pulmonary TB, malignancy, AIDS, adrenal insufficiency. There was no history of fever, weight loss, decrease in appetite or shortness of breath.

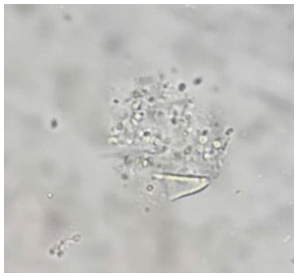
On examination, patient was afebrile, normotensive and no lymphadenopathy. Cutaneous examination showed multiple erythematous, discrete, non-tender, firm papules, and plaques over tongue. Chest Xray findings were unremarkable. Complete blood count, Liver and kidney blood chemistries, blood sugar, electrolytes, serum cortisol, urine and stool microscopy, electrocardiograph were all normal. HIV test was negative. CBNAAT for tuberculosis (TB) was also negative thus ruling out oral tuberculosis.

A biopsy was taken. Later he developed ulcerative lesion over the plaque. This led to high fever in last 20 days. There were no other systemic complaints. The biopsied tissue was sent to Microbiology in normal saline and to Pathology in formalin. Histopathological examination showed inflammatory infiltrates containing lymphocytes, neutrophils and few eosinophils seen.

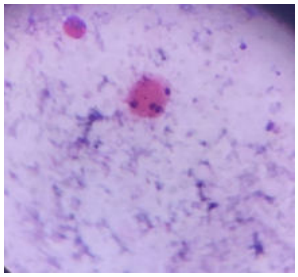
Mycological evaluation revealed yeast cells, intracellularly as well as extracellularly in direct smear via KOH (fig.1), gram stain and giemsa stain (fig.2). After inoculating the sample on sabouraud dextrose agar (SDA) with and without antibiotics and actidione, white cottony dry growth was observed on SDA with antibiotic (25^{o}C)(fig.5) and yeast like pasty white growth was observed at 37^{o}C after 21 days(fig.6). The Lactophenol Cotton Blue mount of the teased mycelial growth revealed hyaline, septate fine hyphae along with tuberculate, thick walled, macroconidia of size approx. 8-10 µm and elliptical microconidia of size 2-4 µm.(fig.3), giemsa stain of yeast like growth showed yeast of 2-4 µm.

For conversion test the growth was inoculated on brain heart infusion agar with 6% sheep blood at 37^{o}C, after multiple subcultures yeast-like growth was observed of approx. 4µm. (fig.4) These findings confirmed that the isolate was *Histoplasma capsulatum*.

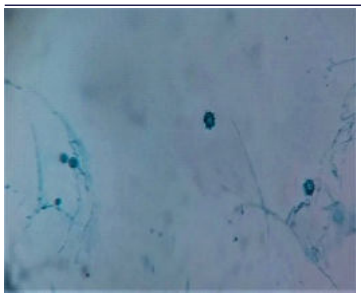
After confirmation of the diagnosis patient was started on oral itraconazole, 200 mg BD for 6 months. On the 15th day after the initiation of treatment patient showed clinical improvement as he had no fever and the ulcer also started to heal. On 1 month visit ulcer was completely painless and was healed halfway.



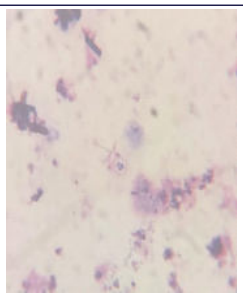
1.KOH mount of biopsy.



2. Intracellular yeast cells.



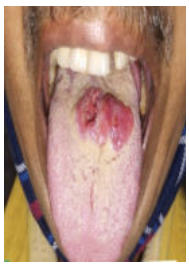
3.Tuberculate macroconidia with microconidia on LCB



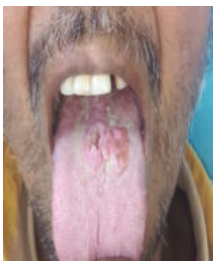
4. Yeast phase on geimsa stain

5. Dry growth on SDA at 25^{o}C.

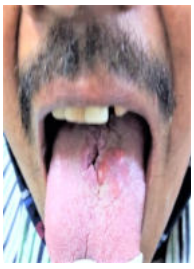
6. pasty growth on SDA at 37^{o}C



7. lesion before treatment



8. Lesion after 15 days of treatment



9. Lesion after 1 month

DISCUSSION

Histoplasmosis is primarily a pulmonary disease with it's reservoir in the environment as soil. Humans acquire the infection via inhalation of conidial spores present in the environment, like caves which are residence of bats and soils which has droppings chickens. Like most fungal diseases, predisposing factors for histoplasmosis are unclear. There is recent experimental evidence demonstrating that susceptibility to *H. capsulatum* strongly depends on genetic predisposition.[5] This is an intracellular pathogen which remains in the reticuloendothelial system i.e., macrophages and giant cells.[6] The outcome of infection with *H. capsulatum* is determined by dynamic interactions between innate immunity, adaptive immunity and fungal virulence factors.[7] The microconidia formed in the mould phase of *H.capsulatum* are easily aerosolized, inhaled into the lungs, and then phagocytized by alveolar macrophages. Moreover, control of *H.capsulatum* infection is largely based on activation of cellular immunity in concert with innate responses.[8] If cell-mediated immunity is deficient because of underlying illnesses or immuno-suppressive drugs, the organisms remain alive within macrophages continue the progression of infection. In many reported cases, disseminated forms are more associated with immunodeficient subjects, notably those with HIV infection. Oral histoplasmosis has frequently been reported in HIV-seropositive patients.[9] Only few cases of isolated oral histoplasmosis in immunocompetent patient has been seen since 1946.[10]

The disease has wide range of clinical presentations, ranging from asymptomatic infection, chronic pulmonary infections, to disseminated infections.[11] Patients infected with *H. capsulatum* show diverse clinical manifestations, making diagnosis difficult. The differential diagnosis of histoplasmosis with other ulcerative oral diseases is often made by a tissue biopsy or culture of *H. capsulatum*. Males are more frequently affected than females by 4:1 ratio[1]. Oral histoplasmosis is usually diagnosed after the discovery of lesions in the upper aerodigestive tracts in the absence of pulmonary signs. These lesions may remain the only location for a long period of time.[12] These mucosal lesions appear in almost every part of the oral mucosa, yet the commonest sites are tongue, palate, and buccal mucosa.[13,14] These lesions could be nodular, ulcerative, verrucous, or plaque-like.[15] Later these can develop into ulcerating, indurated and painful lesions.[16] Oral histoplasmosis mimics other oral ulcerative lesions such as chronic traumatic ulcers, squamous cell carcinoma, lymphomas, Crohn disease, ulcerative necrotic gingivitis or stomatitis, tuberculosis, and necrotizing sialometaplasia.[17] Amphotericin B and certain azoles are effective against H capsulatum.[18] Itraconazole and fluconazole have been effective in treating head and neck histoplasmosis with 85% to 100% and 86% of cases, respectively. The refractory cases to initial azole treatment should be converted into amphotericin B.[19] However, treatment with itraconazole has also been reported as favorable.[20] These data, combined with other reports,[10,21] suggest that, with localized lesions without detection of systemic signs or symptoms, drugs with less toxicity, such as the itraconazole, should be chosen for therapy.

Histoplasmosis is not very common in India with maximum cases reported along the Gangetic plains. The first case of histoplasmosis in India was reported by Panja and Sen in 1954 from Calcutta[22]. After 1994 the major number of cases were from Uttar Pradesh and West Bengal along the Gangetic plains. New Delhi, Tamil Nadu and Maharashtra, previously not considered endemic, have reported some cases in recent times. Isolated case from Chandigarh, Bihar, Rajasthan, Madhya Pradesh, Gujarat, Chhattisgarh and Kerala have also been reported[23]. Mahajan et al[24] and Raina et al[25], have mentioned four cases of Histoplasmosis with varying presentation from Himachal Pradesh. No other documentation has been done elsewhere from Himachal Pradesh.

These sporadic cases from Himachal Pradesh, specially from Kangra valley, makes us ponder that whether Histoplasmosis is an emerging disease of this region.

The uniqueness of this case is that it presented as plaque which became an ulcer on the tongue thus mimicking malignancy in an immunocompetent person with no underlying features of dissemination or immunosuppression. Further, we need to highlight the case to create awareness in all clinicians and laboratory personnel regarding the presentation and diagnostic modalities needed to recognize such cases at the earliest so that treatment can be initiated.

CONCLUSION

One should do a proper analysis before making a diagnosis of histoplasmosis especially in immunocompetent patients who live in non-endemic areas. Exclusive mucocutaneous oral histoplasmosis in an immunocompetent person is rare but such cases are emerging more and more so thorough clinical and microbiological investigations must be done before confirming the diagnosis. Itraconazole is a good treatment option in such cases with good clinical outcome.

Declaration of Conflicting Interests

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