Oral Lesions - Leading Diagnosis of Disseminated Histoplasmosis

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Histoplasmosis is a systemic mycotic infection caused by *Histoplasma capsulatum*. Although rare in India, it is endemic in over 300 countries. If immunity is good in a healthy person, even if this fungus is inhaled, it may cause mild symptoms and can be controlled by supportive therapy. However, in persons with very low immunity, as in the case of human immunodeficiency virus-positive persons, a serious disseminated form could be life-threatening in delayed diagnosis and delay in proper treatment. Due to pulmonary symptoms, it is commonly misinterpreted as tuberculosis and treated accordingly without results. However, oral lesions which occur can reveal the correct diagnosis by biopsy procedure and microscopic confirmation of this rare disease. We had a 76-year-old patient suffering from pulmonary signs of cough, weakness, and with gums and tongue lesions, who was referred by a general dental practitioner for diagnosis of oral lesions. The tongue and gums lesions biopsy revealed the correct diagnosis of granulomatous lesion with yeast-like organisms of giant cells, indicating *histoplasmosis capsulatum* diagnosis which was later treated by immunology experts in the hospital with proper antifungal agents like amphotericin B and management of this disseminated histoplasmosis with other investigations. Therefore, systemic diseases also need oral examination to rule out many unusual diseases.

**Keywords:** Disseminated form, *Histoplasma capsulatum*, Human immunodeficiency virus, Tuberculosis

INTRODUCTION

Histoplasmosis is a systemic granulomatous fungal disease caused by *Histoplasma capsulatum* and is rare in India, and only a few cases have been reported. It is commonly seen in certain regions of USA, South America, Africa, Indonesia, Malaysia, Ohio and the Mississippi River and is less reported from Asia and Europe.¹ Histoplasmosis occurs when the soil is contaminated with bird and bat dropping, common sites in caves, chicken droplets, contaminated soil, etc.,⁴,⁵ and the environmental air gets contaminated with such fungus which is inhaled by the persons working in such areas. Even in places where demolition of buildings and construction work is in progress, the air contamination is positive. Normally, it is not so common to be in disseminated form, unless the person is in immune deficiency situation like human immunodeficiency virus (HIV) or other reasons of very low immunity and disseminated form can affect various organs and areas of the body. When widespread, it is potentially fatal if not treated without delay and properly. Simple forms can be cured without much problem. The lungs, oropharyngeal region, aerodigestive track, oral lesions, ulcers in gums, tongue, palate, nodules, etc., are common occurrence sites. Pulmonary signs are common, with a cough and weakness, similar to tuberculosis and hence are usually misinterpreted⁴,⁵ with tuberculosis.

Histoplasmosis may occur in primary pulmonary form, chronic form or disseminated form, mainly in immunodeficient persons, namely HIV or other forms of immunodeficiency, and rarely does it occur fatally⁶ with widespread organ involvement if not treated early with proper antifungal medicines. In disseminated form, oral lesions are commonly seen and sometimes skin manifestations also occur.

In our article, we are discussing the diagnosis of histoplasmosis due to oral lesions and suspicion by oral diagnosticians; the patient was HIV seronegative in investigations and was disseminated state.

CASE REPORT

An old person, age 76 years, thin and weak, came with the complaint of gums and tongue problem, referred by another dentist for consultation and the needful.
First, gave time to the patient to tell about the complaints and brief about himself, profession/business and general health and specific medical history if any. He replied that he is having this gum problem and tongue swelling for a few days. The previous dentist tried to treat the gum problem with mandibular anteriors, but bleeding was excessive and did not continue. Regarding the tongue, he had swelling on the dorsum of the tongue and felt all the food as totally tasteless.

**General Health**
He had bypass surgery done about 20 years back. He had a cough for few days with blood in the sputum. He had considerable generalized weakness. He also had hypertension. He also suffered from diabetes for quite some time and was taking insulin injection. He felt he had lost weight. He had injured his leg and wound which was not healing for a long time, giving him pain. He also had an eye operation (cataract) done.

Blood pressure: 110/70; pulse-normal now with medicines. No oedema of feet and no skin lesion. The liver problem-recently checked by his physician-positive.

**On Examination**
Tongue has dome-shaped circular swelling in the center of the tongue and a lot of white fur on the tongue with an adjacent small swelling and ulcers in the region. It was firm in consistency (Figure 1).

Mandibular anterior region 42, 41/31, 32, 33 lingual gingiva, there was swelling with corrugated surface and it was painless. Anteriorly, gingival papillae swollen slightly. No lymph nodes in the cervical area noticed on examination (Figures 2 and 3).

Advised intraoral periapical radiograph X-ray 42, 41/31, 32, 33 region and incisional biopsy of the tongue lesion and gingiva 43, 42, 41/31, 32, 33 region (Figure 4). The X-ray revealed radiolucency in 42, 41/31, 32 apical region of the mandible and interdental bone loss up to one-third of the roots.

Before proceeding for biopsy, toluidine blue staining test was done: It was negative on gums and dorsum surface (false positive slightly due to fur coating) (Figure 5a and b).

The patient agreed to biopsy and gave consent to proceed.

Under antibiotic cover, an incisional biopsy was done with local anesthesia of the tongue lesion and the gum lesion, mandibular anteriors lingual surface (Figure 6a and b).

**Histopathology Report**
A. Gums: Section shows extensively ulcerated squamous mucosa overlying a very dense granulomatous disease.

It consists of groups of plump histiocytes and many multinuclear giant cells. The cytoplasm is filled with parasite composed of sharply defined capsule of oval to round yeast structures containing a dot like parasite with a halo.
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Figure 4: Intra oral X-ray 42, 41/31, 32, 33 region-reveals radiolucency 42, 41/31, 32 and interdental bone loss

Figure 5: (a and b) Toluidine blue staining

Figure 6: (a and b) Biopsy of gingival lesion and tongue lesion with suture

B. Tongue: This is similar, but with pseudoepitheliomatous squamous mucosa and sparse population of the parasite.

Diagnosis
Histoplasmosis of gums and tongue; to look for the cause of immune deficiency, if any.

After the lesions microscopic diagnosis of histoplasmosis, the patient was immediately referred to the specialist in immunodeficient cases management, as other symptoms and signs were highly suspicious of disseminated form and immediate treatment and further investigations were necessary.

After referring, he was immediately started with the treatment with antifungal amphetericin-B, after admission to the hospital for further investigations. Further investigations were done basically to rule out HIV seropositive or not, but in our case, he was HIV negative. Further investigations were done as he had chest infection, breathlessness and cough with blood, and hepatomegaly was observed on examination. The culture was also done, which was found to be positive. Weight loss and weakness, etc., confirmed it was a disseminated form in this old person of 76 years. Full body positron emission tomography (PET) scan was also advised as early history of heart problem with bypass surgery due to which proper observation and care was essential in the hospital. After initial phases, he was feeling better, and then he was discharged after a week with the need of follow ups and treatment.

DISCUSSION

This rare histoplasmosis caused by dimorphic fungus *H. capsulatum* was first diagnosed by American pathologist Samuel Darling in 1906. Histoplasmosis capsulatum is a dimorphic fungus, an etiologic organism has three common types: (1) *H. capsulatum* var. *capsulatum*, (2) *H. capsulatum* var. *duboisii*, and (3) *H. capsulatum* var. *farcinimous*. The first two types affect human beings and it is an intracellular organism parasitizing reticuloendothelial system in histoplasmosis affecting various organs. This rare fungus exists as a saprophyte in the environment and can be obtained from soil contaminated with bird roosts, chicken coops and bat droppings in caves, construction sites and commonly the mycelia and spores are inhaled through the respiratory tract from the environment by the persons in the vicinity. Aerobic and Aerobic gastric encroachment of hyphae elements then convert in yeast and survive and replicate in host macrophages. It is usually self-limited in normal and healthy persons having good immunity. However, in low immunity persons, it allows disease evolution commonly in HIV seropositive patients and those with immunocompromised persons, when it could lead to disseminated infection which could be life-threatening if not diagnosed early and properly treated it could be fatal.

Systemic involvement of pulmonary symptoms, pneumonitis with a persistent cough and breathlessness, even causing weight loss, and chest pain with chronicity is commonly misinterpreted as tuberculosis. In India, tuberculosis is common.

Later, other organs such as liver and spleen involve in systemic fibrous illness such as tuberculosis or malignancy and liver failure. The oral cavity in disseminated form is common, with lesions of the tongue, gums, ulcers in oral mucosa, cheeks, palate, etc., or granular, nodular forms which do not respond to common medicines. Skin lesions may also occur.
We received the patient from a dental practitioner for the lesion on the gingiva, mandibular anterior region, and dorsum of the tongue with nodular swelling which did not respond to common medicines, namely antibiotics and gums treatment. Thus, the patient was referred for diagnosis and the needful to the oral diagnostician/oral medicine specialist.

This patient had a chronic cough, chest pain, and generalized weakness. He also had insulin-dependent diabetes. The tongue swelling on the dorsum of the tongue was firm, nodular (Figure 1) with ulcer and gingival marginal swelling with corrugated surface extending to mandibular anterior teeth region on the lingual aspect (Figure 2).

To rule out malignancy clinically, both lesions were subjected to toluidine blue staining (Figure 5a and b). The gingival lesion was negative, but the tongue lesion was false positive due to fungal coating and was not considered. Incisional biopsy was subsequently performed on tongue and lingual gingiva swelling (Figures 6a and b).

It was the histopathological report which confirmed the diagnosis of histoplasmosis as both tongue and gingiva specimen revealed similar diagnosis with yeast-like features and giant cells and hollow areas with parasitic organism “H. capsulatum” (Figure 7 and 8). The patient was also having liver involvement signs. Clinical investigations for HIV seropositivity were negative. Thus, he was not suffering from acquired immune deficiency syndrome.

Disseminated form of histoplasmosis was hence confirmed and was referred to an immunology specialist and the patient was admitted to hospital. After admission to a hospital, further investigations were done and he was treated with amphotericin-B intravenous injection, which is the most effective for histoplasmosis. Alternate therapy itraconazole 200 mg twice orally for a long time is also effective with follow-ups and observation. Specimen was also sent for culture testing which was positive.

The patient was also investigated in the hospital for liver failure and management and further investigations, such as PET scanning and diabetes control. It was the oral lesions which diagnosed the disseminated form of histoplasmosis which was not even thought of by general physicians. Hence, it is necessary to take the dental specialist’s oral diagnosis opinions in most of the systemic diseases having oral examination done for all such patients.

Histology-histoplasmosis-presence of tiny spores within cytoplasm of macrophages and the presence of giant cells spores of H. capsulatum in section clearly seen as round bodies surrounded by oval bodies surrounded by a clear space originally interpreted as a capsule (H. capsulatum) although there is no capsule but clear space in the cell wall of the fungus and clear space is filled with granular material that separates the cell wall of the fungus from cytoplasm of microphage. Differential diagnosis from other fungal infection such as Cryptococcus neoformans, Penicillium marneffei, Candida glabrata, and leishmaniasis - the absence of clear halo around spores - etc.

**CONCLUSION**

A rare case of histoplasmosis in disseminated form was diagnosed because of oral lesions in the oral cavity. Biopsy of the oral lesions, the most rapid diagnosis of histoplasmosis, which helped in further investigations and the proper management and care of the patient suffering from low immunity-systemic diseases. It is absolutely essential to have oral cavity examination done by a dentist or oral medicine specialist in cases of patients suffering from systemic diseases.
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