

Histoplasmosis of Larynx in Immunocompetent Patients Mimicking Carcinoma: Report of Two Cases

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ABSTRACT

Histoplasmosis is a fungal infection primarily acquired through inhalation, and is rarely encountered outside endemic areas. In non-endemic areas, histoplasmosis poses a diagnostic challenge, especially since the presenting lesions can mimic carcinoma. We report two unusual cases of laryngeal histoplasmosis in association with oral mucosal ulcers in two immunocompetent patients from Haryana, India, the state where the prevalence of histoplasmosis is very low. (*J Infect Dis Antimicrob Agents* 2008;25:145-9.)

INTRODUCTION

Histoplasmosis is caused by a dimorphic fungus, *Histoplasma capsulatum*. Human infections may manifest as pulmonary or disseminated histoplasmosis. Laryngeal involvement is usually noted in chronic disseminated histoplasmosis, but a few cases of primary laryngeal histoplasmosis have been reported. To our knowledge, less than 100 cases of laryngeal histoplasmosis have been reported in published medical literature.^{1,2} Oral and oropharyngeal manifestations often coexist with laryngeal histoplasmosis.³ Patients with histoplasmosis are on the rise because of the ongoing HIV pandemic and the increasing occurrence

of compromised conditions including of diabetes mellitus, malignancies, and the use of cytotoxic drugs.⁴ We report on two cases of primary chronic laryngeal histoplasmosis in association with oral mucosal lesions in two immunocompetent patients from Haryana, a state of North part of India (Figure 1), where histoplasmosis is rarely seen.

Case 1

A 47-year-old man came to the Ear, Nose, and Throat (ENT) outpatient department. He had had a hoarse voice and painful ulcer on the tongue for the previous three months. The patient was a farmer and

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Figure 1. The map of India, showing the state of Haryana (square) and the region of the Gangetic belt [comprising the states of the Uttaranchal, Uttar Pradesh, Bihar, and the West Bengal, (circles)].

lived in a village about 100 kilometer from the tertiary referral hospital. There was no history of weight loss or fever. On oral examination, an ulcerative lesion of 1 centrimeter x 1.5 centrimeter was noted on the posterolateral aspect of the left side of tongue. On indirect laryngoscopy, an exophytic lesion was seen involving the laryngeal surface of the epiglottis, the left aryepiglottic fold, and the left vocal cord. A diagnosis of probable carcinoma of the larynx was made, and biopsy was then obtained under direct laryngoscopy. The biopsy report was inconclusive showing chronic inflammation, hence another biopsy

was taken from the tongue ulcer. This biopsy revealed typical features of *H. capsulatum* (Figure 2). No atypia nor malignancy was noted. A repeat biopsy was then taken from the laryngeal lesion, which then confirmed the diagnosis of histoplasmosis. Disseminated histoplasmosis and an immunocompromised state were excluded by conducting a complete blood count, blood sugar, urine culture, liver function tests, chest X-ray and enzyme-linked immunosorbant assay (ELISA) for HIV, which were all normal. The patient had no lymphadenopathy or hepatosplenomegaly. The final diagnosis was orolaryngeal histoplasmosis. The patient

had then received itraconazole 200 mg twice daily. The patient gradually improved after the treatment, and all lesions resolved over a period of 4-6 weeks. The patient was asymptomatic on subsequent follow-up visits.

Case 2

A 45-year-old vegetable vendor came to the ENT outpatient department with a history of hoarse voice for the previous four months. On examination, an exophytic lesion was noted on the anterior aspect of both vocal cords. A probable diagnosis of laryngeal growth was made, and a biopsy was taken. This biopsy revealed chronic inflammatory tissue, hence, a repeat biopsy was taken but it was also inconclusive. Subsequently, the patient developed painful lesions on the anterior part of the hard palate (Figure 3). A biopsy from this lesion showed both intracellular and extracellular yeast cells, suggestive of *H. capsulatum*. A review of the previous biopsy taken from the laryngeal lesion was done, and similar yeast cells could now be identified in that biopsy. Finally, a diagnosis of mucosal histoplasmosis was made. All routine clinical investigations in the patient were normal and no infectious or other causes of immune suppression could be identified in this patient. He had received itraconazole 200 mg twice daily, and there was a remarkable response. On follow-up, the patient was completely asymptomatic.

DISCUSSION

Chronic ulcerative and granulomatous lesions of the upper aerodigestive tracts are frequently seen. The differential diagnosis usually includes malignancy and tuberculosis. Fungal laryngitis, especially in immunocompetent patients, is often overlooked and misdiagnosed because it closely mimics carcinoma. However, the possibility of fungal infections should

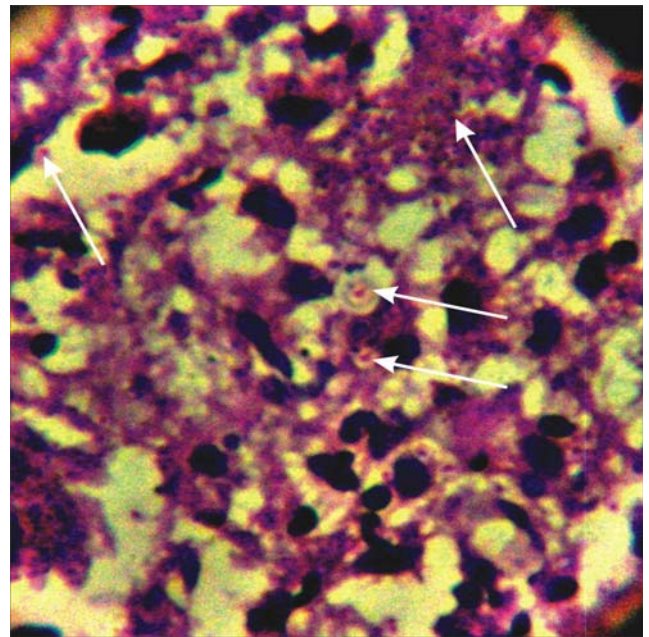


Figure 2. Periodic acid Schiff-stained histopathological section from the oral ulcer in Case 1, showing yeast cells with a clear halo around them (arrows).



Figure 3. Ulcerative lesion on the hard palate in Case 2.

always be kept in mind, and biopsy should always be performed before resorting to radical surgery.⁵

Histoplasmosis is one such fungal infection, which can involve the upper aerodigestive tract.⁶ Histoplasmosis is caused by the dimorphic fungus, *H. capsulatum*, which exists in the environment, in the soil in mycelial form but gets converted into yeast cells inside the human body. Infection is primarily acquired by inhalation, but there are rare cases where cutaneous inoculation of *H. capsulatum* has occurred. Soil is the natural habitat of *H. capsulatum*, and the fungus is often found in soils enriched by avian and bat excrement. Such soils may remain infectious for years. This dimorphic fungus is endemic in the Mississippi and Ohio river valleys in the United States of America.^{2,7} Histoplasmosis is rarely encountered in non-endemic regions. Reported cases in these regions are likely due to geographic microfoci of disease, or to reactivation of latent infection in hosts with a previous travel history to endemic areas. Otolaryngological manifestations of histoplasmosis are usually seen in the form of flat plaque-like non-tender elevations or nodules that later ulcerate and become painful.⁸ Mucosal surfaces of gingivae, tongue, lips, and pharynx are common sites of involvement. Lesions may also involve any area of the larynx, but the anterior part of larynx is more commonly involved. Sobrinho and colleagues made an extensive review of laryngeal histoplasmosis with diverse presentations.¹

The common presenting manifestations of laryngeal histoplasmosis include sore throat, hoarseness, and dysphagia. The gold standard for achieving the diagnosis is isolating the microorganism on culture. Diagnosis is often confirmed by taking biopsies from suspicious areas for histological examination. This usually reveals macrophages containing yeasts, which stain prominently with periodic acid Schiff and Grocott (silver) procedures. Cultures of the organism can also

be obtained from the sputum or biopsy material. The organisms can usually be recovered on Sabouraud dextrose agar medium. Unfortunately, there was no confirmed fungal cultures in both our cases.

In India, histoplasmosis is uncommon, and is usually reported from the Gangetic belt (Figure 1). A few cases have been reported from West Bengal, Andhra Pradesh, Bihar, Assam, Orissa, Tamil Nadu, Uttar Pradesh, and Kerala (Figure 1). It is usually seen in immunocompromised conditions like AIDS and diabetes mellitus.

Both of the patients discussed in this study were residents of Haryana, the state where histoplasmosis is rarely seen. Because of their presenting complaints of hoarseness of voice and the indirect laryngoscopic findings of exophytic lesions in the larynx, a probable diagnosis of carcinoma of the larynx was made. Histoplasmosis was discovered incidentally when repeated biopsies from oral ulcers were undertaken.

A high index of suspicion of histoplasmosis should be kept in mind in cases of ulcerative lesions of the upper aerodigestive tracts, where histological examination of the biopsies fails to show dysplasia or where there is a failure to respond to anti-tuberculous treatment.

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