Histoplasmosis Presenting as a Laryngeal Ulcer in an Immunocompetent Host

Mary John¹, Jency Maria Koshy², Sangeetha Mohan³, Preethi Paul⁴

Abstract

Histoplasmosis is a granulomatous disease of worldwide distribution caused by a dimorphic fungus Histoplasma capsulatum. Majority of primary infections in immunocompetent hosts are asymptomatic or may present with flu-like illness. Histoplasmosis may occur in three forms: (i) Primary acute pulmonary form, (ii) chronic pulmonary and (iii) disseminated form. The manifestations of disseminated form of histoplasmosis are fever, weakness, weight loss, hepatosplenomegaly, and mucocutaneous lesions. The mucosal involvement could be oropharyngeal or laryngeal involvement. We report an unusual case of histoplasmosis presenting as a laryngeal ulcer in an immunocompetent host.

Introduction

Histoplasmosis is a granulomatous disease of worldwide distribution caused by a dimorphic fungus Histoplasma capsulatum (H. capsulatum).¹ H. capsulatum is acquired by inhalation of mycelial fragments of the fungus. Histoplasmosis is less frequently reported in Asia and Europe.²,³ Histoplasmosis has been reported in immunocompetent and immunocompromised individuals with the disseminated forms being more common in the latter group. Its presentation can be varied. We report an unusual case of histoplasmosis presenting as a laryngeal ulcer in an immunocompetent person.

Case Report

A 53 years old man, government employee from Himachal Pradesh presented with history of fever, cough and generalised weakness for 2 months. He was initiated on antituberculous medication 3 weeks prior to presentation which he discontinued as symptoms persisted. He was a chronic smoker and consumed alcohol regularly for 20 years.

On examination, he was febrile with rest of the systemic examination being normal. Hematological and biochemical parameters including liver function tests were normal. Cultures of blood, sputum and urine were sterile. Sputum for acid fast bacilli was negative. Chest X ray revealed a non-homogenous opacity in the right upper zone. A computed tomographic (CT) scan of the chest revealed centriflobular emphysematous changes with parenchymal scarring of the right apical segment. Echocardiogram did not reveal any evidence of infective endocarditis.

One week later, he developed hoarseness of voice with continuing fever. Flexible laryngoscopy revealed multiple ulcers on the laryngeal surface of the epiglottis and the vocal cords. Clinical impression was that of a laryngeal carcinoma, and a biopsy was taken.

Biopsy of the laryngeal ulcer revealed ill-defined granulomas comprised of epithelioid cells and lymphocytes, and special stains revealed histoplasmosis (Figures 1, 2).

Since histoplasmosis has been noted to involve the adrenal glands, a CT scan of the abdomen was done which revealed bilateral adrenal gland enlargement, (Figure 3) although there was no clinical evidence of adrenal insufficiency.

The patient was initiated on Itraconazole and discharged from the hospital. However, he continued to have fever even after 1 month of treatment. Hence he was re-admitted for administration of Amphotericin B which had to be stopped due to an anaphylactic reaction. He was initiated on Voriconazole to which

Fig. 1: Vocal cord biopsy showing dense infiltrate of histiocytes and lymphocytes. H&E, 200x
he responded. He continued his treatment for 1 year during the course of which the hoarseness of voice improved and he gained weight. He has been asymptomatic thereafter.

**Discussion**

Histoplasmosis is acquired by inhalation of dust particles from soil contaminated with bird or bat droppings that contain small spores (microconidia), the infectious form of fungus. Histoplasma is known to occur naturally in caves inhabited by bats. The outbreaks of histoplasmosis have been reported in cave explorers.

Majority of primary infections in immunocompetent hosts are asymptomatic or may present with flu-like illness. Histoplasmosis may occur in three forms: (i) Primary acute pulmonary form, (ii) chronic pulmonary and (iii) disseminated form. The manifestations of disseminated form of histoplasmosis are fever, weakness, weight loss, hepatosplenomegaly, and mucocutaneous lesions.

The mucosal involvement could be oropharyngeal or laryngeal involvement. The oral lesions may occur in any part of the oral cavity and the lesions vary from nodules to painful shallow or deep ulcers. The incidence of oral manifestation is 25-45% in the disseminated form of the disease.

Laryngeal involvement is usually associated with dissemination. In a study involving 79 cases of histoplasmosis, Goodwin et al reported that the oropharyngeal and laryngeal involvement in acute, subacute and chronic disease were 19%, 31% and 66%, respectively. Of the 58 oropharyngeal and laryngeal lesions; only seven were located in the larynx.

Laryngeal involvement of histoplasmosis poses a diagnostic difficulty because clinically it can be mistaken for papillomatosis or even malignancy and microscopically it can be confused with blastomycosis (due to similar microscopic appearance), tuberculosis (due to presence of necrosis and granulomas) and squamous cell carcinoma because of atypical epithelial response (pseudo-epitheliomatous hyperplasia) seen in these cases.

Skin lesions in histoplasmosis range from papules and plaques with or without crusts, pustules and nodules to mucosal ulcers and erosions, molluscum contagiosum-like lesions, acneiform eruptions, erythematous papules and keratotic plaques. This patient did not have any skin manifestation.

Our patient also had evidence of adrenal gland involvement on imaging studies (Figure 3) even though there was no clinical manifestation. Studies have revealed that clinical manifestation of adrenal insufficiency is uncommon, and occurs in only about 7-20% despite a high proportion (80%) of adrenal gland affection detected via imaging studies and autopsy findings. The adrenal gland affection may be silent or may present as unilateral or bilateral adrenal masses.

Gopalakrishnan et al noted five immunocompetent men (mean age 55.6 yrs.) from a nonendemic area with adrenal histoplasmosis presenting with constitutional symptoms. Three patients had adrenal insufficiency at presentation with bilateral adrenal involvement and the other two developed adrenal insufficiency during the course of the illness and had unilateral adrenal mass.

The granulomatous inflammation within the adrenals is due to a large number of macrophages amidst high concentration of steroid hormones that promotes growth of the organism. The adrenal function recovers following cure with antifungal therapy unlike that seen with treatment of tuberculosis, where lifelong cortisol replacement is needed.

In conclusion, a high index of suspicion is needed to make a diagnosis of histoplasmosis early especially in immunocompetent host resident in non-endemic areas. Clinical features and laboratory features are identical to the commonly seen granulomatous infections such as disseminated tuberculosis. It also mimics laryngeal carcinoma.
Oropharyngeal ulcers and adrenal gland enlargement with prolonged fever provide specific clues suggesting disseminated histoplasmosis. Diagnosis needs to be established via smears and/or cultures of tissues obtained from these affected tissues as early diagnosis and antifungal treatment results in remission or cure, usually with no sequelae.\(^\text{15}\)

**Acknowledgement**

We would like to acknowledge Otolaryngology Department for taking the biopsy of the patient.

We also would like to acknowledge Dr Arunaloke Chakrabarti and Dr M.R ShivPrakash from PGI Chandigarh, Mycology Division of the Department of Medical Microbiology for their expert opinion.

**References**