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LARYNGEAL HISTOPLASMOSIS: A RARE ENTITY

Pathology

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ABSTRACT

Histoplasmosis is a granulomatous disease of worldwide distribution caused by a dimorphic fungus Histoplasma capsulatum. Histoplasmosis is infrequently reported in Asia and Europe. Primary laryngeal histoplasmosis is a rare disease that may mimic tuberculosis or even laryngeal cancer, and must be considered in the differential diagnosis of a patient with hoarseness and moreover in the differential diagnosis of tumors in the vocal folds, causing hoarseness. Other differential diagnosis of histoplasmosis includes paracoccidiomycosis, leishmaniasis, blastomycosis, leprosy, syphilis, actinomycosis and lymphoma. We reported an unusual case of laryngeal histoplasmosis in a man aged 50 years who presented with provisional diagnosis of malignancy.

KEYWORDS

Histoplasmosis, Larynx, Hoarseness, Dimorphic Fungus

INTRODUCTION

Histoplasmosis is a fungal infection also known by other names like Darling's disease, Ohio Valley disease, Reticuloendotheliosis, Spelunker's lung and Caver's disease.[1] The aetiological agent is a dimorphic fungus, Histoplasma capsulatum, which causes chronic granulomatous disease.[2] Histoplasma capsulatum is an endemic fungus found in moist and fertile soil. Most primary infections in the immunocompetent host are asymptomatic or there may be mild flu-like illness, while immunosuppressed patients usually presents as disseminated histoplasmosis.[3] Histoplasmosis may occur in three forms: (i) Primary acute pulmonary form, (ii) chronic pulmonary and (iii) disseminated form. The clinical manifestation of disseminated form includes fever, weakness, weight loss, hepatosplenomegaly, and mucocutaneous lesions.[4] Histoplasmosis infection involving the larynx is an extremely rare manifestation.[3] Less than 100 cases of laryngeal histoplasmosis have been reported in English literatures since it was first described in 1940 by Brown and colleagues. The clinical symptoms and signs may mimic tuberculosis or laryngeal malignancy.[5]

CASE REPORT:

CLINICAL PRESENTATION:

A 50 year old male known case of diabetes mellitus came to hospital with complaints of hoarseness of voice since 1 month. Hoarseness of voice started gradually and was not relieved by medications.

Upon initial physical examination, oral cavity, bilateral tympanic membrane and rest of the systemic examination were normal. Routine investigations like complete blood count, biochemical parameters, routine urine examination, sputum examination and chest X-ray were also found to be normal.

Followed by this, indirect laryngoscopy was done, both vocal cords were mobile and showed bilateral growth, right vocal cord showed 7mm pedunculated polypoidal reddish growth and left vocal cord showed 5mm sessile localized growth. Biopsy was taken from the polypoidal growth and was sent to the pathology department. On clinical examination the growth was suspected to be a malignant lesion.

GROSS EXAMINATION:

Multiple whitish bits of tissue measuring 2.0x1.0 cm were received in the pathology department. Tissue processing, H&E and PAS staining was done.

MICROSCOPY:

Microscopic examination showed hyperplastic stratified squamous epithelium overlying the fibroconnective tissue containing numerous foamy histiocytes filled with numerous histoplasma which were PAS positive and showed halo effect. Along with these neutrophils, lymphocytes and patches of necrosis were seen. These histopathological findings were consistent with the diagnosis of Laryngeal Histoplasmosis.

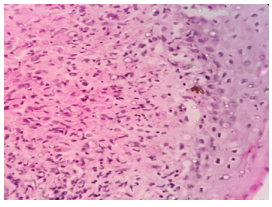

Figure 1 Laryngeal biopsy showing hyperplastic squamous epithelium and macrophages filled with numerous histoplasma (H&E, 10X).

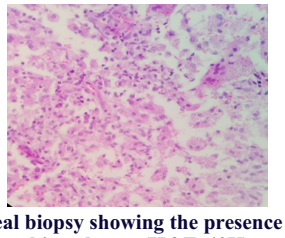

Figure 2 Laryngeal biopsy showing the presence of macrophages filled with numerous histoplasma (H&E, 40X).

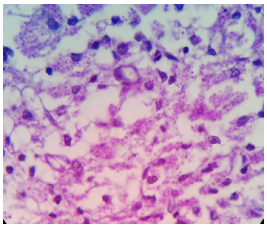

Figure 3 Laryngeal biopsy showing Histoplasma Capsulatum showing PAS positivity with halo effect (PAS, 100X)

DISCUSSION

Histoplasmosis is a granulomatous disease of universal distribution, caused by a dimorphic intracellular fungus, Histoplasma capsulatum. This fungus invades the reticularendothelial system.[6] The clinical

spectrum of the disease is variable and can manifest as a severe multisystem disease affecting bone, liver, spleen, lungs, gastrointestinal tract, skin, adrenal glands, larynx or other extrapulmonary sites. It usually occurs as an acute pneumonia, chronic lung cavity, lung nodules, mediastinal fibrosis and granulomatous mediastinitis.[7-8] Laryngeal histoplasmosis may present with hoarseness, dysphonia odynophagia, dysphagia, dyspnea, fatigue, weight loss and generalized unrest. It can also be seen on some occasion leukoplakia lesions and exophytic masses laryngeal and cervical lymphadenopathy.[9] The main predisposing factors for histoplasmosis, includes increasing age and decreasing cell-mediated immunity due to immunosuppressive agents. Laryngeal histoplasmosis, an uncommon presentation of disseminated disease, should be considered in the differential diagnosis for certain patients presenting with hoarseness, particularly those who are immunocompromised. The disease can manifest in several ways after primary inhalation of the spores, determined by inoculum size and immune status of the host. Various presentations can be classified as acute pulmonary, chronic pulmonary and disseminated disease.[10] Laryngeal involvement occurs in the chronic disseminated form of histoplasmosis. Typical initial manifestations include hoarseness, dysphagia, and odynophagia, as well as fatigue and weight loss.[11] Distinguishing laryngeal histoplasmosis from laryngeal carcinoma can be challenging, as in our case this was earlier misdiagnosed as squamous cell carcinoma. 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 (pseudoepitheliomatous hyperplasia) seen in these cases.[4] Clinical suspicion and timely diagnosis of this disease is important in order to ensure that the patients receive appropriate treatment. When histoplasmosis is suspected, special stains and cultures must be used for identification of the organism. Diagnosis can be achieved by using clinical examination and histopathologic examination. Other methods for diagnosis are cultures, antigen detection, or antibody assays, including complement fixation and immunodiffusion.[10]

Histopathologic examination can be performed on biopsies of oral and laryngeal masses. Special stains such as Periodic acid-Schiff stain or Gomori methenamine silver stain can be used and reveals multiple small, oval, budding yeast, typically found within macrophages. Biopsy may also shows granulomatous tissue infiltrated with giant cells, lymphocytes, and numerous macrophages.[6]

Growth of Histoplasma capsulatum from tissue or body fluids is the definitive diagnostic test. Samples can be obtained from various sites in patients with disseminated infection, including blood, skin, or mucosal lesions. Organisms can be successfully isolated on Sabouraud's agar, although this process can take up to 6 weeks.[10]

The only diagnostic certainty is achieved by isolating the microorganism. Biopsy shows granulomatous tissue, frequently necrosed, with an infiltrate of giant cells, lymphocytes, plasma cells and a large number of macrophages. The organisms are not easily seen with the hematoxyline-eosin dye. However, with the Periodic acid-schiff stain or Gomori methenamine silver, the macrophage appears with a variable number of oval and round bodies, surrounded by a clear zone. These bodies represent an intracellular Histoplasma capsulatum.[12-13]

CONCLUSION

Isolated laryngeal Histoplasmosis is a rare entity. Though it looks like cancer, biopsy confirms the diagnosis. Organisms can be detected in the culture medium Sabouraud and may take 6 weeks for growth. Serological test for anti-Histoplasma using immunodiffusion and complement fixation methods can aid in diagnosis. The treatment is mainly medical with Itraconazole being the drug of choice. Some patients may need tracheostomy to relieve acute respiratory obstruction. Prognosis is usually good with a few fatal cases in disseminated disease.

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