CASE REPORT

Laryngeal histoplasmosis

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SUMMARY

Histoplasmosis is a fungal infection, having interesting synonyms such as Cave disease, Darling's disease, Ohio Valley disease, reticuloendotheliosis, Spelunker's lung and Caver's disease. The aetiological agent is a dimorphic fungus, *Histoplasma capsulatum*, causing chronic granulomatous disease. The route of transmission is by inhalation of dust particles from soil contaminated by excrement of birds or bats, harbouring the small spores or microconidia, which is considered the infectious form of fungus. The spectrum of illness ranges from subclinical infection of the lung to progressive disseminated disease. The major bulk of histoplasmosis infections are asymptomatic or present with mild influenza like illness and involve immunocompetent individuals. However, the immunocompromised or immunodeficient cases have disseminated/haematogenous infections with multiple organs involved and are usually fatal unless treated immediately. Laryngeal involvement is associated with the disseminated form of the disease. Histoplasmosis of larynx is a rare entity and poses diagnostic difficulty to otolaryngologists because clinically it may be mistaken for malignancy. We report an unusual case of laryngeal histoplasmosis in a man aged 60 years who presented with provisional diagnosis of tuberculosis/malignancy.

BACKGROUND

Chronic granulomatous lesions can involve any part of the body, with one of the sites being the larynx.^{1–9} The common differentials in Indian

setup are malignancy and tuberculosis with fungal infections being relatively uncommon. The possibility of fungal laryngitis should always be kept in mind whenever a clinical diagnosis of malignancy is made, and biopsy from the involved site must be taken, as the fungal lesion can be treated medically without surgery or chemotherapy.

CASE PRESENTATION

A man aged 60 years, smoker, presented to the ear, nose and throat outpatient department with primary symptoms of hoarseness of voice since 4 months. General and systemic examinations showed normal findings. On local examination, there was no abnormality in the ears, nose and throat. However, an indirect laryngoscopic examination revealed a growth in the aryepiglottic fold. Biopsy was taken, and the sample was sent for histopathological analysis. No enlarged lymph nodes were found. Gross examination of the biopsy sample showed multiple soft tissue pieces, which were tan brown with an aggregate size of 1.5 × 1.5 cm. The tissue was processed according to the routine laboratory protocol, and H&E staining was performed. Microscopic examination of the tissue sections revealed a polypoidal mass, showing granulation tissue mixed with dense inflammatory infiltrate. Langhans as well as foreign-body giant cells and a part of minor salivary gland covered by thickened benign squamous epithelium were also seen (figure 1A–C). Furthermore, numerous clusters of round structures measuring ~2–4 µm with a

Figure 1 (A) H&E stained section showing granulation tissue mixed with dense inflammatory infiltrate, a part of minor salivary gland covered by benign squamous lining (H&E, ×4). (B, C) Section shows non-caseating epithelioid cell granulomas along with numerous clusters of round structures surrounded by halos (H&E ×10, H&E ×40). (D–F) PAS-stained section highlighting the intracellular histoplasma spores within the macrophages/epithelioid cells (PAS, ×10, PAS, ×40 and PAS, ×40).

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surrounding halo were seen. Suspecting them to be some kind of fungal spores and to further depict their nature, we performed periodic acid Schiff (PAS) and mucicarmine staining. The round structures were found to be PAS positive and mucicarmine negative (figure 1D–F), thus confirming them to be spores of histoplasma.

DISCUSSION

Histoplasmosis is among the frequent causes of chronic granulomatous disease, caused by dimorphic (ie, existing as mycelial and yeast forms) fungus, *Histoplasma capsulatum*.² Roberts *et al.*⁹ discovered this organism for the first time in 1905 and initially thought that it was a protozoan, which later on proved to be a fungus.¹⁰ The exact pathogenesis of histoplasmosis is not fully understood. Being a chronic granulomatous disease, macrophages are the main targets of *H. capsulatum*. Regarding the structure, heat shock protein 60 (hsp60) expressed by fungi binds to $\alpha 2$ integrins on the surface of macrophages. Following this, the histoplasma stimulates the macrophages to secrete tumour necrosis factor, which further induces and recruits other macrophages to kill the histoplasma.³ Transmission of infection is through inhalation of the spores (microconidia) present in soil, contaminated by bat or bird droppings. The dimorphic fungus lives predominantly in the mycelial form in the environment, however when the spores are inhaled, the relatively raised body temperature encourages the yeast form. Therefore, histoplasmosis in humans is mainly due to the yeast form of the fungus.⁴

Clinically, histoplasmosis can occur in three forms: (1) primary acute onset pulmonary form, (2) chronic pulmonary form and (3) disseminated form.¹¹ It is the disseminated form of histoplasmosis, which is associated with laryngeal involvement.⁸ Patients with laryngeal histoplasmosis usually exhibit low-grade fever, weight loss, sore throat, hoarseness, cough and dysphagia, which can cause diagnostic difficulty as these symptoms are also seen in malignancy.⁴ On laryngoscopy, mucosa is pearly white, oedematous, inflamed or painful ulcerative, again mimicking the typical findings of malignancy.¹² On histopathology of histoplasmosis, many differentials are to be kept in mind, such as cryptococcosis and blastomycoses (fungal infections having similar microscopic features), tuberculosis (confluent caseating granulomas) and squamous cell carcinoma (pseudo-epitheliomatous hyperplasia with infiltrating atypical malignant squamous cells).²

In our case, the provisional clinical diagnosis of tuberculosis or malignancy was made. However, microscopic examination of the biopsy showed many foamy macrophages containing intracytoplasmic spores, which were highlighted on PAS stain and were mucicarmine negative, ruling out the other two common fungal infections of *Cryptococcus* and *blastomyces* (as the capsule of *Cryptococcus* and the cell wall of *blastomyces* take up the mucin stains).

In such cases, a thorough clinical workup of the patient is necessary to rule out any underlying immunosuppressive

condition such as HIV. Besides this, tuberculosis and malignancy have to be closely looked for as histoplasmosis can even coexist with these conditions or even mask an occult carcinoma.

Ideally, the organism from the biopsy material should be cultured on Sabouraud dextrose agar medium to confirm its fungal nature. Unfortunately, there were no confirmed fungal cultures in our case. Following this, the patient was kept on fluconazole (systemic antifungal) with complete remission of symptoms.

Learning points

- ▶ Histoplasmosis is a chronic granulomatous fungal infection, caused by *Histoplasma capsulatum*.
- ▶ Histoplasmosis mainly involves the lung, with the uncommon disseminated forms involving other rare sites such as larynx.
- ▶ Primary histoplasmosis is a very rare entity, which may mimic other common lesions of the larynx such as carcinoma larynx and tuberculosis.
- ▶ Microscopic examination of the suspicious lesions along with special stains such as PAS stain helps us reaching at the final diagnosis of histoplasmosis.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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