Disseminated Histoplasmosis presenting as oropharyngeal mass lesion

Tauhidul Alam Choudhurya,∗, Ronica Baruahb, Naushad Shahb, Brajendra Lahkarc, Kuddush Ahmedd, Bhaskar Jyoti Sarmahe

a Department of Nephrology, Dispur Hospitals, Guwahati, India
b Pathologist, Ekopath Metropolis Lab Services Pvt Ltd, Guwahati, India
c Department of Internal Medicine & Critical Care, Dispur Hospitals, Guwahati, India
dDispur Hospitals, Guwahati, India
e Department of Radiology, Dispur Hospitals, Guwahati, India

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ABSTRACT

A 62 year old man from Silchar in North East India presented with complaints of painful swallowing, hoarseness, fever, anorexia and weight loss. Oropharyngeal examination revealed reddish ulcer-nodular lesion involving left tonsillar area and base of tongue which was clinically suspicious of malignancy. Radiological examination revealed involvement of bilateral adrenals by a mass. The biopsy of the oropharyngeal lesion showed many fungal spores morphologically favoring Histoplasmosis. Treatment with Amphotericin B followed by Itraconazole resulted recovery of lesions.

1. Introduction

Histoplasmosis is a worldwide systemic mycosis caused by *Histoplasma capsulatum*, a dimorphic fungus found in moist fertile soil contaminated by bird or bat droppings. Human and animal infections are caused by inhalation of fungus in dust [1]. In India, Histoplasmosis is endemic in West Bengal and Gangetic delta [2]. In humans Histoplasmosis may occur in three form: (i) Primary acute pulmonary form, (ii) chronic pulmonary and (iii) disseminated form. Disseminated Histoplasmosis (DH) is the mostly seen in immunocompromised individuals [3]. Oropharyngeal involvement is seen in 30%–50% of cases and have a tendency to develop more destructive and focal lesions. These lesions often mimic malignancy and hence disseminated Histoplasmosis must be kept in mind in order to avoid misdiagnosis [1].

2. Case

62-year-old man, an engineer by profession with Type 2 Diabetes Mellitus and hypertension of long duration presented with complaints of painful swallowing, weight loss, asthenia, anorexia and fever for two to three years (date of presentation being 25.9.17, taken as day zero). He was admitted with altered sensorium of two days duration. He gave history of loss of 15kg weight over 2–3 years. He was a chronic smoker until four years back. No history of cough or bleeding from mouth was given. Clinical examination revealed 42 kg weight with dehydration, pallor, tachycardia, muscle wasting, loss of subcutaneous fat and blood pressure of 100/70 mm of Hg. He was semi-conscious at the time of admission. Clinical systemic examination was non-contributory with no palpable organomegaly. Oropharyngeal examination revealed a reddish ulcer-nodular lesion involving left tonsillar area and base of tongue (Fig. 1A). The oropharyngeal lesion was biopsied twice previously (day −90, prior to patient's presentation to us) and reported as chronic inflammatory lesion once and granulomatous inflammation with a suspicion of tuberculosis the next time. Ziehl Neelsen stain, real time polymerase chain reaction for mycobacterial tuberculosis and non-tubercular mycobacteria were done using the paraffin block and were negative in the previous biopsy.

Computerized Tomography (CT) scan of the neck showed soft tissue thickening of base of tongue and the left tonsillar pillar. Computerized Tomography of Thorax showed no significant abnormality. The oropharyngeal lesion was biopsied twice previously and reported negative for malignancy. All laboratory and radiological investigation findings are given in Table 1 (see Fig. 2).

Biopsies were taken from the oropharyngeal lesions in left base of tongue and tonsil. Histopathology showed multiple bits of squamous lined tissue with ulceration and pseudoepitheliomatous hyperplasia. Subepithelium shows dense chronic inflammatory cells, few

Abbreviations: DH, Disseminated Histoplasmosis; CT, Computerized Tomography; MRI, Magnetic resonance imaging; GMS, Grocott methanamine silver stain; PAS, periodic acid-Schiff stain; HIV, human Immune deficiency virus

∗ Corresponding author. Room no-51, 2nd floor, Dispur Hospitals, Ganeshguri, Guwahati, Assam, India.
E-mail address: drtauhid77@gmail.com (T.A. Choudhury).

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granulomas, numerous histiocytes and occasionally foreign body giant cells. Many yeast both extracellular and within macrophages were seen as basophilic dot with a surrounding artefactual halo (pseudo capsule) suggestive of Histoplasma species. The features of Histoplasma are similar to those of Leishmania but it lacks the kinetoplast which is present in Leishmania. Special stains like Periodic acid Schiff stain (PAS) and Grocott’s Methanamine silver stain (GMS) done which shows many narrow based budding yeast confirming Histoplasma. (Fig. 3A and B).

Fungal identification by DNA sequencing using paraffin block was done three months prior to patient’s presentation to our medical facility (day −90). This had tested negative. Fungal culture was not done with the biopsy tissue as the sample was received in formalin. Serological tests for Histoplasmosis were not available. Hence, the diagnosis was entirely based on characteristics morphological features of the fungi on histopathology, while differentiating it from other fungi on morphology only (see Fig. 4).

The treatment included rehydration, Ryle’s tube feeding and treatment with Liposomal Amphotericin- B (5mg/kg body weight). The patient showed symptomatic improvement and serum creatinine decreased to 2.0 mg/dl over next 10 days. The patient was subsequently discharged with advice to continue oral Itraconazole. On six monthly follow up, the patient was well-nourished and oral lesions had subsided (Fig. 1).

3. Discussion

Histoplasmosis is caused by inhalation of fungus in dust contaminated by bird or bat droppings. Areas such chicken coops, bird roosts, caves and building sites harbour high level of Histoplasma capsulatum. People with exposure to such areas along with immunosuppression are susceptible to Histoplasmosis [2,3]. Gupta et al. analyzed 95 published studies with 204 cases from India. Histoplasmosis is reported from all over India including Delhi, Andhra Pradesh, Bihar, West Bengal and Vellore in Tamil Nadu. Most Indian cases were reported along the rivers Ganges, Yamuna and Brahmaputra and in people associated with agricultural activity [4–6].

Histoplasmosis is an important opportunistic infection in immunocompromised patients, particularly HIV infected individuals. In 95% HIV positive patients with Histoplasmosis, it presents as disseminated disease. In healthy individuals it usually does not present as life threatening and debilitating illness [3]. Histoplasmosis is more common in men (male: female ratio 4:1) and the age in the adults ranges from 40 to 65 years. The most common presenting symptoms are fever, mucocutaneous ulcerative lesions followed by hepatosplenomegaly. The duration of illness to diagnosis ranged from 2 to 24 months. Disseminated Histoplasmosis is increasingly being reported in immunocompetent individuals in India. According to the reported Indian studies, the immunocompetent individuals are more prone to getting disseminated Histoplasmosis [6]. Our patient is unusual as he had no
history of occupational exposure, was immunocompetent and yet presented with disseminated disease.

Although Histoplasmosis is a primarily lung disease, initial pulmonary infection in our country remains underdiagnosed or may be misdiagnosed as tuberculosis. Lymphadenopathy and cutaneous lesions are also common, especially in HIV infected patients. Involvement of adrenal gland is more commonly seen in immunocompetent individuals. Oral and oropharyngeal involvement is seen in 30%–50% of disseminated Histoplasmosis and tend to mimic malignancy. Tongue, palate and buccal mucosa are frequently involved. The oropharyngeal lesion in our patient was biopsied thrice due to high degree of suspicion for malignancy [2,3,6].

The gold standards for laboratory diagnosis include demonstration of yeast on pathological examination of tissue and isolation of the mold in the culture of clinical specimens; however, antigen detection serology has provided a rapid, non-invasive, and highly sensitive method for diagnosis and is a useful marker of treatment response [7]. Histopathology is an important component of establishing the correct diagnosis. The diagnosis is based on the identification of 2–4 μm, oval, narrow-based budding yeasts that are present on special stained sections like methenamine silver or periodic acid-Schiﬀ’s. The organism can be found both in the macrophages and freely within the tissue [8]. On histopathology Histoplasma features are similar to those of Leishmania and Penicilliosis. Distinction from Leishmaniasis is based on the presence of a kinetoplast in the latter and Leishmania are PAS and GMS negative. Distinction from Penicilliosis is based on the fact that H. capsulatum displays narrow-necked budding while P. marneffei divides by septation [9].

The published studies show that most cases responded well to antifungal therapy with improvement or cure achieved in 78% cases while the mortality rate given is 14% in studies where outcome data is available. Amphotericin B is given as initial drug in about 47% of cases owing to the severity of disease. Studied showed that 45% of cases receive oral Itraconazole as the speciﬁc antifungal therapy. There were reports of relapse in few cases who received oral Itraconazole. A high mortality (30%) was observed in cases who received amphotericin B as initial antifungal drug which is likely due to the severity of illness at presentation [6].

To conclude, Histoplasmosis although not very uncommon in India remains frequently underdiagnosed or misdiagnosed. Our case shows the frequent problems faced in diagnosis of Histoplasmosis. Our patient underwent multiple biopsies with clinical suspicion of malignancy and in the duration of two to three years between presentations of symptoms to diagnosis he lost 15 kg weight and was admitted in a serious condition. Another cause of delay in diagnosis was that he was immunocompetent and did not have any history of occupational exposure. Our case highlights the importance of knowledge and awareness of Histoplasmosis with its clinical presentations which are confusing with other common diseases in India such as tuberculosis, febrile illness, malignant oropharyngeal nodular lesions and elaborates the laboratory findings while differentiating it from other infections.

Conflict of interest

None.

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