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CASE STUDY

NODULAR VARIANT OF ORAL HISTOPLASMOSIS WITHOUT PULMONARY INVOLVEMENT

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ABSTRACT

Histoplasmosis is a mycotic disease caused by the dimorphic fungus Histoplasma capsulatum which exists as moulds in fertile and humid soil, rich in bird and bat droppings and as yeast in infected tissues. It is classified clinically as acute pulmonary, chronic pulmonary or disseminated form. Oral manifestations account for 25-40% of the disseminated form of the disease and can present as solitary, variably painful, shallow or deep ulcer or less commonly in the form of nodules. It is commonly found in immune compromised patients. Diagnosis of histoplasmosis can be established by identification of fungus from infected tissues and/or culture studies. Presence of fungal yeasts are best demonstrated by staining the sections with Periodic Acid Schiff (PAS) and Grocott Gomori methenamine silver (GMS) stain which demonstrate the characteristic 1-2 micron yeasts of Histoplasma capsulatum. Treatment modalities include, administration of antifungal drugs like intravenous Amphotericin B, oral Itraconazole or Ketoconazole but proper monitoring of hepatic function is essential. A unique case of localised, nodular variant of Histoplasmosis involving the hard palate in an immune competent patient without pulmonary involvement has been discussed with emphasis on clinicopathological and histological features along with treatment modalities.

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INTRODUCTION

Histoplasmosis is a mycotic disease caused by the dimorphic fungus Histoplasma capsulatum which exists as moulds in fertile and humid soil, rich in bird and bat droppings and as yeast in infected tissues. (Neville 2nd ed; De and Nath, 2015; Mignogna *et al*., 2001) The first case of histoplasmosis was reported by Darling from Panama in 1908. (Prabhu *et al*., 1993) Ever since, cases of histoplasmosis have been reported globally, especially, from the Ohio and Mississippi river valleys in the United states. (Neville 2nd ed) Case of disseminated histoplasmosis in India was first reported by Panja and Sen from Calcutta in 1954. Though cases have been reported from various states of India but it is more frequent in the Gangetic delta areas of West Bengal. (Debopriya Chatterjee *et al*., 2017) Clinically histoplasmosis has been classified into three types-i) Acute pulmonary, ii) Chronic pulmonary, iii) Disseminated. The disseminated form of the disease is most fatal and is usually seen in immune compromised individuals. The disease can affect the spleen, adrenal glands, liver, lymph nodes, GIT, CNS, kidneys and oral mucosa. Oral manifestations account for 25-40% of the disseminated form of the disease. (Vidyanath *et al*., 2013) and can present as solitary, painful, shallow or deep ulcer or less commonly in the form of nodules. (Gulia *et al*., 2010; Alcure *et al*., 2006; Ferreira *et al*., 2002) Diagnosis of histoplasmosis can be established by identification of fungus from infected tissues and/or by culture studies. (Debopriya Chatterjee *et al*., 2017) Haematoxylin and Eosin stained sections of biopsy tissue shows diffuse infiltrate of macrophages, often organised into granulomas. Occasionally, giant cells can be seen in association with these granulomas. Spores of histoplasmosis may be identified in the sections with difficulty. Presence of fungal yeasts can be confirmed by staining the sections with Periodic Acid Schiff (PAS) and Grocott Gomori Methenamine silver (GMS) stains which demonstrate the characteristic 1-2 micron yeasts of Histoplasma. (Neville 2nd ed) The acute pulmonary histoplasmosis is usually self limiting and requires no treatment. Chronic and disseminated forms of histoplasmosis if left untreated may cause death in 20 % cases. Treatment modalities include the administration of intravenous Amphotericin B. Alternatively, oral administration of Itraconazole or Ketoconazole for 3-18 months is also curative but proper monitoring of hepatic function is essential. (Neville 2nd ed) Here we report an interesting case of nodular variant of histoplasmosis affecting the palate in an immune competent patient without pulmonary involvement.

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Case report

A 45- year- old male poultry worker from rural area reported to our department with the chief complaint of swelling in the palate and mobility of regional teeth since one month which gradually increased in size. He also complained of frequent cough, fever and progressive weight loss in the recent past. Extraorally, no abnormality was detected except for the presence of enlarged left submandibular lymph node (Fig 1a). Intraoral examination revealed poor oral hygiene with multiple missing and mobile teeth along with retained roots. There was presence of a 2.5 x 3.0 cm. diffuse, soft, nodular, non tender, non pulsatile, non compressible, non reducible swelling in the hard palate without any surface ulceration (Fig.1b). Based on these clinical findings the case was provisionally diagnosed as malignancy or chronic granulomatous infection. Orthopantomogram showed presence of multiple carious teeth, retained roots and generalised alveolar bone loss in both jaws (Fig 2a). Postero anterior (PA) view radiograph of chest showed no abnormality (Fig. 2b). All haematological parameters were within normal limits. Pre operative serology revealed that the patient was ELISA negative for hepatitis, tuberculosis and HIV. An incisional biopsy was taken from the representative site of the lesion. Routine Haematoxylin and Eosin staining was performed and the sections showed the presence of dense infiltrate of chronic inflammatory cells chiefly composed of lymphocytes and macrophages in the connective tissue. The most striking feature was the presence of small, round, intracytoplasmic, basophilic bodies surrounded by clear halo within the macrophages. These basophilic bodies characteristically resembled spores of the fungus Histoplasma capsulatum (Fig. 3).

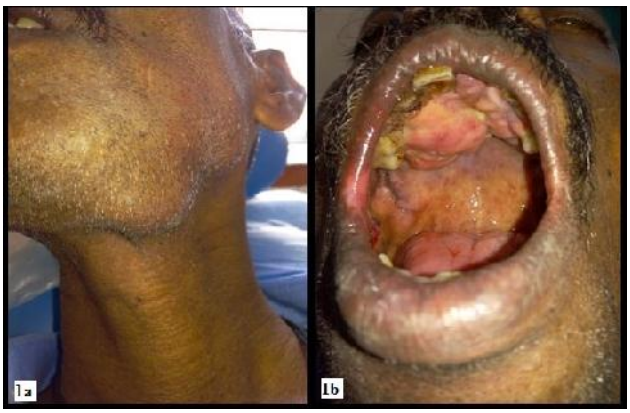

Fig 1 (a): Extraoraly there was presence of enlarged, left submandibular lymph node and (b): Intraoraly there was presence of a 2.5x3.0 cm, diffuse, soft, nodular, non tender, non pulsatile, non compressible, non reducible swelling in the hard palate without any surface ulceration

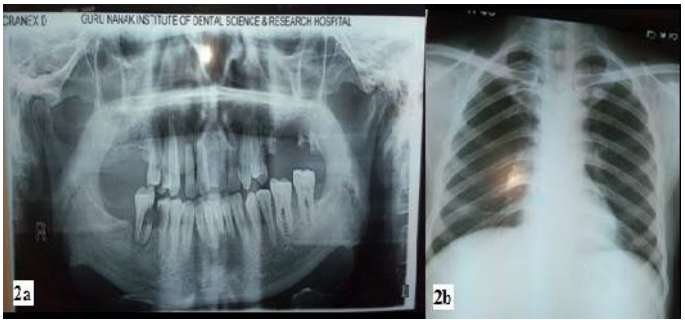

Fig. 2 (a) Orthopantomogram showed presence of multiple carious teeth, retained roots and generalised alveolar bone loss in both jaws and (b) Postero anterior (PA) view radiograph of chest showed no abnormality

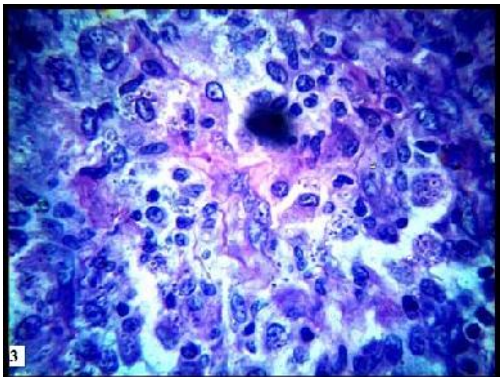

Fig. 3. Haematoxylin and Eosin stained sections (100x) showed the presence of dense infiltrate of chronic inflammatory cells chiefly composed of lymphocytes and macrophages in the connective tissue. The most striking feature was the presence of small, round, intracytoplasmic, basophilic bodies surrounded by clear halo within the macrophages resembling fungal spores

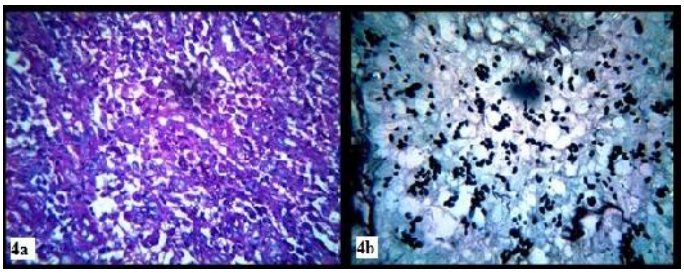

Fig. 4 (a): PAS stained the fungal cell wall magenta colour& (b) GMS stained the 1-2 micron yeasts of Histoplasma with the characteristic black colour

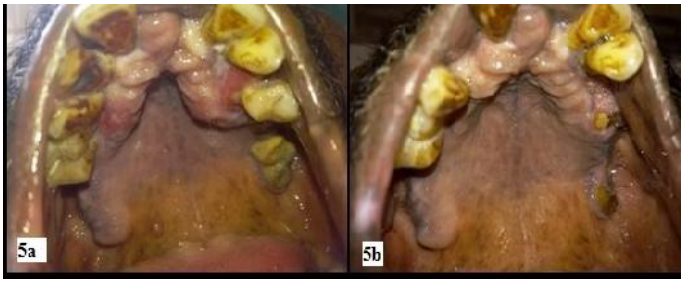

Fig 5 (a) 1 month after starting Itraconazole therapy and (b) 3 months after Itraconazole therapy

To establish a confirmatory diagnosis, the sections were stained with Periodic acid Schiff (PAS) and Grocott Gomori methanamine silver (GMS) stains. PAS stained the fungal cell wall magenta colour while GMS stained the 1-2 micron yeasts of Histoplasma with the characteristic black colour (Fig.4 a &b). Based on the clinical and histopathological findings the case was finally diagnosed as 'Nodular variant of Oral Histoplasmosis'. The patient was treated with oral Itraconazole 200 mg BD for three months with monitoring of hepatic status. Regular check up of the patient was done at 15 days interval. After 3 months the patient showed complete recovery and no recurrence has been reported over a period of six months (Fig.5 a & b).

DISCUSSION

Histoplasma capsulatum is a dimorphic fungi, which exists as yeast in body temperature in the human host and as mould in its natural environment. Infection of humans with this fungus causes the disease histoplasmosis. The first case of histoplasmosis, reported by Darling in 1908 from Panama, was caused by H.capsulatum var.capsulatum. The African variant of

Histoplasmosis caused by H.capsulatum var.duboisii was reported by Dubois and Vanbreuseghen from Africa in 1952. (Prabhu *et al*., 1993) Few cases of histoplasmosis have been reported from India as well. The first case of histoplasmosis in India was reported by Panja and Sen from Calcutta in 1954. The disease is endemic in the states of West Bengal and Assam, particularly in the river delta area. Few cases have also been reported from northern and southern parts of India. (De and Nath, 2015) Infection with histoplasmosis occurs due to inhalation of fungal microconidia and their subsequent uptake by the alveolar macrophages where they are transformed into the yeast form. The whole process is calcium and iron dependent. The yeasts grow and multiply within the resting macrophages from where they disseminate to the regional lymph nodes and the reticuloendothelial system. Cell mediated immunity develops after that in two weeks which produces interferon γ (IFNγ), responsible for phagocytosis thus controlling the spread of the disease. In healthy adults, the macrophages, lymphocytes and epithelial cells form granuloma surrounding the fungus which ultimately fibrose and calcify. In immune compromised individuals the infection is not confined and can disseminate to various organs causing progressive disseminated histoplasmosis. (Hage *et al*., 2008) The patient under discussion was a poultry worker by profession where he handled poultry products without any protective barrier. This could have been the source of the microconidia of Histoplasma that has been inhaled by the patient. Of the three clinical variants of histoplasmosis the disseminated form is most fatal. Oral manifestations are usually seen in pulmonary or disseminated variants. However primary oral mucosal lesions may also arise due to direct inoculation of fungus in oral mucosa. (Psevdos and Tanowitz, 2008) Our patient was a 45 yr old male who presented with a large nodular mass in the hard palate without any surface ulceration. This finding was consistent with the description of oral manifestation of histoplasmosis given by various authors. (Vidyanath *et al*., 2013; Gulia *et al*., 2010; Alcure *et al*., 2006; Ferreira *et al*., 2002) Chronic and disseminated forms of histoplasmosis show presence of upper lobe infiltration and cavitation in PA view radiograph of chest. But no abnormality was detected in chest radiograph of our patient. (Prabhu *et al*., 1993) Fungal culture remains the gold standard diagnostic test for H. capsulatum. It can be grown on Sabouraud dextrose agar incubated at 25 degree Celsius. After several weeks may be up to six weeks, growth of a white to light tan mold occurs. Two types of conidia are produced on the hyphae: macroconidia and the microconidia. (Davis *et al*., 2001) Such culture couldn't be performed in our case due to financial constraint of the patient.

Haematoxylin and eosin stained sections of biopsy tissue of the patient showed the presence of diffuse infiltrate of chronic inflammatory cells comprising of lymphocytes and macrophages in the connective tissue. Characterstic 1-2 micron yeasts of H.capsulatum were present within the macrophages. PAS and GMS staining further confirmed the presence of Histoplasma capsulatum in the tissue sections. These histological findings were consistent with those reported in the literature. (Vidyanath *et al*., 2013; Psevdos and Tanowitz, 2008; Iqbal *et al*., 2014) Treatment modalities include intravenous administration of Amphoterecin B or oral administration of Itraconazole or Ketoconazole. Our patient was treated with oral Itraconazole 200 mg BD for 3 months following which the patient recovered completely and no recurrence has been reported over a period of 6 months.

Conclusion

Oral histoplasmosis is rare fungal infection which is frequently undiagnosed. An awareness of the disease, recording of clinical history and adequate investigative procedures would help diagnosis of the disease. Establishment of early diagnosis and proper therapeutic modalities proves curative in most cases.

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