Disseminated Histoplasmosis Without Pulmonary Involvement in An Immunocompetent Host - A Case Report

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Abstract:
Histoplasmosis is a dimorphic fungal infection caused by histoplasma capsulatum. It is the most prevalent endemic mycosis in the United States, but now it is a disease of world wide occurrence. Most infections are asymptomatic or self-limited, some individuals develop acute pulmonary infections or severe and progressive disseminated infection. Progressive disseminated histoplasmosis occurs in about one in 2000 patients with acute infection. Besides lung it may affect skin, lymph nodes, GIT, CNS, adrenals, liver and spleen. The patient of disseminated histoplasmosis usually presents with fever, anorexia, weight loss, myalgia and manifestations according to organ involved. Here we described a 45 year-male who presented to us with fever, weight loss, generalized lymphadenopathy, growths in the oral cavity and chylous ascites. The particular interest of this paper is to present a case of disseminated histoplasmosis in an immunocompetent host without pulmonary involvement, and to demonstrate the differences between this entity and other similarly presented diseases like disseminated tuberculosis, lymphoma and metastatic malignancy.

Key words: histoplasmosis, disseminated histoplasmosis, histoplasma capsulatum, immunocompetent host, Bangladesh.

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Introduction:
Histoplasmosis is the most common endemic mycosis in human. It has recently emerged as an important opportunistic infection among human immunodeficiency virus (HIV)-infected persons living in areas where it is endemic.

Histoplasma capsulatum is a dimorphic fungus that remains in a mycelial form at ambient temperatures and grows as yeast at body temperature and transmitted by inhalation of the spores. It enters the reticuloendothelial system and resides in macrophages. Most individuals with intact cellular immunity are asymptomatic. Severe disseminated histoplasmosis develops in people with primary or secondary deficiency of cellular immunity.

Its presentation varies depending on the size of the inoculum, host’s immune status, and presence of underlying lung disease. Approximately, 10% cases of histoplasmosis develop into progressive disseminated histoplasmosis (PDH).

Disseminated histoplasmosis can be fatal if untreated. In Bangladesh it is very uncommon. The successfully treated 1st reported case in Bangladesh was in 1982. We report our experience to increase awareness of the clinical spectrum of disseminated histoplasmosis and its similarity to other infections and malignancies and update the reader on recommended therapeutic modalities.

Case Report:
A 45-year old male was admitted with the complaints of fever, abdominal pain, painful growths in the oral cavity, generalized lymphadenopathy, ascites and weight loss for 4 months. He was an insurance worker and occasionally worked in a fishing farm for last five years. He gave no history of extra-marital sexual exposure or close contact with a known tuberculosis patient. The patient was toxic and cachectic. He was anaemic and febrile. His pulse was 100 per minute and BP was 130/80 mmHg. He had tender lymphadenopathy involving sub mental, sub-mandibular, abdominal and inguinal regions, some were matted and some discrete and mobile. There were two growths in the oral cavity. One was over the middle of the tongue, which was raised, fungating, ulcerated, covered with necrotic tissue and another one was over the hard palate, rounded and ulcerated (Fig-1).
There was mild tenderness in the left hypochondrium with ascites. Haemoglobin was 9gm/dl, ESR 40mm in 1st hour, WBC- 20,000/cmm, platelet 5 lac/ cmm. Chest skiagram, tuberculin test, FBS, SGPT, HBsAg, antiHCV, creatinine were within normal limit. Ascitic fluid– chylous (TG-921) and exudative. Ascitic fluid for bacterial, fungal & adenosine deaminase culture were negative. USG and CT scan of abdomen showed pre and paraaortic lymphadenopathy with huge ascites. Endoscopy and colonoscopy were normal. Anti-HIV (ELISA) was negative.

Biopsies were taken from tongue growth, submandibular and inguinal lymph nodes and stained with H.E and PAS. The tissue was densely infiltrated with chronic inflammatory cells including eosinophils (Fig.2). These included many histiocytes with a small number of lymphocytes and plasma cells, the histiocytes show cytoplasmic vacuoles. In addition, many of these cells contain histoplasma capsulatum (PAS positive and Giemsa negative).

He was treated with intravenous amphotericin-B at a dose of 0.9mg/kg body weight and total dose was 2.0gm over two and half month. His oral lesion over hard palate was completely healed, the lymph nodes became smaller, and ascites was resolved. The patient was discharged with oral itraconazole 400mg/day. In his next follow-up after one and half month, his general condition was improved with weight gain, increased appetite, and regression of lymph nodes. He was advised to continue itraconazole in the same dose for a total duration of one year.

Fig-2 shows histoplasma capsulatum in the tongue and lymphnode
Discussion:
Histoplasmosis is an endemic infection in most of the USA, Asia and Africa. Highly infectious soil is found near areas inhabited by bats and birds, as their excretions contaminate the soil, thereby enriching the growth medium for the mycelium. Birds cannot be infected, whereas bats can be. It cannot be transmitted from an infected person or animal to someone else. An estimated 40 million people in the United States have been infected with H. capsulatum, with 500,000 new cases occurring in each year. In Bangladesh sporadic cases have been reported in different literature.

Disseminated histoplasmosis may present either as self-limited disease or progressive disseminated histoplasmosis. Progressive disseminated histoplasmosis of course can occur in immunocompetent patients at extremes of age and immunocompromised patients. Clinical presentations vary depending on the size of the inoculum, host’s immune status and presence of underlying lung disease. Overt symptoms occur in only 5% of individuals after low-level exposure, but in 75% cases after heavy exposure in healthy hosts. Approximately 10% cases of histoplasmosis develop progressive disseminated histoplasmosis. In 80% of patients, symptoms are nonspecific and include fever, chills, myalgia, nonproductive cough, and chest pain. The acute syndrome can range from mild (lasting 1-5 d) to severe (lasting 10-21 d); the latter is associated with weight loss, fatigue, and night sweats. Fatigue may persist for weeks after the acute symptoms resolve. Patients may develop a variety of clinical manifestations including acute or subacute pulmonary disease, progressive disseminated disease, pericarditis, arthritis or, less commonly, fibrosing mediastinitis. Hepatomegaly, splenomegaly, and bone marrow suppression may occur.

Histoplasmosis can be diagnosed by growth of histoplasma in culture, fungal stains (Bone marrow aspirate, peripheral blood smear, lymph node biopsy, bronchoalveolar lavage fluid, transbronchial biopsy specimen and biopsy from cutaneous lesions), serologic tests for antibodies, and antigen detection. Skin testing is rarely useful as a diagnostic measure because of high positivity in endemic areas and false-negative results associated with chronic pulmonary and disseminated disease. Among all these, bone marrow examination has the highest diagnostic yield. Antigen detection in urine and serum by radioimmunoassay is useful in immunocompromised patient when antibody production may be impaired. It is highly sensitive in disseminated infection. It can also be used for monitoring response to treatment especially in AIDS patient. Other laboratory abnormalities include anemia, leukopenia, pancytopenia, elevated liver enzymes, increased ferritin and serum lactate dehydrogenase.

The case was diagnosed as disseminated histoplasmosis on the basis of clinical presentation and histopathology of involved lymph nodes and tongue. Although culture was negative, histomorphological features were characteristic for diagnosis (Fig: 2). The progressive disseminated histoplasmosis is reported to occur in one or two per 1000 patients of any age due to many predisposing factors. Fever, cough, weight loss, lymphadenopathy and hepatosplenomegaly are usual mode of presentation. But our case was presented with oral growth and abdominal lymphadenopathy with chylous ascites. It is as yet a rare disease in Bangladesh.

Awareness of this infection is important because 100% mortality is seen in untreated group which comes down to 70% when adequately treated with Amphotericin-B. Disseminated disease is to be differentiated from more common diseases in our country like tuberculosis, lymphoma or metastatic malignancy.

References: