CASE REPORT

Disseminated Cryptococcosis Mimicking Lymphoreticular Malignancy in a HIV Negative Patient

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Abstract

Disseminated cryptococcosis, a life threatening mycosis, usually presents with respiratory tract, central nervous system and skin involvement. Herein we report a case of disseminated cryptococcosis presenting with hepatic, lymph nodal and bone marrow involvement in addition to the central nervous system and lung involvement in a previously healthy, HIV negative individual. The unique presenting manifestation highlights the need for careful consideration of this entity in conditions mimicking disseminated tuberculosis and lymphoreticular malignancy.

Key Words

Cryptococcosis, Lymphoreticular malignancy, HIV

Introduction

Cryptococcus is an encapsulated fungal organism that causes disease in apparently immunocompromised hosts. Human immunodeficiency virus (HIV) infection has emerged as the leading cause of immunodeficiency predisposing to disseminated cryptococcal infection. Common presentations of cryptococcosis are related to pulmonary, central nervous system (CNS) and skin involvement. Rarely, liver, prostate and bone marrow involvement has been reported. We report a case of disseminated cryptococcal infection in a HIV negative young male presenting with hepatitis, pulmonary infiltrates, CNS involvement, bone marrow involvement, generalized lymphadenopathy and hepato-splenomegaly mimicking disseminated tuberculosis or non-Hodgkin's lymphoma.

Case Report

A 30-year-old businessman presented with the complaints of fever of 3 months and jaundice of 20 days duration. Fever was moderate grade, intermittent and associated with evening rise without any localizing features. Jaundice was progressive and not associated with pruritus or clay colored stools. There was history of anorexia and significant weight loss (>5 kg, >10% of baseline) over last 3 months. There was no history of chronic cough, dyspnoea, chest pain and hemoptysis, hematemesis or melena, abnormal behavior or movements, dysuria, oliguria or hematuria, blood transfusions, multiple injections in past, drug abuse or contact with commercial sex worker. He was a teetotaler and there was no history to suggest diabetes mellitus or

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tuberculosis in past. Examination revealed average built male with mild pallor, deep icterus, bilateral cervical and axillary lymphadenopathy (1-1.5 cm diameter, multiple, firm, non-tender and discrete), hepatomegaly (4 cm below right subcostal margin, non tender), splenomegaly (3 cm below left subcostal margin, non tender) and bilateral basal crepitations in chest. Rest of the general as well as systemic examination was unremarkable. With this presentation a clinical possibility of disseminated tuberculosis/fungus or non-hodgkin's lymphoma was made. Investigations revealed hemoglobin 8.5 g/dl, total leukocyte count 20,000/ml with polymorphs 82%, lymphocytes 11%, monocytes 2% and eosinophils 5%, erythrocyte sedimentation rate 56 mm first hour, platelet count 260 X 103/ml and normocytic normochromic red blood cell morphology. Peripheral smear for malarial parasite was negative on three consecutive occasions. Renal function tests and urine examination were normal. Liver function tests revealed serum bilirubin 21.5 mg/dl (12.9 mg/dl conjugated), alanine and aspartate transferase levels of 142 /48 IU/L, alkaline phosphatase of 1060 IU/L and low total serum protein and albumin of 5.6 and 2.3 g/dl respectively. Serology for HBsAg, anti-HCV and anti-HIV-1 and HIV-2 was negative. Roentgenogram chest showed diffuse basal infiltrates bilaterally. Mantoux test (5TU) showed no induration after 48 hours. Ultrasonogram revealed hepato-splenomegaly and lymph nodes at porta without any free fluid in the peritoneal cavity. Blood culture grew Klebsiella pneumoniae sensitive to aminoglycosides and third generation cephalosporins. Sputum for acid-fast bacilli was negative thrice on consecutive days. Sputum and urine cultures did not grow any organisms. Fine needle aspiration cytology of the cervical lymph node revealed round to oval yeast forms of cryptococcus (surrounded by PAS positive capsule). Cerebrospinal fluid (CSF) examination showed protein 18 mg/dl, sugar 60 mg/dl (blood sugar 96mg/dl), cells 2/ml, all lymphocytes, negative India ink preparation and no organisms on culture. Cryptococcal antigen in CSF by latex agglutination was positive in 1:8 titers. Histopathological examination of lymph node (Figure 1), liver and bone marrow showed evidences of inflammation and cryptococcal infection. Thus, a diagnosis of disseminated cryptococcosis in a HIV negative host was made. Patient received therapy for K pneumoniae as per the sensitivity pattern initially, followed by Amphotericin B 1mg/kg/d for 32 days (total dose of 1350 mg) along with supportive management. His fever, lymphadenopathy, hepato-splenomegaly, anorexia and liver functions improved after therapy.

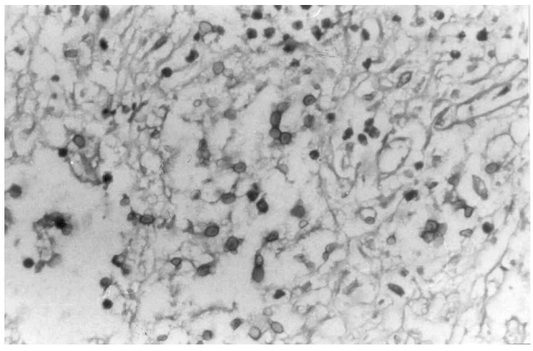

Fig 1: Lymph node biopsy showing marked lymphodepletion and numerous yeast and budding forms of cryptococci having PAS positive capsule (PAS, X 200).

Discussion

Diagnosis of cryptococcal infection depends upon demonstration of growth of the organisms on Saboraud's media with characteristic biochemical reactions (urease, phenoloxidase). Demonstration of encapsulated yeast like organisms on India ink or PAS staining followed by positive mucicarmine or Masson Fontana staining and/or demonstration of cryptococcal capsular polysaccharide antigen in titers more than 1:8 in serum or CSF is also confirmatory of the diagnosis. Demonstration of both, encapsulated yeast like organisms on PAS and mucicarmine staining in the capsule of the organism in the lymph node, liver and bone marrow and in addition, positive serology for cryptococcal capsular polysaccharide antigen in the CSF in the present case confirmed the diagnosis of disseminated cryptococcosis.

The presenting feature of cryptococcosis as fever with jaundice is very uncommonly reported in literature (1) however concomitant liver, lymph node and bone marrow involvement was unique to our patient in view of HIV negative status. Till date, only 10 cases have been reported to have hepatitis, cholangitis or cholecystitis as presenting manifestation of cryptococcal infection. Of these 10 cases eight were HIV negative. One of the patients reported with hepatitis was from the same geographical location as in this patient (2).

None of the patients without immunocompromised status has been reported to have bone marrow involvement due to cryptococcosis. Though, a detailed work up for defect in the cell mediated, humoral or phagocytic arms of the immunity was not carried out in the present case, except anti HIV-1 and HIV-2 serology, he did not have any clinical pointers to suggest an underlying primary or acquired immunodeficiency prior to the onset of the illness. Histopathological examination of lymph nodes, bone marrow and liver ruled out underlying lymphoreticular/hematological malignancy and sarcoidosis. Though 2 cases of familial cryptococcal infection have been reported (3), no definite genetic predisposition is known for both immunocompromised as well as immunocompetent hosts.

Cryptococcus neoformans occurs in two variant forms: Cryptococcus neoformans var neoformans and Cryptococcus neoformans var gattii Cryptococcus neoformans var neoformans is distributed worldwide and causes most cryptococcal infections in humans. Cryptococcus neoformans var gattii is localized to tropical and subtropical Asia and regions of Australia where there is abundance of Eucalyptus trees. Cryptococcus neoformans var neoformans causes infection in the immunocompromised hosts whereas Cryptococcus neoformans var gattii infects immunocompetent hosts and seldom infects HIV positive individuals. As we were unable to culture cryptococcus in this patient so a definite species categorization of Cryptococcus neoformans could not be ascertained.

There are no definite guidelines for management of cryptococcal infection in an immunocompetent host. We followed recently published Infectious Disease Society of America (IDSA) guidelines (4) for management of this patient.

Our case presents unique challenge for diagnosis; involvement of liver, lymph node, CNS and bone marrow as a presenting manifestation of disseminated cryptococcosis in a HIV negative (immunocompetent) host, which to the best of our knowledge is not reported in the literature. Thus we conclude that a high index of suspicion for cryptococcal infection should be considered in conditions mimicking disseminated tuberculosis or lymphoreticular/ hematological malignancy.

References

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