

Case Report

Disseminated Cryptococcosis with Hepatic Dysfunction as the Initial Manifestation in an Immunocompetent Adult

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Abstract

Disseminated cryptococcosis is rare in immunocompetent hosts and hepatic manifestations as the presenting feature is further rare. We report a case of disseminated cryptococcosis with hepatic involvement as an initial manifestation in a previously healthy, immunocompetent adult. A young married female presented with progressive jaundice, anorexia, weightloss, cough with expectoration, and hepatosplenomegaly. Biochemical profile showed liver function derangement with increased transaminases, alkaline phosphatase, bilirubin with deranged coagulation assay, and decreased albumin. The patient was treated initially for disseminated tuberculosis with associated sepsis, but she succumbed on the third day. Diagnosis of cryptococcosis was made on the basis of sputum culture, serology, and liver histopathology.

Keywords: Cryptococcosis, hepatic, HIV, immunocompetent

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Introduction

Cryptococcus neoformans is an encapsulated yeastlike fungus. It is an important cause of infection in patients with HIV, lymphoid malignancies, and in those receiving corticosteroid therapy. It is rare in immunocompetent hosts. The most common sites involved are central nervous system (CNS), lung, skin, prostate, and eye in decreasing order. Though disseminated cryptococcosis can involve every organ in the body, hepatic involvement as a presenting feature is rare.^{1,2} We are reporting a case of disseminated cryptococcosis in an immunocompetent young female with hepatic and pulmonary involvement as the presenting features mimicking disseminated tuberculosis and malignancy.

Case Report

A 25-year-old female, married one year back and housewife by occupation, was presented with the complaints of yellowish discoloration of the sclera and urine since three months; cough with scanty white sputum for two months; anorexia, weight loss, and nausea since two months; low-grade intermittent fever without chills since one month; pain in the right upper abdomen since 20 days; and two episodes of scanty hemoptysis one day back. The jaundice was progressive and was not associated with pruritus or clay colored stools. The cough was associated with scanty sputum, which was blood stained for the last one day. The weight loss was significant (10 kg over the last two months). There was no history of orthopnea, dyspnea, chest pain, diarrhea, constipation, or jaundice in the past. She had not received any injections, drugs, or blood transfusions in the past and had no past history of

tuberculosis (TB), TB contact, diabetes, asthma, or sexual promiscuity. There were no clinical features to suggest the presence of immunodeficiency disorder in the patient. The menstrual history was normal. On examination, the patient was conscious, oriented, and average built. She was in respiratory distress with pallor, icterus, and pedal edema. There was nocyrosis, lymphadenopathy, clubbing, petechiae, bruising marks, skin lesions, or asterixis. The pulse rate was 104/min, respiratory rate 24/min, and blood pressure 92/50 mm of Hg. Examination of the chest revealed bilateral lower zone end-inspiratory crepitations with air entry fair and equal on both sides. The abdomen was distended. A tender liver was palpable 3 cm below the right costal margin in the midclavicular line with nodular surface. Tip of the spleen was palpable and a free fluid could be detected by shifting dullness. Bowel sounds were normal.

The initial investigations revealed a hemoglobin of 10.3 mg/dL, total leukocyte count of 36,500/cumm (neutrophils: 68% and lymphocytes: 27%), and platelet count of 135,000/cumm. The peripheral smear showed microcytic hypochromic RBCs, leukocytosis, but no hemoparasite or abnormal immature / blast cells of myeloid or lymphoid lineage were seen. Random blood sugar was 70 mg/dL; renal function tests showed a urea of 72 mg/dL; creatinine of 0.2 mg/dL; sodium of 129 meq/L; potassium of 4.2 meq/L; liver function tests showed a total bilirubin of 18.8 mg/dL; alanine transaminase of 159 IU/L; aspartate transaminase of 328 IU/L; alkaline phosphatase of 2272 IU/L; total protein of 6.3 mg/dL, with albumin of 1.9 mg/dL. Serum amylase was 64 U/L. Prothrombin time was control: 13 sec and test: 21.1 sec with INR: 1.82; partial thromboplastin time with kaolin was control: 29 sec and test: 36.9 sec. Serology was negative for HIV, hepatitis B, and C viruses. Urine analysis showed trace albumin; 1-2/HPF pus cells and RBCs; nocast or crystals. Sputum smear did not show any AFB. Cultures of blood and urine were sent along with sputum PCR for TB and sputum cultures for TB, fungal, and bacterial organisms. Chest X-ray (PA view) showed bilateral in homogeneous infiltrates (Figure 1) and ECG revealed a sinus tachycardia. Ultrasound abdomen was done and showed enlarged liver (span 17 cm), edematous gallbladder wall with internal echoes sugges-

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Figure 1. Chest X-ray showing bilateral infiltrates.

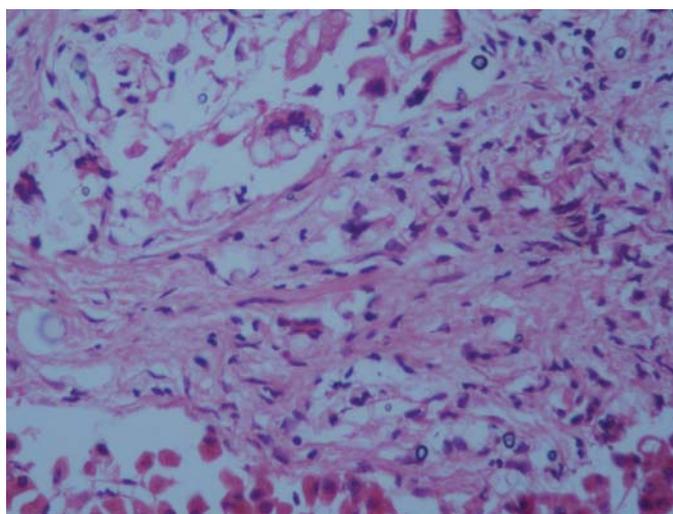


Figure 2. Liver biopsy showing capsulated spores of *Cryptococcus* (H&E, x 400).

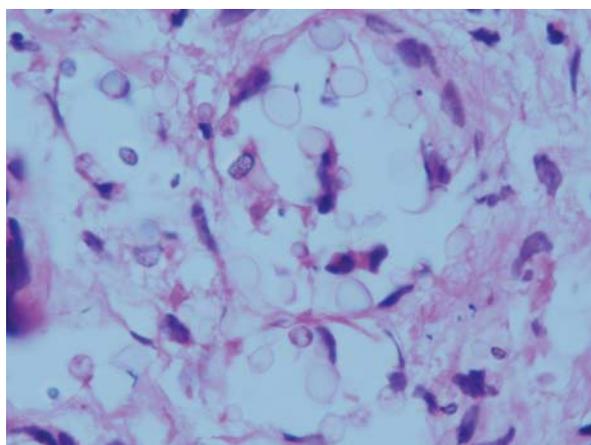


Figure 3. Liver biopsy showing capsulated spores of *Cryptococcus* (H&E, x 1000).

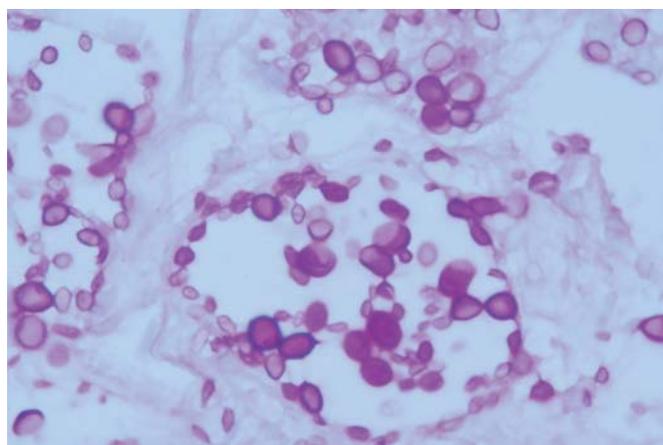


Figure 4. Liver biopsy showing capsules of cryptococcal spores with mucicarmine staining (mucicarmine, x 1000).

tive of sludge but no calculus, enlarged portal and peripancreatic lymph nodes with largest being 11 mm × 9 mm, splenomegaly (span 13.5 cm), bulky hypoechoic pancreas, and free fluid; rest of the study (common bile duct, portal vein, kidneys, and urinary bladder) was unremarkable. The ascitic fluid analysis revealed: total protein 1.6 mg/dL; albumin 0.4 mg/dL; glucose 66 mg/dL; calculated serum ascitic albumin gradient 1 (< 1.1 mg/dL); total cells: 750 cells/cumm (lymphocytes: 70%, polymorphs: 5%, mesothelial cells: 25%); ADA: 7.24 IU/L; few RBCs; and negative gram and AFB staining.

Based upon the initial evaluation, a provisional diagnosis of disseminated TB with associated sepsis was made and the patient was treated with broad spectrum antibiotics, modified ATT, and appropriate supportive care. The patient, however, deteriorated the next day and succumbed on the third day despite higher antibiotics, intensive ventilation, and inotropic support. The pending reports received just before the patient succumbed were: *Klebsiella* growth on blood culture, sterile urine culture, and negative sputum PCR for TB. Postmortem liver biopsy was done with consent. Histopathologic examination (Figures 2, 3, 4) showed

many capsulated fungal spores with foreign body giant cell reaction around them. With mucicarmine, the capsule stained pink. Her serum sample (preserved in a central laboratory as a part of hospital policy) tested for cryptococcal antigen was found to be positive. Sputum cultures (sent earlier) for fungal organisms grew cream-colored mucoid colonies of *Cryptococcus neoformans* on Sabouraud's media; however, cultures for AFB (received after six weeks) and bacterial organisms yielded no growth. The triad of serology, sputum culture, and liver histopathology confirmed the diagnosis of disseminated cryptococcosis with associated gram-negative sepsis in this HIV-negative patient.

Discussion

Cryptococcosis is a systemic infection caused by an encapsulated yeast-like fungus, *Cryptococcus neoformans*. It is worldwide in distribution. There are two variants of *Cryptococcus*: *C. neoformans* and *C. gatti*.^{3,4} The *neoformans* variety causes disease in immunocompromised patients including those with AIDS, and is found in most countries. The *gatti* form is seen mainly in

tropical areas and generally occurs in healthy individuals.

The two most common sites for infection with this encapsulated yeast are the lung and CNS.⁵ The respiratory tract is the most common portal of entry for this yeast and symptoms there range from asymptomatic colonization of the airway to life-threatening pneumonia.^{6,7} The clinical picture depends on the immune status of the host. Patients of HIV with pulmonary cryptococcosis are almost invariably symptomatic, presenting with fever, cough, dyspnea, and weight loss. However, one-third of immunocompetent hosts with pulmonary cryptococcosis are asymptomatic. Patients of CNS cryptococcosis present with signs of subacute meningitis or meningoencephalitis. Involvement of skin, bone, and prostate gland may also occur. Radiologic features on the chest X-ray can show variable appearances such as focal or diffuse interstitial infiltrates, pleural effusion, hilar lymph node enlargement, or rarely cavities.^{8,9} Hepatobiliary manifestations on presentation are rare in cryptococcosis and in an immunocompetent patient are further rare with few cases reported till date in which jaundice, deranged liver functions, or hepatic failure were the main features.¹²

The diagnosis of cryptococcosis depends on the demonstration of the organism by staining smears, cerebrospinal fluid (CSF), or sputum with India ink or nigrosin. Biopsy material depicts large yeast cells using periodic acid Schiff or Grocott stains; the mucicarmine stain is specific for cryptococcal capsule which it stains pink.¹⁰ The organism can also be readily cultured on conventional mycological media such as Sabouraud's agar. Sources of culture material include CSF, sputum, and biopsies.¹¹ Latex agglutination tests for cryptococcal antigen in body fluids are sensitive and specific.¹²

If not diagnosed and treated early, the patients with disseminated cryptococcosis may die. Possible reasons for delay in diagnosis and therapy are a low degree of suspicion, lack of characteristic signs and symptoms, and mimicking common differential diagnosis like TB and malignancy. In a country like India, with a high prevalence of TB and logistic constraints for investigations, it is not possible to pick up the diagnosis unless there is a high degree

of suspicion.

Our case of disseminated cryptococcosis with hepatobiliary dysfunction as the initial presentation in an immunocompetent patient was a diagnostic challenge. Henceforth, the hepatic manifestations should be considered as one of the primary presentations of disseminated cryptococcosis and must be given more importance in the era of effective antifungal therapy.

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