

Case Report

Spontaneous Peritonitis Secondary to *Cryptococcus Neoformans*

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OPEN ACCESS**Keywords**

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Abstract

Cryptococcus neoformans is encapsulated yeast, which causes significant infections in immune compromised individuals, with a very high morbidity and mortality. We present a case of disseminated cryptococcal infection with peritonitis in a 33 year-old female patient with a history of alcoholic liver cirrhosis, complicated by hepato-renal syndrome. She presented to the Emergency Department with altered mental status and was found to have spontaneous peritonitis, with elevated leukocyte count in the ascitic fluid. She developed septic shock requiring significant vasopressor support and renal replacement therapy. She had multiple recent admissions for treatment of hepatic encephalopathy and her Model for End Stage Liver Disease score on admission was 38. She was initially started on broad-spectrum antibiotics with vancomycin and imipenem as well antifungal therapy with fluconazole. The blood and peritoneal fungal cultures grew *Cryptococcus neoformans*. The patient developed multi-organ failure with refractory shock, acute respiratory distress syndrome and disseminated intravascular coagulopathy. Given the grave prognosis, the patient's family decided on a palliative care approach and the patient died.

Cryptococcal peritonitis is a rare manifestation of disseminated cryptococcal infection and its clinical presentation may be similar to that of spontaneous bacterial peritonitis. The ascitic fluid cell count can be either polymorphonuclear or lymphocyte predominant. Early clinical suspicion, isolation of the organism and timely initiation of appropriate antimicrobial therapy are crucial.

ABBREVIATIONS

SFP: Spontaneous Fungal Peritonitis; SBP: Spontaneous Bacterial Peritonitis; PMN: Polymorphonuclear; INR: International Normalized Ratio; WBC: White Blood Cell count; MELD: Model for End stage Liver Disease

INTRODUCTION

Spontaneous peritonitis, bacterial (SBP), is a common and life-threatening complication in patients with liver cirrhosis and ascites, with a mortality of 10 to 50% [1,2]. It should be suspected in patients with ascites who develop fever, abdominal pain, abdominal tenderness, ileus, and worsening hepatic encephalopathy, though 13% of patients may lack any signs or symptoms of SBP at the time of presentation [1,2]. The diagnosis is made if the polymorphonuclear cell (PMN) count in the ascites fluid is ≥ 250 cells/mm³, culture results are positive and secondary causes of peritonitis are excluded [3,4].

Cryptococcus neoformans is encapsulated yeast, member of the genus *Cryptococcus* and family of *Tremellaceae*, found mainly in the excreta of birds and their nest, especially pigeons as well in tree barks. This organism causes significant infections in immunocompromised individuals with human immunodeficiency virus infection (HIV), organ transplantation, malignancy and prolonged glucocorticoid therapy. The most common infections include meningitis, pneumonia and disseminated disease. However, cryptococcal infections in patients with cirrhosis have recently been described and are usually fatal. Cryptococcal peritonitis is the second most common peritoneal infection in patients with cirrhosis [5-7].

We present a case of disseminated cryptococcal infection with peritonitis in a patient with cirrhosis. We will also discuss possible causes of this fungal peritonitis and review the literature on this complication.

CASE PRESENTATION

A 33 year-old Native American female with a history of alcoholic liver cirrhosis presented to the hospital with altered mental status. She had multiple recent admissions for treatment of hepatic encephalopathy. Her family stated she had symptoms of mild abdominal discomfort, nausea, and vomiting for a few days preceding the Emergency Department visit and that she had a therapeutic paracentesis three weeks ago.

On physical exam, the patient was cachectic and afebrile with a pulse of 110 beats per minute. The remainder of the exam revealed jaundiced skin with spider angiomas and abdominal exam with significant ascites, reduced bowel sounds and mild tenderness to deep palpation. In the Emergency Department, the patient became more somnolent and required endotracheal intubation and mechanical ventilation for airway protection.

Initial laboratory values revealed a bilirubin of 20.4 mg/dL, INR of 4.8, creatinine of 1.5 mg/dL, lactate of 7.3 mg/dL. Hematologic values included a WBC count of 6.8 K/uL, hemoglobin of 6.8 g/dL and platelets of 84,000/dL. The calculated model for end stage liver disease (MELD) score was 38. Her HIV serology was negative. The patient developed profound septic shock and required vasopressor support. Tracheal aspirate, urine and blood cultures were obtained on admission. Given her rapid clinical deterioration, the patient was empirically started on vancomycin, imipenem and fluconazole. A bedside paracentesis performed on hospital day one revealed a WBC count of 6,439 /uL with 86% neutrophils.

On hospital day four, blood and peritoneal cultures grew *Cryptococcus neoformans*. The patient developed multi-organ failure with refractory shock, acute respiratory distress syndrome, disseminated intravascular coagulopathy and acute kidney injury requiring continuous renal replacement therapy. We were unable to perform a lumbar puncture due to the severe coagulopathy. Given the grave prognosis, the patient's family decided on a palliative care approach and the patient died.

DISCUSSION

Spontaneous Fungal Peritonitis (SFP) with fungus as secondary to *Cryptococcus neoformans* is a rare event, occurring in less than 5% of HIV-negative patients [8]. Its clinical presentation may be similar to that of SBP but at times it may be occult. The typical peritoneal fluid cell count is polymorphonuclear predominant (greater or equal to 250 cell/mm³) but can be mononuclear with a lymphocytic predominance [9]. The mortality rate is very high, upwards of 70 to 80% [5,10]. *Cryptococcus neoformans* infection can occur in immunosuppressed patients, with HIV being the most frequent predisposing factor [11]. Previous reported cases document that in non-HIV patients, chronic liver disease is the predominant risk factor for cryptococcal peritonitis [5,12]. Jean noted that patients with HIV, immunosuppressive therapy and liver cirrhosis are the three main predisposing conditions for cryptococemia.

Patients with cirrhosis are immune compromised for several reasons. First, there is a relative serum complement deficiency leading to reduced opsonic recognition of fungi as well as deterioration of the humoral immunity [13,14]. In addition, the

function of PMNs is reduced in patients with cirrhosis [15,16]. Finally, the use of invasive procedures and antibiotics and the possibility of translocation of organisms from the gastrointestinal tract put these patients at risk for life-threatening fungal infections [13].

Our patient developed profound septic shock with multi-organ failure, and received only empiric fluconazole, as her family decided to withdraw life support. However, the Infectious Diseases Society of America and American Thoracic Society initial treatment guidelines for *Cryptococcus neoformans* infections recommend amphotericin B and flucytosine for severe disseminated disease and immune compromised patients. Lumbar puncture is indicated in all immune suppressed patients and those with severe disease to evaluate for fungal meningitis [17,18]. Due to her significant coagulopathy, we were unable to perform a lumbar puncture in our patient.

A recent review of Spontaneous Fungal Peritonitis (SFP) in patients with cirrhosis reported that *Cryptococcus neoformans* is the second most common organism, is difficult for clinicians to diagnose and is associated with a high mortality. Patients with SFP have a significantly worse prognosis than patients with SBP. [12]. The high mortality of this infection in patients with cirrhosis, including liver transplant candidates is also noted in a number of other case series [9,10].

In summary, *Cryptococcus neoformans* peritonitis is a life-threatening infection in patients with cirrhosis and is often associated with septic shock. Mortality is very high and clinicians must have a high level of suspicion for this infection, as it can mimic SBP and there is often a delay between ascitic fluid examination and culture positivity. Clinicians should consider a diagnostic work-up and empiric treatment for cryptococcal peritonitis if cell counts in ascitic fluid reveal an elevated leukocyte count but bacterial cultures remain negative after 48 hours. Two recent reports in the literature suggest that performing cytology and India ink preparation on ascitic fluid and testing cryptococcal antigen in the serum and ascitic fluid may assist in the diagnostic evaluation of patients with suspected cryptococcal peritonitis. This may lead to earlier confirmation of this infection and initiation of appropriate antifungal therapy [11,19, 20].

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