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CASE REPORT

Cryptococcal Peritonitis in a Patient with Decompensated Liver Cirrhosis

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Abstract

***Cryptococcus* is a rare pathogenic fungus that is known primarily for causing meningeal and pulmonary disease in immunocompromised patients. There are scarce reports of other varieties of cryptococcal infections, such as disseminated and peritoneal disease. Here we present a very rare case of an elderly female patient with a history of non-alcoholic steatohepatitis (NASH) cirrhosis who presented with symptoms of dyspnea and abdominal distention and was found to have *Cryptococcus neoformans* pleuritis and peritonitis without evidence of disseminated disease. The patient was treated with antifungals consisting of amphotericin and flucytosine followed by fluconazole. This case describes a previously unknown pattern of disease spread and adds to the body of knowledge on *Cryptococcus*. Additionally, it reinforces growing evidence in the literature that cirrhosis is a risk factor for *Cryptococcus*.**

Keywords: Cryptococcus, Peritonitis, Cirrhosis

1. Introduction

Cryptococcus is a rare pathogenic fungus. There are two species of *Cryptococcus* that are associated with human infections, *Cryptococcus neoformans* and *Cryptococcus gatti*. Morphologically, *Cryptococcus* species are encapsulated yeasts, often found in bird droppings and decaying wood.[1] Infections typically affect immunocompromised hosts. Conditions such as acquired immunodeficiency syndrome (AIDS), liver cirrhosis, and the use of chronic immunosuppressive medication are associated with infection.[2] Inoculation typically occurs through inhalation of spores, which are contained in the immunocompetent host, but which can disseminate hematogenously when an individual is immunosuppressed.[3] *Cryptococcus* infections typically manifest as fungemia, central nervous system, or pulmonary infections. Peritonitis is an exceedingly rare site for cryptococcal infection. Treatment of cryptococcal disease is based primarily on the 2010 Infectious Diseases Society of America Guidelines and consists of antifungal medications. Specific regimens depend on the type of infection and type of host; however, they are not well established in patients presenting with non-meningeal, non-pulmonary disease.[4] We present a case of an elderly female with NASH cirrhosis who developed spontaneous *Cryptococcus neoformans* peritonitis and pleuritis.

2. Case

A 76-year-old female with a past medical history of non-alcoholic steatohepatitis (NASH)-induced cirrhosis with complications including hepatic encephalopathy, recurrent ascites and pleural effusions, also with hypothyroidism and obesity presented to our facility with complaints of generalized weakness, shortness of breath with minimal exertion, worsening abdominal pain and distension and bilateral lower extremity swelling over several weeks. She had no fevers, chills, headache, cough, focal weakness or numbness. She lived on a farm with some livestock but denied any recent exposure to bird or pigeon droppings. At presentation, she was afebrile and normotensive with a heart rate of 80 and an oxygen saturation of 97% on room air. She was not ill-appearing and non-icteric. Her

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pulmonary examination was significant for diminished breath sounds in the right mid and lower lung zones. On abdominal exam, she had moderate distension, dullness to percussion, a positive fluid wave and mild generalized tenderness. There was pitting edema in the lower extremities bilaterally up to the thighs. There was no asterixis. Initial laboratory investigations revealed normal renal and hepatic function. There was no leukocytosis and inflammatory markers were within normal limits. A computed tomography (CT) scan of the chest, abdomen, and pelvis demonstrated a large right-sided pleural effusion (Fig. 1) and moderate abdominal ascites and cirrhosis of the liver. She subsequently had a diagnostic thoracentesis and paracentesis. Both pleural and ascitic fluid cultures grew *Cryptococcus neoformans*. Interestingly, her blood cultures and serum cryptococcal antigen were negative. Lumbar puncture was obtained, and cerebrospinal fluid studies were negative for cryptococcal antigen. She was started on intravenous amphotericin B liposome at 4 mg/kg/dose daily and oral flucytosine 25 mg/kg/dose daily for two weeks and transitioned to fluconazole 400 mg daily at discharge for eight weeks, with plans to reduce the dose to 200 mg afterwards for an extra 12 months. The patient was discharged from the hospital in stable condition with follow up established with infectious disease. Follow up records indicated the patient was doing well and tolerating treatment for approximately two months. Subsequently, the patient was readmitted to the hospital for worsening abdominal pain which was not investigated with invasive studies as the patient elected for comfort measures and passed away shortly thereafter under hospice care.

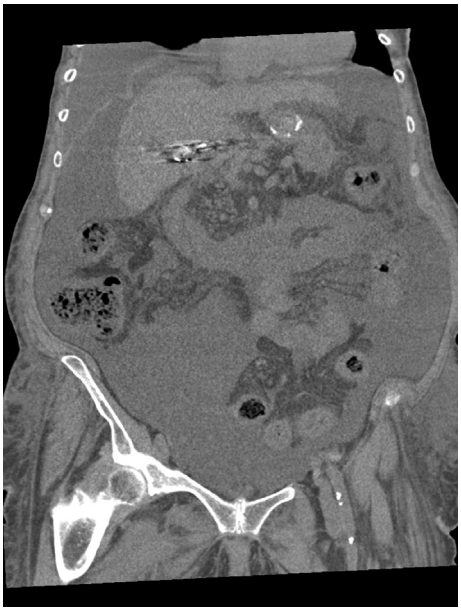

Fig. 1. Coronal view of an abdominal computed tomography without contrast demonstrated cirrhosis with moderate abdominal ascites, diffuse anasarca, and a large right sided pleural effusion.

3. Discussion

To our knowledge, there have been no reported cases of isolated cryptococcal pleuritis and peritonitis without evidence of disseminated disease. Because the pleural effusion was right-sided, in the setting of cirrhosis with known peritoneal cryptococcus without fungemia, a hepatic hydrothorax was postulated as the conduit for contiguous spread. Ultimately, peritoneal and pleuritic Cryptococcal infection without fungemia yielded a rare clinical scenario without specific management guidelines.

Cirrhosis remains an under recognized risk factor for development of cryptococcus infections. Classically, Acquired Immunodeficiency Syndrome (AIDS) has been associated with cryptococcus. Albert-Braun et al. reviewed existing reports of peritonitis and found 17 reports in underlying liver disease from alcohol or hepatitis, compared to three cases in patients with AIDS.[5] In their retrospective review, Yinnon et al. identified only 20 cases in the literature of cryptococcus peritonitis. Of those, ten were associated with peritoneal dialysis, five were associated with liver disease, and three were associated with AIDS.[6] A similar report by Mabee et al. supported these findings in their review of cryptococcal peritonitis. Cirrhosis from alcohol or hepatitis was present in almost one third of the cases the authors identified.[7] Notably, cirrhosis secondary to NASH was not identified in their review. High morbidity and mortality were observed in both reviews, possibly because of late recognition of disease.[6,7]

Several mechanisms describing the immunocompromised state in cirrhosis have been proposed. In liver dysfunction, it is possible decreased serum complement levels, impaired chemotaxis, and impaired phagocytic function of neutrophils contribute to infectious susceptibilities.[8] Additionally, patients with cirrhosis frequently have complications such as gastrointestinal bleeding and invasive procedures which may predispose patients to bacterial translocation from the gut into the bloodstream.[9]

In our patient's case, we initiated antifungal therapy, targeting peritoneal and pulmonary involvement after CT head and lumbar puncture ruled out CNS infection. There are currently no standardized guidelines regarding the management of cryptococcal peritonitis. Management with antifungals and choice of antifungals has often been

done on a case-by-case basis. Our patient initially improved after two weeks of inpatient treatment and was discharged on fluconazole with scheduled outpatient follow-up. Her clinical decline which lead to her death two months later may have been accelerated by her cryptococcal infection.

4. Conclusion

We present a case of cryptococcal peritonitis and pleuritis without fungemia in a patient with NASH cirrhosis. This presented a challenge in the management due to a scarcity of reported cases. Further documentation of cryptococcal peritonitis and pleuritis cases could guide clinicians faced with this rare and life-threatening clinical circumstance. Importantly, this report adds to the existing body of literature documenting cirrhosis as a risk factor for cryptococcal infections; to our knowledge this is the first documented case of NASH as the etiology of cirrhosis in patients with such infections.

Disclaimers

This manuscript has not been published or presented at another forum.

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Conflict of interest

There is no conflict of interest.

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