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FUNGAL PERITONITIS BY *CRYPTOCOCCUS NEOFORMANS*: A CASE-REPORT

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Abstract: This paper describes a rare case of fungal spontaneous peritonitis caused by Cryptococcus neoformans in a 77-year-old woman with decompensated hepatic cirrhosis due to non-alcoholic fatty liver disease. The patient presented with disabling abdominal pain and hepatic encephalopathy, leading to hospitalization. Diagnostic paracentesis revealed serohematic fluid, and subsequent culture identified C. neoformans on the 6th day of admission. Treatment was initiated with fluconazole, later escalated to liposomal amphotericin B based on sensitivity testing. The patient's hospital course was complicated by sepsis, acute kidney injury, anemia, urinary tract infection, and atrial fibrillation. Despite these challenges, the patient survived the acute infection phase, ultimately transitioning to palliative care after 28 days. This case highlights the importance of considering fungal etiology in cirrhotic patients with peritonitis, especially when risk factors are present. It also underscores the need for early detection, prompt treatment, and a multidisciplinary approach to management. The paucity of clear guidelines for antifungal use in this patient population emphasizes the need for further research to optimize diagnostic and treatment protocols for fungal peritonitis in cirrhotic patients.
Keywords: Fungal peritonitis, *Cryptococcus Neoformans*, Hepatic Cirrhosis.

INTRODUCTION

Spontaneous peritonitis, often referred to as spontaneous bacterial peritonitis (SBP), is an acute infection of ascitic fluid without an evident intra-abdominal source, predominantly affecting patients with advanced liver disease and ascites[1]. SBP is typically bacterial, caused by enteric organisms due to bacterial translocation across the gut wall[2]. Clinically, SBP manifests through symptoms such as fever, ascites,

and altered mental status, though it can also present asymptomatically, complicating timely diagnosis. While bacterial infections are the most common cause, spontaneous peritonitis can occasionally be attributed to fungal pathogens, a scenario that carries a significantly higher mortality rate and presents unique diagnostic challenges[3].

Among the rare fungal etiologies, *Cryptococcus neoformans* is particularly uncommon. This pathogen is more frequently associated with central nervous system infections in immunocompromised individuals, rather than with peritoneal infections. When *Cryptococcus neoformans* invades the peritoneal cavity, it creates a complex clinical scenario that complicates diagnosis and management, often resulting in poorer patient outcomes.

Despite the severity of fungal peritonitis, especially caused by *Cryptococcus neoformans*, the current literature is sparse. Most research has focused on bacterial causes, leaving a substantial gap in understanding fungal peritonitis in cirrhotic patients[1]. Existing guidelines primarily address bacterial infections, with little consideration given to fungal pathogens, which contributes to delayed diagnosis and suboptimal treatment. This gap in research and clinical guidance directly impacts patient survival, underscoring the need for more comprehensive studies.

OBJECTIVE

The aim of this paper is to describe a rare case of fungal spontaneous peritonitis caused by *Cryptococcus neoformans* in a female patient with decompensated hepatic cirrhosis and ascites. By presenting this case, we highlight the importance of considering fungal etiology in cirrhotic patients with peritonitis, especially when risk factors are present. We also discuss the diagnostic approach, treatment challenges, and outcomes, providing valuable insights for clinicians managing similar cases.

CASE REPORT

On December 28th, 2022, a 77-year-old retired woman with a history of hepatic cirrhosis due to non-alcoholic fatty liver disease (NAFLD) presented to our clinic for elective paracentesis. The patient reported a three-day history of disabling abdominal pain, accompanied by confusional episodes noted by her caregiver. Notably, there were no reports of fever or bleeding.

MEDICAL HISTORY

The patient's medical history was significant for:

- Hypertension and associated heart failure
- Refractory ascites, with a hospitalization ten years prior
- Recent placement of a transjugular intrahepatic portosystemic shunt (TIPS) 21 days before presentation
- No history of alcohol use

INITIAL PRESENTATION AND MANAGEMENT

Upon examination, the patient appeared uncomfortable and disoriented. Paracentesis yielded five liters of serohematic fluid. Given the patient's altered mental status, suggestive of hepatic encephalopathy, the decision was made to admit her for further management and close monitoring.

HOSPITAL COURSE

- Day 1-3: The patient was closely monitored, with supportive care provided for hepatic encephalopathy.
- Day 4: Blood work revealed significant leukocytosis with a left shift, raising concerns for an underlying infection. Empiric antibiotic therapy with piperacillin/tazobactam was initiated for a presumed infection of undetermined origin.

- Day 6: A pivotal development occurred when the ascitic fluid culture returned positive for *Cryptococcus neoformans*. This unexpected finding prompted an immediate change in the treatment strategy. Antibiotic therapy was discontinued, and antifungal treatment with fluconazole was initiated (loading dose of 800 mg, followed by 400 mg daily maintenance dose).
- Day 6-8: A second therapeutic paracentesis was performed, accompanied by albumin replacement following an established protocol. The patient's condition remained guarded, necessitating close monitoring and supportive care.
- Day 9: Based on fungal sensitivity testing results, the antifungal regimen was escalated. Fluconazole was replaced with liposomal amphotericin B, planned for a 14-day course.

COMPLICATIONS AND FURTHER MANAGEMENT:

The patient's hospital course was marked by several significant complications:

- Sepsis: The patient developed hypotension requiring vasopressor support. Blood cultures grew *Staphylococcus haemolyticus*, necessitating the reinitiation of broad-spectrum antibiotics (piperacillin/tazobactam and linezolid).
- Acute Kidney Injury: The patient developed KDIGO stage II acute kidney injury, requiring nephrology consultation, careful fluid management, and temporary dialysis support.
- Anemia: Requiring transfusion of packed red blood cells.
- Urinary Tract Infection: Diagnosed on day 26, treated with appropriate antibiotics.
- Atrial Fibrillation: New-onset high-response atrial fibrillation was detected on day 27, managed with rate-control strategies.

Throughout these complications, the 14-day course of amphotericin B was completed, and the albumin replacement protocol was continued as needed.

OUTCOME AND DISCHARGE

Following the completion of antifungal therapy, the patient showed signs of clinical improvement. On day 28, after a comprehensive family meeting and consideration of the patient's overall condition and prognosis, the decision was made to transition to palliative care.

The patient was discharged on January 27th, 2023, with the following management plan:

- Analgesia for symptom control
- Prophylactic norfloxacin
- Double lumen abdominal catheter for ongoing management of ascites
- Arrangements for ascitic fluid drainage in her home city
- Scheduled follow-up at our outpatient clinic

DISCUSSION

Cryptococcus neoformans is an opportunistic encapsulated fungus primarily known for causing respiratory infections and central nervous system infections in immunocompromised patients, particularly those with HIV. However, fungal spontaneous peritonitis caused by this species is a rare but potentially severe complication in patients with advanced liver disease and cirrhosis[4].

The risk factors for fungal spontaneous peritonitis, particularly in cirrhotic patients, are multifaceted and include:

- Severity of liver disease: Child-Pugh C classification and MELD score > 30 points

- Biochemical markers: High serum bilirubin and urea levels, low ascitic fluid protein (< 1 mg/mL)
- Medical interventions: Antibiotic prophylaxis for spontaneous bacterial peritonitis, hepatorenal syndrome[3,5]
- Invasive procedures: Routine paracentesis in refractory ascites, potentially leading to percutaneous inoculation of commensal fungi
- Other factors: Continuous corticosteroid use, high APACHE score, renal replacement therapy, malnutrition, and placement of nasogastric tubes

In our case, the patient exhibited several of these risk factors, including advanced cirrhosis, refractory ascites requiring paracentesis.

The mortality rate associated with fungal peritonitis is alarmingly high, with studies reporting 30-day mortality of 55.78%, 90-day mortality of 70%, and 180-day mortality of 74%[6]. These poor outcomes may be attributed to several factors:

- Delayed diagnosis: Fungal cultures typically require 3-5 days for results, potentially delaying targeted treatment
- Limited antifungal treatment options: Some antifungals have hepatotoxic effects, complicating their use in patients with liver disease
- Underlying severe liver dysfunction: Advanced cirrhosis itself carries a poor prognosis

This highlights the importance of maintaining a high index of suspicion for fungal peritonitis in cirrhotic patients, especially when risk factors are present. The initial empiric treatment with broad-spectrum antibiotics, followed by prompt initiation of antifungal therapy upon culture results, likely contributed to the patient's survival[4,6]. Ferreira da Silva et al. highlighted the utility of Cryptococcal antigen (CrAg) testing for detecting systemic cryptococcal involvement[7]. This suggests that CrAg testing could be a valuable tool for early diagnosis and monitoring of treatment response, particularly when cultures for fungi are not routinely performed.

The choice of antifungal therapy in this case-fluconazole followed by liposomal amphotericin B-aligns with current recommendations for cryptococcal infections[4]. Ferreira da Silva et al. also reported a similar treatment approach due to the unavailability of flucytosine, highlighting a common challenge in resource-limited settings[7]. However, the gold-standard duration of therapy for cryptococcal peritonitis in cirrhotic patients remains unclear, underscoring the need for further research in this area.

The complications observed during treatment, including sepsis, acute kidney injury, and cardiac arrhythmias, underscore the complex management required for these patients. Multidisciplinary care involving hepatology, infectious diseases, nephrology, and critical care was crucial in navigating these challenges.

While our patient survived the acute infection, her eventual transition to palliative care highlights the overall poor prognosis associated with advanced liver disease complicated by fungal peritonitis. This outcome emphasizes the need for early detection and aggressive management of fungal infections in cirrhotic patients.

Future research directions should focus on developing rapid diagnostic tests for fungal peritonitis, optimizing antifungal regimens for patients with liver disease, and investigating preventive strategies for high-risk individuals.

CONCLUSION

Fungal spontaneous peritonitis, particularly caused by *Cryptococcus neoformans*, presents a rare yet potentially fatal complication in patients with cirrhosis. This case report emphasizes the critical importance of early recognition and prompt treatment, given the high mortality rates associated with this condition. Given the gaps in current clinical practice guidelines, particularly regarding the use of antifungal agents in cirrhotic patients with fungal peritonitis, there is a need for more comprehensive research to establish optimal diagnostic and treatment protocols.

In the broader context of cirrhosis management, this case serves as a reminder of the importance of vigilance for atypical infections. Improving outcomes for patients with fungal peritonitis will require a combination of heightened clinical awareness, advances in diagnostic and therapeutic approaches, and a deeper understanding of the unique challenges posed by fungal infections in the setting of liver cirrhosis.

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