

Disseminated Cryptococcus Presenting as a Pleural Effusion in a Cirrhosis Patient

William Jones, MD, Elizabeth Craig, DO, Charles Duckworth, MD
Memorial Health University Medical Center, Savannah, Georgia

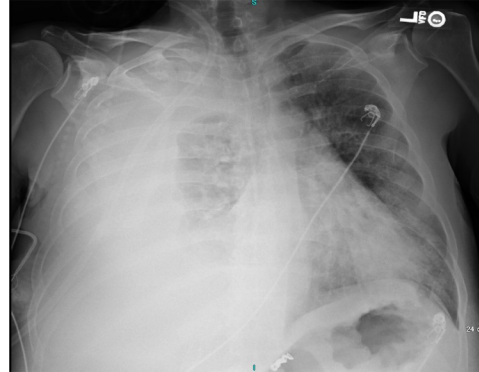
Introduction

- *Cryptococcus neoformans* is an encapsulated yeast classically known as an opportunistic infection notorious for affecting patients with acquired immunodeficiency syndrome (AIDS) and other immunosuppressed patients.
- Over the last few decades, there have been very few cases of pleural effusions as the initial presentation of disseminated cryptococcosis, particularly with cirrhosis as the only risk factor for an immunocompromised state.

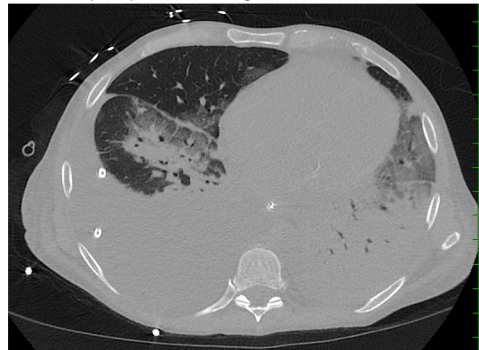
Case Description

- A 48 year old male with a past medical history of alcoholic cirrhosis presented to the ED with shortness of breath.
- His past medical history is significant for multiple hospitalizations for decompensated hepatic cirrhosis, ascites, pleural effusions, portal hypertension gastropathy, and s/p TIPS with revision. MELD-Na score of 31 on admission.
- He presented with a 3-day history of worsening shortness of breath. Chest x-ray on admission showed a right sided pleural effusion concerning for hepatic hydrothorax.
- He received a thoracentesis on admission and on hospital day 1 he was started on micafungin after preliminary pleural fluid analysis grew yeast.
- On hospital day 2, blood cultures and pleural fluid cultures returned concerning for *Cryptococcus* or *Blastomycosis*. His antifungal coverage was changed to fluconazole.
- The patient also developed respiratory failure requiring intubation for 7 days as well as vasopressor support. During this period, the patient's pleural fluid finalized as *Cryptococcus neoformans* and his cryptococcal antigen titer return high at 1:128.
- Antifungal therapy was again adjusted to cover cryptococcal meningitis as he developed a worsening encephalopathy despite treatment for hepatic encephalopathy. He received 14 days of amphotericin B as well as 9 days of flucytosine, which was discontinued after an elevated serum level.
- His ICU admission was complicated by worsening hepatic and renal function. His MELD score climbed to 42. Renal dysfunction was thought to be due to hepatorenal syndrome, however he did not receive renal replacement therapy.
- On hospital day 12, the patient was stable for transfer to the floor for continued antifungal treatment and transfer to a liver transplant center planning.
- Unfortunately, he developed shock requiring vasopressor supports and required intubation on hospital day 14.
- He expired from cardiovascular collapse the next day despite maximum rates of multiple vasopressors. Blood and ascites cultures performed on the day of expiration eventually returned *Klebsiella pneumoniae*.

Results



Chest x-ray from admission showing right pleural effusion with passive atelectasis and near complete opacification of the right hemithorax.



CT chest without contrast on hospital day 2 showing moderate right pleural effusion with chest tube, small left pleural effusion, bilateral lower lobe consolidation, and diffuse ground glass attenuations.

Discussion

- *C. neoformans* is an encapsulated yeast typically known for infecting immunocompromised hosts, classically patients with AIDS or patients receiving immunosuppression therapy.
- The pathophysiology normally involves inhalation causing primary lung lesion then dissemination, usually to the meninges and brain.
- While AIDS and patients receiving immunosuppression therapy are predisposing factors for disseminated cryptococcosis, cirrhosis appears to be an increasingly more common risk factor.
- Interestingly, this patient presented initially with a large pleural effusion that later grew *C. neoformans* with eventual disseminated cryptococcosis with fungemia.
- In a 2015 case report by Wang et al, they reported only 5 cases of pleural effusion as the initial clinical presentation of disseminated cryptococcosis in the English language literature. The 5 patients studied all had an obvious cause of immunosuppression, making our patient with cirrhosis an even more unique case.
- In a small VA study investigating outcomes of cryptococcosis in cirrhotic patients, they found mortality to be 81%. In the same study, patients with liver cirrhosis were significantly less likely to receive antifungal therapy early in their hospital course. Mortality was noted to be particularly high in cirrhotic patients with a 30 day mortality rate of 82%.

Conclusion

- Cirrhotic patients appear to be at an increased risk for cryptococcal infections.
- The mortality rate of cirrhotic patients with cryptococcus appears to be high.
- Clinicians should be aware of cryptococcus as a pathogen in cirrhotic patients and consider early antifungal therapy given the mortality with cryptococcal infection.

References

1. Revankar, Sanjay G. "Cryptococcosis - Infectious Diseases." *Merck Manuals Professional Edition*, Merck Manuals, 2 June 2022. <https://www.merckmanuals.com/professional/infectious-diseases/fungi/cryptococcosis>.
2. Chen M, Wang X, Yu C, Dai C, Chen D, Yu C, Xu X, Yao D, Yang L, Li Y, Wang L, Huang X. Pleural effusion as the initial clinical presentation in disseminated cryptococcosis and fungaemia: an unusual manifestation and a literature review. *BMC Infect Dis*. 2015 Sep 22;15:385. doi: 10.1186/s12879-015-1132-4. PMID: 26395579; PMCID: PMC4580115.
3. Singh, Nina, et al. "Cryptococcus Neoformans Infection in Patients with Cirrhosis, Including Liver Transplant Candidates." *Medicine*, vol. 83, no. 3, 2004, pp. 188-192. <https://doi.org/10.1097/01.md.0000125760.45299.69>.
4. Jean SS, Fang CT, Shau WY, Chen YC, Chang SC, Hsueh PR, Hung CC, Luh KT. Cryptococcosis: clinical features and prognostic factors. *QJM*. 2002 Aug;95(8):511-8. doi: 10.1093/qjmed/95.8.511. PMID: 12145390.

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA or any of its affiliated entities.