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DISSEMINATED CRYPTOCOCCAL DISEASE IN LIVER CIRRHOSIS: Is it more common than reported in the literature?

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Introduction

- Cryptococcus is an environmental yeast that is typically associated with human immunodeficiency virus (HIV), and transplant recipients
- Invasive disease has been described in patients with liver disease, however it is not a common occurrence.
- We describe a case of disseminated *Cryptococcus neoformans* infection in a patient with liver cirrhosis

Case presentation

- 53-year-old male, with history of Hepatitis C infection, liver cirrhosis, Sjogren's syndrome, venous thromboembolism (VTE), was admitted to the hospital for worsening debility and weakness
- In a recent hospital admission for acute kidney injury (AKI), he was found to have spontaneous bacterial peritonitis secondary to *Klebsiella pneumoniae* and *E. coli*, and bacteremia with the latter organism. Patient was treated with IV Ertapenem
- On latest admission, patient's model for end-stage liver disease (MELD)-Na was 25. Physical exam was significant for abdominal distention with mild diffuse tenderness, shifting dullness, positive fluid-wave sign, and bilateral 1+ edema to the knee
- Peritoneal fluid was positive for *Cryptococcus*, and multiple blood cultures (total of 6 different days) were positive for *Cryptococcus*. Lumbar puncture (LP) showed pleocytosis with monocytes predominance, CSF culture positive for *Cryptococcus* and an elevated CSF Cryptococcal antigen (Crypto Ag)
- Patient was treated with Liposomal Amphotericin B and Flucytosine.
- Repeated LPs showed persistently elevated opening pressures, requiring ventricular-pleural shunt
- He finished a course of 4 weeks of induction therapy, followed by transition to oral Fluconazole for consolidation

Laboratory data

- Lumbar puncture on admission: 30 WBCs, 0 RBCs, 25% neutrophils, 51% monocytes, protein 87.7, glucose 95. OP 31/CP 13. CSF Crypto Ag > 2560
- CSF culture on admission: POS for *Cryptococcus neoformans*
- Peritoneal fluid culture 06/30/18 and 07/30/18: POS for *Cryptococcus neoformans*
- Blood cultures 07/03, 07/04, 07/06, 07/07, 07/09 07/10/18: POS for *Cryptococcus neoformans*

Lumbar puncture	Opening pressure (cm H ₂ O)	Closing pressure (cm H ₂ O)
7/10/18	31	13
7/18/18	44	8
7/20/18	29	14
7/22/18	34	UO*
7/24/18	25	14
7/26/18	26	16.5
7/28/18	30	11
7/30/18	26	13
08/1/18	32	14

Table 1. Lumbar punctures with opening and closing pressures.
*UO: Unable to obtain closing pressure

Discussion

- *Cryptococcus neoformans* is an encapsulated, ubiquitous, opportunistic yeast traditionally associated with HIV, solid organ transplant patients
- In the past 25 years, an epidemiology shift has been observed to HIV negative patients
- Liver cirrhosis, diabetes mellitus, autoimmune disease, and malignancy is now more commonly reported with cryptococcal disease (CD)
- Disseminated disease is defined as: POS culture from ≥ 2 sites or POS blood culture

Discussion

- Invasive CD is a rare but highly morbid infection in patients with liver disease. Peritonitis is common in these patients, especially with high MELD-Na scores
- Challenges in diagnosis are due to atypical presentation, mild-moderate fluid pleocytosis, and slow culture turnaround time
- Meningitis with *Cryptococcus* poses a high morbidity condition, especially if complications like elevated intracranial pressure arises. Multiple sites of seeding of *Cryptococcus neoformans* in an immunocompetent patient is rare
- Prompt initiation of adequate therapy and close monitoring of complications are key for improvement in patient's survival
- Treatment is prolonged and challenging

Conclusion

- Cryptococcal invasive disease in non-HIV patients has a high morbidity and mortality rate, especially in liver disease
- Presentation is atypical and diagnosis is challenging, high degree of suspicion is required in these patients

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