Cryptococcus Neoformans: A case of Cryptococcal Meningoencephalitis in an immunocompetent patient

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Objectives

- Identify risk factors for Cryptococcal Meningitis
- Understand the importance of immunocompromised state, and elevated risk of infection
- Signs and symptoms in a patient with aC. Neoformans infection
- Differential Diagnosis and testing in a patient with this presentation
- Diagnosis and appropriate management for a patient with cryptococcal meningitis
- Understand current treatment, and side effects associated

Introduction

- Cryptococcal Meningoencephalitis is an opportunistic fungal infection caused by ubiquitously present encapsulated yeast; cryptococcus neoformans (C. neoformans) or cryptococcus gattii(C. gattii).
- Transmission is through direct inhalation of the fungal spore into airways.
- It is an uncommon disease in immunocompetent hosts, however, about 12% of cryptococcal meningitis cases are reported in immunocompetent patients.
- Even though rarely present, the mortality is higher in immunocompetent patients.
- This is believed to be due to the strong immune response seen in immunocompetent patients leading to severe organ damage with higher affinity for the central nervous system.[1]
- We report a case of a young male who presented multiple times to the emergency room for evaluation of intermittent headaches.
- Lumbar puncture was performed after he developed worsening confusion, which led to the diagnosis of cryptococcal meningitis and subsequent treatment.

Diagnosis

- MRI Brain: multiple regions of restricted diffusion involving bilateral cerebellar hemispheres, medulla, anterior aspects of bilateral thalami
- Initial LP: opening pressure 40 mm H20, protein 83 mg.dL, glucose 5 mg.dL, wbc 393.
- Cryptococcal antigen titer 1:1280
- CSF culture with light growth C. Neoformans

Case Presentation

- A 48-year-old male with known history of migraines and non-alcohol cirrhosis, presented to the emergency room with progressive headache and slurred speech for the past month.
- He was alert to person, able to move all extremities with full strength, but unable to recall his address or date of birth at presentation.
- Initial CTA head/neck, MRI brain showed multiple regions of restricted diffusion involving bilateral cerebellar hemispheres, medulla, anterior aspects of the bilateral thalami, and evidence of increased intracranial pressure and vasogenic edema.
- Given his lethargy and cervical rigidity, lumbar puncture was performed, and the initial opening pressure was 40 mm H2O, protein 83 mg/dL, glucose 5 mg/dL, wbc 393, RBC 22.
- Cryptococcal antigen was 1:1280, and CSF cultures had light growth of cryptococcus neoformans, consistent with a cryptococcal meningitis diagnosis.
- He was started on liposomal amphotericin B and flucytosine, along with serial lumbar punctures to monitor for a decrease in CSF pressures.
- Despite appropriate treatment, his neurologic status declined. He developed spontaneous movement of the lower extremity without ability to follow commands and decreased responsiveness to stimuli.
- He became oliguric with worsening renal function and hyperkalemia further requiring CRRT and was intubated due to respiratory failure.
- The patient remained hypotensive in the setting of septic shock despite being on maximum dosing of four IV pressors.
- On his 7th day of liposomal amphotericin B, the patient was found to be in PEA arrest, and resuscitation efforts were unsuccessful.

Labs and Imaging

CSF Studies	
Appearance	Clear
WBC	393
Segmented PMN	31
Protein	83.8
Glucose	5
Crypotcoccal antigen Titer	1:1280

Lumbar Puncture	Opening Pressure
LP #1	40
LP #2	23
LP #3	17

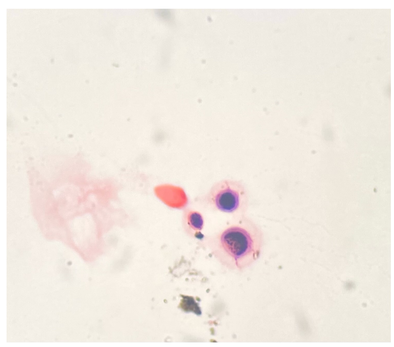

Figure 1: CSF studies completed during the first lumbar puncture. Three different lumbar punctures were completed. The first with an opening pressure of 40. Two other therapeutic lumbar punctures were completed to get opening pressure below 20. On the bottom right is the staining of the body fluid culture representing Cryptococcal Neoformans

Discussion

- Cryptococcal Neoformans is an encapsulated yeast that can be found in aged pigeon droppings which causes mild infections, from airway colonization to severe infections like meningitis or disseminated disease
- Approximately 1 million cases are reported annually, and incidence has increased over the past few decades due to corticosteroid use
- Patients usually present with neurologic symptoms that include lethargy, fever, stiff neck, nausea, and vomiting.
- Duration of symptoms from onset to presentation is typically 1-2 weeks in HIV cases and 6-12 weeks in non-HIV cases
- Workup and evaluation should include CT or MRI followed by lumbar puncture
- Blood and CSF should be cultured for fungi and tested for cryptococcal antigen
- Opening pressure must be measured at first spinal tap, and a pressure over 25 is a predictor of poor prognosis
- CSF usually presents with low glucose and high protein levels
- Visualization can be made with India Ink staining
- Treatment includes induction therapy with Amphotericin B(0.7 to 1.0 mg/kg/day) and flucytosine(100 mg/kg/day) for 4 weeks, and maintenance therapy with fluconazole 200mg/day for 6 to 12 months
- Complications can involve persistent infection with cultures after 4 weeks of treatment, elevated CSF pressure, Immune Reconstitution Inflammatory Syndrome, and Hydrocephalus

Conclusion

- Cryptococcal meningitis is a severe infection mostly present in immunocompromised patients that continues to be a challenge to manage, due to no new drug development.[2]
- Given its rapid progression, and affinity for the central nervous system, early diagnosis is imperative.
- Our case serves as a unique example of a patient with an accurate diagnosis, appropriate treatment, but inadequate response to therapy, implicating the importance of early diagnosis and management for patients with similar presentations without any immunocompromising factors.

References

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