False Negative Latex Antigen Testing in a Cirrhotic Patient with cryptococcosis: a case report

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BACKGROUND
• Cryptococcus neoformans is an ubiquitous fungal pathogen that predominantly affects immunocompromised patients
• Liver cirrhosis is a risk factor for disseminated cryptococcal disease in HIV-uninfected patients
• Literature on the presentation and optimal management of cryptococcal disease in HIV-uninfected, cirrhotic patients is limited

CASE REPORT
A 56 year old male with alcoholic cirrhosis presented with progressively worsening shortness of breath and subjective fevers. He also had been having mild headaches with no focal neurologic complaints.

His physical exam revealed decreased breath sounds in the right lower lobe. He did not have edema and no signs of decompensated cirrhosis. His neurologic exam was normal.

The initial evaluation revealed a pleural effusion in the right lower lobe (Fig 1) which was drained. Four days later, the transudative fluid from the Bactec bottles grew C. neoformans (Fig 2), which was confirmed by Vitek automated testing. Fluconazole was started.

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The patient experienced acute kidney injury after two weeks of treatment requiring renal replacement therapy and intubation for pulmonary edema. His CSF pleocytosis was as high as 66. LAT continued to be negative.

His CSF parameters normalized, and induction negative. After 3 weeks, CSF parameters normalized, and induction negative. After 3 weeks, CSF parameters normalized, and induction negative. After 3 weeks, CSF parameters normalized, and induction negative.

Lumbar puncture was performed, with an opening pressure of 23. CSF studies showed: WBC=136 (94% lymphocytes), RBC=80, Glucose=51, and Protein=33. CSF cryptococcal LAT was positive in >90% of patients with cryptococcosis

Table 1. Reported etiologies for false negative latex antigen testing and efforts to address them

<table>
<thead>
<tr>
<th>Reason</th>
<th>Evaluation</th>
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<tbody>
<tr>
<td>Limitations of Meridian LAT kit</td>
<td>Sensitivity of 87-100% for serum and CSF; positive control done</td>
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<tr>
<td>Interference of other proteins with agglutination</td>
<td>Treatment of both serum and CSF samples with pronase</td>
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<tr>
<td>High burden of antigen</td>
<td>Both serum and CSF samples run with prozone</td>
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<td>Variant organism (i.e., low level antigen producer, acapsular, or fastidious)</td>
<td>In vitro, capsule seen on Gram stain and antigen detected in pleural fluid</td>
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<td>Low antigen level (i.e., pre-treatment or early in disease course)</td>
<td>Serial testing was done as disease progressed</td>
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DISCUSSION
Cryptococcal disease in HIV-uninfected cirrhotic patients most often presents as peritonitis or meningitis

• 20% of cirrhotic patients with cryptococcal disease will have evidence of dissemination
• In patients with pulmonary infection, cirrhosis is a risk factor for dissemination

Cryptococcal LAT is positive in >90% of patients with cryptococcosis

• Negative LAT is more common in HIV-uninfected patients or localized disease
• False negative LAT can be seen if early in disease, high antigen burden, or variant organisms present (Table 1)
• Host response may decrease capsule and/or antigen formation that become wild-type in vivo

Prognosis of cryptococcal disease in cirrhotic patients has been reported to be as high as 82%-100%, partly due to delay in diagnosis and treatment. In one series:

• The median time to detection of cryptococcus in peritoneal fluid was 6 days
• 36% of patients who died did not receive any antifungal therapy

Management is similar for HIV-infected and HIV-uninfected patients and includes combination induction therapy with amphotericin and fluconosine. In those with meningitis, mortality is attributed to sequelae of increased intracranial pressure

REFERENCES


