Navigating Uncertainty in a Critically Ill Patient

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Navigating Uncertainty in a Critically Ill Patient
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Introduction
Aspergillus spores are routinely inhaled. Innate immune defenses prevent fungal growth and disease in immunocompetent individuals. However, immunocompromised patients are at risk of developing invasive aspergillosis. Diagnosis of invasive aspergillosis is often difficult as biopsy is not always feasible and relies on the interpretation of non-invasive testing. Early recognition and initiation of therapy is paramount as the mortality rate is high.

Case Presentation
Patient is a 59 year old female with a history of alcohol abuse admitted with acute encephalopathy and new onset seizure.

History:
- Initially presented 3 weeks earlier for jaundice, found to have acute alcoholic hepatitis, started and discharged on prednisolone
- Now presenting with new onset grand mal seizure and acute confusion
- Obtunded on admission and admitted to the ICU
- Required intubation for airway protection

Admission Workup:
- ALT 111
- AST 140
- Bilirubin 19.7

Chest XR: Diffuse ground glass opacities bilaterally
MRI Brain (Image 1): T2/FLAIR hyperintense lesions in frontal/parietal regions in a scattered distribution
TTE: EF 75% and no vegetations

Hospital Course
Day 1: Started on Vancomycin and Zosyn. TEE with no vegetations. Unable to liberate from mechanical ventilation.
Day 4: Repeat MRI brain with increased size and number of lesions. Chest CT (Image 2): Multifocal air disease bilaterally with ill-defined left lower lobe density. Respiratory cultures growing aspergillus. Started on IV voriconazole

Discussion
When to Test for Invasive Fungal Infections
Testing for invasive fungal infection should be initiated promptly in all patients who have risk factors and the differential includes fungal etiology.

Major Risk Factors for Invasive Aspergillosis
- Neutropenia
- Immunosuppression (transplant, AIDS, Immunosuppressive meds)
- Cirrhosis - COPD
- ESRD/HD - ICU

Radiographic Characteristics

How to Interpret Fungal Biomarkers and Cultures
Beta-D-Glucan: Cell wall component of fungi. Found on all fungi and not specific for aspergillus. (+) test may indicate fungal infection, but not specific
Galactomannan: Polysaccharide on aspergillus walls. More specific for aspergillus and can be diagnostic in the correct context. Sensitivity decreased with antifungal therapy and false (+) can occur with Zosyn. If serum results are (-), BAL can be performed, which provides additional sensitivity.
Fungal Cultures: Does not always mean active infection. We are constantly inhaling conidia. (+) cultures need to be weighed against the probability of aspergillosis as the cause of disease.

Biopsy is the gold standard, but often cannot be obtained in critical illness

Conclusions
- Invasive aspergillosis often presents with non-specific symptoms and knowing the risk factors and radiographic findings can help identify who to test
- Diagnosis is based upon both identifying the organism via biopsy or biomarkers as well as probability that aspergillus is the cause of disease
- Positive sputum fungal stain/culture or positive galactomannan should prompt therapy in the setting of high clinical suspicion and risk factors for aspergillosis

References

Images from commons.wikimedia.org

Fungal Biomarker Testing Characteristics

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Indicates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-D-Glucan (Serum)</td>
<td>77%</td>
<td>85%</td>
<td>Fungal Infection</td>
</tr>
<tr>
<td>Galactomannan (BAL)</td>
<td>88%</td>
<td>81%</td>
<td>Aspergillus</td>
</tr>
<tr>
<td>Galactomannan (Serum)</td>
<td>82%</td>
<td>81%</td>
<td>Infection</td>
</tr>
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