The morbidity and mortality caused by invasive fungal disease (IFD) are still unacceptably high in pediatric patients undergoing allogeneic hematopoietic stem cell transplantation

Diagnosing IFD in children is challenging: cultures are often negative, and the diagnostic efficacy of biomarkers may be of value in children with cancer and hematopoietic stem cell transplantation.

We conducted a retrospective chart review of all pediatric oncology patients at Comer Children’s Hospital (July 2009 to December 2016) to determine the utility of BG and GM for diagnosis of IFD.

Our evaluation shows there is no optimal cut-off for BG and GM assays for detecting IFD in symptomatic high-risk pediatric oncology patients to determine whether we should follow these recent guidelines.

Methods

We conducted a retrospective chart review of all pediatric oncology patients at Comer Children’s Hospital (July 2009 to December 2016) to determine the utility of BG and GM for diagnosis of IFD.

Inclusion criteria:
- Neutropenic fever (FN)
- High risk for IFD (fever > 5 days unresponsive to empiric antibiotics or recurrent fever with persistent neutropenia)

IFD and Invasive Aspergillosis (IA) were diagnosed according to the最新的EORTC/MSG criteria with eligible patients divided to 2 groups:
- Proven or likely IFD: patient has clinical and radiological symptoms highly consistent with IFD and received antifungal therapy with clinical improvement or histological evidence of tissue invasion by filamentous fungi in specimens or a positive culture for fungi from a normally sterile body fluid
- Unlikely or less likely IFD: patient didn’t meet criteria of proven or likely IFD

Data pertaining to possible causes of false positive BG and GM assays was collected such as presence of bacterial infection or receipt of immunoglobulin (IVIG), albumin or certain antibiotics (ie ampicillin/sulbactam or piperacillin/tazobactam)

Results

<table>
<thead>
<tr>
<th>BG assay (n = 76)</th>
<th>GM assay (n = 115)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median value (range)</td>
<td>150 (106-250)</td>
</tr>
<tr>
<td>Number of false positive results (n)</td>
<td>6</td>
</tr>
<tr>
<td>Possible cause of false positive result (n)</td>
<td>---</td>
</tr>
<tr>
<td>Received IVIG</td>
<td>4</td>
</tr>
<tr>
<td>Received albumin</td>
<td>2*</td>
</tr>
<tr>
<td>Received piperacillin/tazobactam or ampicillin/sulbactam</td>
<td>---</td>
</tr>
<tr>
<td>Presence of bacterial infection</td>
<td>2</td>
</tr>
<tr>
<td>Cross-reactivity with non-aspergillus molds</td>
<td>---</td>
</tr>
</tbody>
</table>

*1 patient who received albumin also received IVIG and 1 patient who received albumin also had E coli bacteremia

Conclusions

- Both BG and GM have low sensitivity and low positive-predictive value supporting low utility in IFD diagnosis pediatric oncology patients
- High specificity of the GM assay may be of value in diagnosing IFD; however, it is not helpful in identifying non-Aspergillus molds
- Our evaluation shows there is no optimal cut-off value for BG assay in IFD, but a false positive BG assay cut-off may be as high as 250 pg/mL in the setting of a low risk of clinical and radiological symptoms suggesting IFD
- Novel fungal biomarkers are needed for early IFD detection to improve outcomes

References

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