Breath-Based Diagnosis of Invasive Mucormycosis (IM)

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1776. Breath-Based Diagnosis of Invasive Mucormycosis (IM)
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Background. Timely diagnosis of IM remains a major challenge in clinical mycology. Because of the lack of specific diagnostic methods for IM and the frequently fulminant nature of this infection, IM-associated mortality remains high.

Methods. We examined breath volatile metabolite profiles in a neutropenic murine model of IM, using the 3 Mucorales species that most commonly cause human IM - Rhizopus arrhizus var. arrhizus, R. arrhizus var. delemar, and R. microsporus - and for comparison, Aspergillus fumigatus. We infected female balb/c mice (N = 4 per group) treated with cyclophosphamide and cortisone followed by intranasal administration of 10^6 conidia of each species. 3 days post-infection, we collected breath samples from each mouse via tracheostomy using a flexiVent murine ventilator, examining breath volatile metabolites using thermal desorption gas chromatography/tandem mass spectrometry (GC-MS/MS). We also sampled breath prospectively from five patients eventually diagnosed with proven IM caused by R. microsporus, analyzing breath volatile metabolites using thermal desorption GC-MS/MS.

Results. Each Mucorales species produced a consistent profile of breath sesquiterpene secondary metabolite VOCs in our murine models, which distinguished these species from each other and from murine invasive aspergillosis (Figure A). These fungi shifted their secondary metabolism significantly in vivo, compared with their previously characterized in vitro metabolism. We found overlapping VOC sesquiterpene metabolites between breath samples from the murine model of R. microsporus infection and 5 of 5 patients with R. microsporus IM, with additional sesquiterpene secondary metabolites detected in patient breath, compared with the murine IM model (Figure B). In one patient with serial breath samples, these sesquiterpenes declined in abundance and disappeared with antifungal therapy, in parallel with clinical improvement (Figure C).

Conclusion. The three Mucorales species that cause most human IM have distinct breath sesquiterpene profiles that can be used to identify these infections in vivo noninvasively. These profiles distinguish these infections from each other and from aspergillosis, and may be useful in monitoring clinical response to treatment.
Table: Propensity matched patients at IA Onset

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>CSU (n = 61)</th>
<th>Control (n = 61)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>59.0% (36/61)</td>
<td>54.1% (33/61)</td>
<td>.72</td>
</tr>
<tr>
<td>CSU &gt; 75 mg prior to IA</td>
<td>78.7% (48/61)</td>
<td>70.5% (43/61)</td>
<td>.41</td>
</tr>
<tr>
<td>Leukemia</td>
<td>52.5% (32/61)</td>
<td>49.2% (30/61)</td>
<td>.86</td>
</tr>
<tr>
<td>Allogeneic bone marrow transplant</td>
<td>26.2% (16/61)</td>
<td>29.5% (18/61)</td>
<td>.84</td>
</tr>
<tr>
<td>Graft vs host disease</td>
<td>3.3% (2/61)</td>
<td>11.6% (7/61)</td>
<td>.16</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>48.3% (28/58)</td>
<td>42.9% (24/56)</td>
<td>.58</td>
</tr>
<tr>
<td>Solid organ transplant</td>
<td>11.5% (7/61)</td>
<td>6.6% (4/61)</td>
<td>.53</td>
</tr>
<tr>
<td>Obstructive lung disease</td>
<td>21.3% (13/61)</td>
<td>24.6% (15/61)</td>
<td>.83</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>26.9% (16/61)</td>
<td>29.5% (18/61)</td>
<td>.84</td>
</tr>
<tr>
<td>Pulmonary IA</td>
<td>94.8% (55/58)</td>
<td>94.9% (56/59)</td>
<td>.99</td>
</tr>
<tr>
<td>Coinfection</td>
<td>23.0% (14/61)</td>
<td>21.3% (13/61)</td>
<td>.99</td>
</tr>
</tbody>
</table>

Data presented as median (interquartile range) or % (n with feature/n with data available).

Figure. Kaplan–Meier curves comparing 6-week survival

Disclosures. All authors: No reported disclosures.

1779. Catheter-free Period Over 2 Days Is Associated with Better Outcome in Catheter-related Bloodstream Infection due to Candida

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Background. Regardless of active antifungal drugs, mortality of candidemia remains high. Although it is well-known that central venous catheter (CVC) is one of the most important risk factors of candidemia and should be removed immediately, little is known about optimal timing of CVC replacement after removal. Here, we analyzed contributing risk factors associated with 30-day mortality for catheter-related bloodstream infection (CRBSI) due to candida and optimal timing of CVC replacement.

Methods. We conducted a retrospective cohort study at St. Luke#129;s International Hospital between 2004 and 2015. We compared each clinical component in patients who died within 30 days and were alive at 30 days. Also, catheter-free period (from removal to replacement) was compared between group A and B.

Results. Among 228 patients (pts) with candidemia, 166 patients (73%) were on CVC at diagnosis. Of them, 144 patients (65%) removed CVC after the result of candidemia. Seventy-one patients (31%) replaced CVC. Fifteen patients (6%) died within 30 days (group A) and 56 patients (25%) were alive at 30 days (group B). Median age was 74 in group A and 72 in group B (P = 0.331) (Table 1). In univariate analysis, hematological malignancy (OR 6.75, 95% CI 1.01–44.9) and CVC replacement < 2 days after removal (OR 5.63, 95% CI 1.16–27.3) showed statistically significant increase in group A vs group B (Table 2). In multivariate analysis, CVC replacement < 2 days was independent risk factor for 30-day mortality (Table 3).

Conclusion. This is the first study to demonstrate the optimal timing of CVC replacement in CRBSI due to candida. CVC replacement < 2 days was an independent risk factor for 30-day mortality.

Disclosures. F. M. Marty, Astellas Pharma US: Consultant and Grant Investigator, Consulting fee and Grant recipient; Chimerix: Consultant and Grant Investigator, Consulting fee and Grant recipient; Fate Therapeutics: Scientific Advisor, Consulting fee; Gilead Sciences: Consultant and Grant Investigator, Consulting fee and Grant recipient; LFR: Consultant, Consulting fee; Merck: Consultant, Grant Investigator and Scientific Advisor, Consulting fee and Grant recipient; Roche Molecular Systems: Consultant, Consulting fee; Shire: Consultant and Grant Investigator, Consulting fee and Grant recipient; D. P. Kontoyiannis, Pfizer: Research Contractor, Research support and Speaker honorarium; Astellas: Research Contractor, Research support and Speaker honorarium; Merck: Honorarium, Speaker honorarium; Cadara: Honorarium, Speaker honorarium; Amypx; Honorarium, Speaker honorarium; F2G: Honorarium, Speaker honorarium