Breath-Based Diagnosis of Invasive Mucormycosis (IM)

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Citation
Koshy, S., N. Ismail, C. L. Astudillo, C. M. Haeger, O. Aloum, M. T. Acharige, D. Farmakiotis, et al. 2017. "Breath-Based Diagnosis of Invasive Mucormycosis (IM)." Open Forum Infectious Diseases 4 (Suppl 1): S53-S54. doi:10.1093/ofid/ofx162.124. http://dx.doi.org/10.1093/ofid/ofx162.124.

Published Version
doi:10.1093/ofid/ofx162.124

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1776. Breath-Based Diagnosis of Invasive Mucormycosis (IM)
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Session: 216. The Fungus Among-us - Clinical Advances
Saturday, October 7, 2017: 8:30 AM

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. arhizus, 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 10⁶ 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.
Background. The safety of corticosteroid use (CSU) during active infection is controversial. In the invasive aspergillosis (IA) literature, CSU is typically defined using the time period prior to IA onset. Clinicians caring for patients with IA are unable to control CSU prior to IA onset. The more clinically relevant question is whether CSU after IA onset is harmful.

Methods. Patients hospitalized at our institution from 2004 to 2014 with IA were retrospectively identified. CSU, defined as the average daily prednisone equivalent dose during the 7-day period following IA onset, was calculated for each patient. A CSU cut-off of 7.5 mg was used to assign patients to treatment (>7.5 mg) or control (<7.5 mg, including no CSU) groups. A propensity score (PS) was generated to predict group assignment. Nearest neighbor matching was performed with a caliper width of 0.2. A Cox proportional hazards model was used to assess survival 6 weeks after IA onset.

Results. PS matching generated 61 matched pairs (122 patients). Baseline characteristics did not differ significantly between groups (Table). CSU was associated with increased mortality (PS adjusted hazard ratio [HR] 2.91, 95% CI 1.32–6.40). In univariate analysis, characteristics associated with increased mortality (P < 0.05) included no CSU in patients who died within 30 days and those alive at 30 days. Also, cather-free period (from removal to replacement) was compared between group A and B. Fisher's exact test and Mann–Whitney U test were used in univariate analysis and multivariate linear regression was used for controlling confoundings.

Conclusion. CSU after IA onset is associated with increased mortality. In IA patients with CSU, efforts to reduce corticosteroid dose may be beneficial.

Table. Propensity matched patients at IA Onset

| CSU (n = 61) | Control (n = 61) | P value |
|-------------|-----------------|---------|
| Age, years  | 57.6 (49.2–65.9) | 53.2 (42.5–63.2) | 0.27 |
| Male        | 59.0% (36/61)    | 54.1% (33/61)    | 0.72 |
| CSU >7.5 mg prior to IA | 78.7% (48/61)    | 70.3% (43/61)    | 0.41 |
| Leukemia    | 52.5% (32/61)    | 49.2% (30/61)    | 0.86 |
| Allergic bone marrow transplant | 26.2% (16/61)    | 29.5% (18/61)    | 0.84 |
| Graft vs host disease | 3.3% (2/61)     | 3.3% (2/61)      | 1.00 |
| Neutropenia | 48.3% (28/58)    | 42.9% (24/56)    | 0.58 |
| Solid organ transplant | 11.5% (7/61)    | 6.6% (4/61)      | 0.53 |
| Obstructive lung disease | 21.3% (13/61)  | 24.6% (15/61)   | 0.83 |
| Diabetes mellitus | 26.0% (16/61)  | 29.5% (18/61)   | 0.84 |
| Pulmonary IA | 94.8% (55/58)   | 94.9% (56/59)    | 0.99 |
| Coinfection | 23.0% (14/61)    | 21.3% (13/61)    | 0.99 |

Data presented as median (interquartile range) or % (n with feature)/n without data available.

Figure. Kaplan–Meier curves comparing 6-week survival

1779. Corticosteroid Use Following the Onset of Invasive Aspergillosis is Associated with Increased Mortality: A Propensity Score-Matched Study Takahiro Matsu, MD1, Nobuyoshi Mori, MD2, Eri Hoshino, MPA, MPH2, Aki Sakaura, MD1, Keiichi Furukawa, MD, FSHEA1, Infectious Diseases, St. Luke's International Hospital, Tokyo, Japan; 1Center for Clinical Epidemiology, St. Luke's International Hospital, Tokyo, Japan

Session: 216. The Fungus Among-us – Clinical Advances Saturday, October 7, 2017: 8:30 AM

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’s129; 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. Fisher129; s exact test and Mann–Whitney U test were used in univariate analysis and multivariate linear regression was used for controlling confoundings.

Results. Among 228 patients (9%) 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 independently associated with 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. All authors: No reported disclosures.