

00565 Breakthrough invasive fungal infection among patients with haematologic malignancies: a prospective multi-centre study

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Background: We aimed to describe the current epidemiology and outcomes of breakthrough invasive fungal infections (BtIFI) in hematological patients in Spain.

Materials/methods: BtIFI were prospectively diagnosed (13 months-12 hospitals) when occurring in patients with ≥ 3 days of antifungals within the last week and according to the revised EORTC definitions. Antifungal susceptibility was tested in the Spanish National Center for Microbiology.

Results: 64 episodes of BtIFI were documented. Most frequent prior antifungals were: Posaconazole (37.5%), echinocandins (35.9%) and Fluconazole (31.2%), administered for primary prophylaxis (79.7%), secondary prophylaxis (12.5%) and preemptive therapy (7.8%). Most common comorbidities were AML (47.7%) and 28 (43.8%) HSCT. Table 1 details the microbiological characteristics of the 20 (31.3%) proven cases. Probable Aspergillosis (44%) and possible BtIFI (25%) were also documented. Upon diagnosis, antifungal therapy was usually changed (57, 89.1%), most commonly to liposomal Amphotericin B (26, 40.6%). After the first 100 days, 34.4% and 20.3% of patients experienced complete and partial response. 100-day mortality was 53% and, in most cases (22, 65%), BtIFI was the attributable cause of mortality or played an essential role in the death.

Conclusions: BtIFI is associated with a change in the epidemiology entailing the appearance of rare fungi like Mucorales, *Geotrichum* or *Fusarium* and non-albicans *Candida* infections. Probable Aspergillosis is still the most frequent IFI. Most proven BtIFI were resistant to the prior antifungal administered. Overall and attributable mortality were high.

Table 1. Microbiological characteristics.

| | Proven (n=20) | Previous antifungal (S, R or NA) |
|-------------------------------|----------------------|---|
| <i>Aspergillus</i> | 2 | |
| • <i>A. niger</i> | 1 | Caspofungin (NA) |
| • <i>A. flavus</i> | 1 | Fluconazole (R) |
| <i>Candida</i> | 11 | Micafungin (R) |
| • <i>C. orthopsilosis</i> | 1 | Fluconazole (R) and Posaconazole (R) |
| • <i>C. glabrata</i> | 2 | Posaconazole (R) and Anidulafungin (R) |
| • <i>C. guilliermondi</i> | 2 | Voriconazole (R) and Fluconazole (R) |
| • <i>C. krusei</i> | 2 | Posaconazole (S) and Micafungin (NA) |
| • <i>C. parapsilosis</i> | 2 | Micafungin (R) |
| • <i>C. tropicalis</i> | 1 | Fluconazole (S) |
| • <i>C. albicans</i> | 1 | |
| <i>Geotrichum sp.</i> | 2 | Posaconazole (R) and Posaconazole (NA) |
| Mucorales | 4 | |
| • <i>Lichtheimia sp.</i> | 1 | Caspofungin (R) |
| • *** <i>Cunninghamella</i> | 1 | Fluconazole (R) |
| • sp.** | 1 | Fluconazole (R) |
| • <i>Rhizopus sp.</i> | 1 | Caspofungin (R) |
| • <i>Rhizomucor sp.</i> | 1 | |
| <i>Fusarium solani</i> | 1 | Fluconazole (R) |

