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Blood 142 (2023) 5871–5872

The 65th ASH Annual Meeting Abstracts

ONLINE PUBLICATION ONLY

613.ACUTE MYELOID LEUKEMIAS: CLINICAL AND EPIDEMIOLOGICAL

Rare Invasive Fungal Infections in Hematologic Patients: A Large Unicentric Series

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Introduction:
Invasive fungal infections (IFI) are a major cause of infectious mortality in immunocompromised hematologic patients. While *Candida* spp and *Aspergillus* spp account for most cases, IFI by so-called "rare" fungi (about 1% of all IFI) are clinically relevant, with challenging diagnoses (including difficult phenotypic identification and misinterpretation as contaminants) and insufficient data on antifungal susceptibility to guide treatment guidelines.
International efforts to record the epidemiology of these rare IFIs are fundamental to help overcome the lack of data that hinders successful diagnosis and treatment.

Methods:
We reviewed all fungal infections diagnosed in our Hematology Department in adults (18 years and over) from 06.01.2006 to 03.31.2023, selecting cases with identification of rare fungi by mycologic methods. The date of "Diagnosis" (Dx) was that of collection of the first positive sample.

Results:
A total of 67 patients (pts, 52.2% male) with a median age of 63.6 years (mean: 59.2, range: 23.2-90.0) were included; 68.7% had acute leukemias - 89.4% of which myeloid (AML), 13.0% lymphoblastic, 4.4% promyelocytic and 2.2% of ambiguous lineage - and 4.5% had myelodysplastic syndromes; 20.9% had a chronic lymphoproliferative disease, 3.0% had aplastic anemia and 3.0% had plasma cell dyscrasias.
There was an average of 4 cases of rare IFI per year (range: 0-9), with a peak in 2017 (13.4% of total); 50.8% of all infections diagnosed over the nearly 17 years of the study occurred in the 5 years between 2013-2017, a period of renovation work in our hospital.
Time to Dx ranged from 0 (collection on the day of hospitalization) to 98 days (mean: 25.4; median: 22 days). Identification of the fungus took a median of 5 days (mean: 5.6, range: 2-16 days) from the time of collection. In 8 patients (12.9%), the lab report with a fungal identification was released post-mortem; in these pts, results were available a median of 3.5 days after exitus (mean: 5.4, range: 1-13 days).
In 79.1% of pts, a yeast was isolated (68.7% *Geotrichum*-like), while in 20.9% a filamentous fungus was identified (3.0% Mucorales). The most frequent genera were *Geotrichum* (62.7%), *Saprochaete* (5.8%), *Fusarium* and *Alternaria* (4.5% each). *Cryptococcus*, *Trichosporon* and *Penicillium* accounted for 3% of infections each, with 9 additional species identified in single pts.
Fungemia was found in 58.2% of pts (in peripheral blood in 52.2%; in central access blood in 38.8%; in both in 32.8%). Pulmonary isolates were obtained in 26.9% of pts (in sputum in 19.4%; in bronchial aspirate or lavage in 10.4%; in both in 3.0%). Urinary isolates were found in 6.0% of pts; 13.4% had fungi in other biologic samples.
The median overall survival was 20 days; 32.6% of pts died within a week of Dx, 45.6% within the first fortnight and 60.9% within the first month; 26.1% died between 1 and 3 months from Dx; and 13.0% died over 3 months after Dx. At the time of the study, 5 pts (7.5% of the cohort) were still alive, all with yeast infections; survivors had evidence of fungemia in 20% of cases and pulmonary involvement in 60%.

Discussion:
In our large clinical series, AML was responsible for nearly 2/3 of cases of rare IFI, reflecting its overall increased risk for IFI. The rarity of these agents was highlighted by the fact that our tertiary hematology center, serving a population of 2.3 million, had an average of 4 cases of rare IFI per year; yearly variations were in part accounted for by construction work (which releases fungal spores).

Dx varied from the day of admission to over 3 months into hospitalization, reflecting a range from community-acquired to nosocomial infections; the average pt had been in hospital for 3 weeks by the time they were diagnosed.
There were 4-fold more yeast infections than filamentous fungi, with *Geotrichum* and related yeasts accounting for 2/3 of cases. Fungemia was present in over half of patients, and pulmonary infiltrates in 1/4, a proportion that was reversed in survivors.
Fungal identification took up to a fortnight, and over 10% of patients were dead before a Dx was established, not benefiting from directed treatment. The high lethality of these infections was underlined by the fact that 1/3 died within a week of Dx, with a median OS of 3 weeks. About 1/10 of pts died more than 3 months from Dx, with progressive hematologic disease being the most likely cause of death in that pt subset; less than 10% of the cohort is currently alive, and in remission.

Disclosures Geraldes: *Takeda:* Consultancy, Speakers Bureau; *BMS:* Consultancy, Speakers Bureau; *Janssen:* Consultancy, Speakers Bureau; *Amgen:* Consultancy, Speakers Bureau; *Sanofi:* Consultancy, Speakers Bureau; *Gilead:* Consultancy, Speakers Bureau; *Pfizer:* Consultancy, Speakers Bureau.

https://doi.org/10.1182/blood-2023-188856