O184

2-hour Oral Session

Invasive fungal infections: what is new?

Surveillance and antifungal susceptibility of mixed invasive aspergillosis over a 13-year period

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Objectives: Invasive Aspergillosis (IA) is usually considered a monofungal disease and a single *Aspergillus* species is commonly reported as the causative agent. IA purportedly caused by 2 or more filamentous fungi (mixed infections) is uncommon. Failure in antifungal therapy of IA may be due to intrinsic or secondary resistance and co-infection by 2 or more filamentous fungi (mixed infections).
We retrospectively evaluated the incidence, epidemiology and antifungal susceptibility of mixed IA in a general hospital over 13 years (2000-2012).

Methods: The clinical reports of patients with a positive culture were studied. Mixed IA was diagnosed based on EORTC criteria and when two or more different moulds were recovered simultaneously from the same sample. The prevalence of cryptic species was also tested. Antifungal susceptibility to amphotericin B, itraconazole, voriconazole, posaconazole, caspofungin, anidulafungin and micafungin was obtained using CLSI M38-A2. *Cyp51A* gene was sequenced in *A. fumigatus* isolates with high azoles MICs.

Results: We studied 1105 *Aspergillus* species isolates from 910 patients (749 colonized [82%] and 161 [18%] with proven/probable IA). Of these, 152 (16.7%) had 2 or more filamentous fungi. In the colonized patients, 647 (86%) had only 1 species of *Aspergillus* and 102 (14%) had >1 species. Among patients with IA, 112 (70%) were infected by a single species and 49 (30%) by >1 species. The percentage of mixed IA during the study period increased from 0% to 53.3%. The combinations causing IA were: *A. fumigatus* + *Aspergillus* spp. (59.2%), *A. fumigatus* + other filamentous fungi (16.4%), 3 *Aspergillus* spp. (12.2%), 2 *Aspergillus* spp + other filamentous fungi (8.2%) and 2 *Aspergillus* spp (4%). The 4 dominant mixed IA were: *A. fumigatus* + *A.flavus* (27.1%), *A. fumigatus* + *A. terreus* (14.5%), *A. fumigatus* + *Scedosporium* spp (10.4%), and *A. fumigatus* + *A. niger* (6.25%). During the study period, 10 patients (5.8%) presented IA caused by azole-resistant cryptic species (9 were also mixed). The percentage of IA caused by cryptic species increased from 0% to 20%, with *A. lentulus* being the most common. Most patients with IA caused by cryptic species had a poor prognosis. During the last 4 years of the study, 4 patients (3 IA) harboured azole-resistant *A. fumigatus* 'sensu stricto'.

Conclusions: Our results confirm that the incidence of mixed IA (29%) was much higher than reported in the literature. The percentage of mixed IA caused by cryptic species increased significantly during the study period. Mixed IA due to resistant *Aspergillus* isolates will have a profound impact on morbidity and mortality, with a consequent increase in healthcare costs.

Acknowledgements: This study was partially supported by GILEAD and FIS PI13/02783.