O229
1-hour Oral Session
From antifungal susceptibility to resistance

Molecular identification and antifungal susceptibility of cryptic Aspergillus section Fumigati isolated in a multicenter study in Spain (Madrid Aspergillus Resistance Study)

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Background: Invasive aspergillosis (IA) is an emerging disease whose incidence continues increasing. IA is mainly caused by *Aspergillus fumigatus*, however, some cases of IA are caused by cryptic species from *Aspergillus* section *Fumigati*. Their frequency in the clinical setting is between 10 and 15%, but studies about their antifungal susceptibility are scarce. The aim of this study was to analyze the antifungal susceptibility of 80 clinical and environmental strains of *Aspergillus* section *Fumigati* in a Madrid multicenter study (Madrid Aspergillus Resistance, MAR study).

Material/methods: From a total of 1,489 isolates (984 clinical, 505 environmental), 80 strains of cryptic *Aspergillus* section *Fumigati* were isolated in the multicenter study. Sixty four (6.5%) were clinical isolates and sixteen (3.2%) were environmental. Species identification was developed using molecular identification sequencing β-tubulin and rodlet A genes.

Antifungal susceptibility using broth microdilution method was tested for all the strains according to the guidelines of CLSI (Clinical and Laboratory Standards Institute). The antifungals analyzed were amphotericin B (AMB), itraconazole (ITZ), voriconazole (VCZ), posaconazole (POS), terbinafine (TB), anidulafungin (AN), caspofungin (CA), and micafungin (MC). *A. fumigatus* ATCC 2004305 and *A. flavus* ATCC 2004304 were used as control strains. With regard to antifungal susceptibility drugs, due to the lack of defined cutoff values for these antifungal agents against these species, the antifungal susceptibility of *A. fumigatus* was used as the reference epidemiological cutoff values. *A. fumigatus* ATCC 2004305 and *A. flavus* ATCC 2004304 were used as control strains.

Results: Six different species were identified: *A. lentulus* (n=40), *N. udagawae* (n=18), *A. novofumigatus* (n=9), *A. fumigatiaffinis* (n=5), *N. hiratsukae* (n=5), and *A. viridinutans* (n=3). Antifungal susceptibility testing showed heterogeneous patterns among these six species. Most *A. lentulus* and *A. fumigatiaffinis* isolates showed the highest MICs to AMB (2.07 and 2.30, geometric mean (GM), respectively). In addition, *A. lentulus* presented a resistant profile against azoles, showing ITZ and VCZ MICs >1 μg/ml, however, it was susceptible to echinocandins and TB. *A. viridinutans and A. novofumigatus* showed high resistance to all azoles tested with the following geometric means for ITZ, VZ and POS: 5.04/4.32, 4/3.43 and 0.63/0.86. Moreover, *A. novofumigatus* showed the highest MICs against TB (GM 0.68) as well as *A. fumigatiaffinis* (GM 0.66). Finally, *N. udagawae* showed high resistance to AMB (GM 1.78) and VCZ (GM 1.42). *N. hiratsukae* was susceptible to all antifungals tested.

Conclusions: In our knowledge, this is the largest cryptic *Aspergillus* Section *Fumigati* collection tested. Cryptic species showing decreased susceptibility to azoles are recovered from clinical samples and the hospital environment. Resistance to VZ is particularly worrisome, as it is the current pillar of IA treatment. The emergent role of *Aspergillus fumigatus* cryptic species warrants further resistance monitoring. This study was partially supported by FIS (PI13/02783).