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P0330 The presence of MSH2 polimorphisms in Candida glabrata is not a predictor of antifungal resistance acquisition

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Background: *C. glabrata* is prone to acquire echinocandin resistance and the presence of *MSH2* gene polymorphisms may have a role in the antifungal resistance. We here studied whether the *MSH2* gene sequence of a collection of candidaemia *C. glabrata* isolates was associated to acquisition of antifungal resistance.

Material/methods: A total of 81 isolates from patients with candidaemia (one patient each) caused by *C. glabrata* admitted at Gregorio Marañón Hospital (2007-2016) were studied. Antifungal susceptibility to fluconazole, micafungin and anidulafungin were determined using EUCAST EDef 7.2. *MSH2* gene was sequenced; isolates were genotyped using microsatellites and a cluster was defined as a group of ≥2 patients infected by an identical genotype. *In vitro* acquisition of resistance after exposure to anidulafungin and micafungin was studied in 20 isolates. Additionally, a clinical *FKS2*-mutant *C. glabrata* (S663P) from a patient with endocarditis was studied.

Results: All isolates were echinocandin susceptible (geometric mean MICs of micafungin and anidulafungin was 0.0153 and 0.023 mg/L, respectively) and four of them were fluconazole resistant. Genotyping revealed the presence of 9 clusters. *MSH2* mutations [V239L, P208S, A942T, S653F, A313V, E456D, E459K, E7K, L588V, N890I and L810H] were found in 44% (n=36/81) of the isolates and 20/36 of them were involved in five clusters. Isolates within the clusters tended to show the same *MSH2* polymorphism (Table).

Cluster code	Number of isolates	*MSH2* mutation (No. of isolates)
1	4	V239L/A942T (n=3); V239L (n=1)
3	2	E459K (n=2)
6	21	E7K (n=1); L588V (n=1); WT (n=19)
9	5	V239L (n=5)
16	7	P208S/N890I (n=6); N890I (n=1)

In vitro acquisition of resistance to echinocandins was observed in 12/20 isolates. We found *MSH2* mutations in 8 antifungal-resistant isolates [2/4 fluconazole-resistant isolates, 5 induced echinocandin-resistant isolates, and 1 echinocandin-resistant isolate from the patient with endocarditis]. The remaining 9 resistant isolates were *MSH2* wild type.

Conclusions: The presence of *MSH2* mutations in candidaemia *C. glabrata* isolates seems to be associated with specific genotypes rather than to the prediction of antifungal resistance acquisition.