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P2359 Clinical features and outcomes of fungaemia caused by Pdr1-mutant Candida glabrata

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Background: Gain-of-function mutations in the transcription factor gene *PDR1* of *Candida glabrata* not only mediate fluconazole resistance (FR), but also enhance virulence in animal models. However, the clinical features and outcomes of *C. glabrata* fungemia caused by Pdr1 mutant have rarely been assessed.

Materials/methods: In total, 208 bloodstream isolates of *C. glabrata* comprising 26 fluconazole-resistant (F-R; fluconazole minimum inhibitory concentration [MIC], ≥64 μg/mL) and 182 fluconazole-susceptible dose-dependent (F-SDD; MIC ≤32 μg/mL) isolates were assessed. The isolates were obtained from nine Korean university hospitals over six years (2009–2014). For each isolate, *PDR1* was sequenced to identify mutations. For all isolates, clinical features related to risk factors for candidemia and mortality rates were analyzed.

Results: Pdr1 mutations were identified in 24 F-R and 2 F-SDD isolates of *C. glabrata*, while no Pdr1 mutations were detected in 182 F-SDD isolates. A Pdr1 mutation was identified more frequently in patients with previous antifungal exposure (61.5% with a Pdr1 mutation vs. 11.0% without), immunosuppressive therapy (61.5% vs. 18.1%), neutropenia (38.5% vs. 5.5%), central venous catheter (CVC) use (92.3% vs. 55.5%), and a *Candida* score greater than three (23.1% vs. 6.6%) (all *P*-values <0.05). Treatment failure after azole therapy occurred in 60% (3 of 5) of patients with a Pdr1 mutation and in 44.2% (23 of 52) of patients without a Pdr1 mutation. Antifungal therapy and CVC removal after positive blood cultures were performed more frequently in cases with a Pdr1 mutation compared to those without (92.3% and 80.8% vs. 67.6% and 48.9%, respectively, all *P*-values <0.05). However, patients with a Pdr1 mutation showed higher 60-day (65.4% vs. 42.3%) and 120-day (73.1% vs. 46.2%) mortality rates compared to those without a mutation (all *P*-values <0.05). The cumulative survival was lower in patients with a Pdr1 mutation than in those without (median survival, 31 days vs. 74 days with a Pdr1 mutation vs. without, respectively, *P*=0.0562).

Conclusions: This study provides the first evidence that *C. glabrata* bloodstream isolates harboring a Pdr1 mutation in Korea are more frequently associated with antifungal exposure, immunosuppression, neutropenia, CVC use, and poor outcomes than those without a Pdr1 mutation.