Emergence of Candida tropicalis resistant to caspofungin

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Sir, Candida species is the fourth leading cause of nosocomial bloodstream infection in the USA. The incidence and mortality of invasive candidiasis (IC) remain high despite new antifungal agents. Although Candida albicans remains the most common isolated species causing IC, the incidence of IC caused by non-albicans species is increasing.1 Caspofungin, an echinocandin, is approved for treatment of IC.2 Resistance to caspofungin has been rarely reported. We admitted a 28-year-old female with acute myelogenous leukaemia (AML) for fever and otitis media. She was started on caspofungin [70 mg intravenous (iv) loading dose followed by 50 mg iv daily] on her fifth hospital day due to persistent fever despite iv broad-spectrum antibiotics. Defervescence was noted and she was started on induction chemotherapy for AML on the sixth hospital day. She again developed fever with symptoms of oesophagitis on her 21st hospital day. Oesophagogastroduodenoscopy with oesophageal biopsy was performed and showed invasive candidal oesophagitis. Caspofungin was switched to liposomal amphotericin B. Her repeat blood cultures grew Candida tropicalis susceptible to fluconazole. Amphotericin B was switched to fluconazole and the patient improved slowly. She completed 4 weeks of fluconazole treatment.

We subsequently performed additional in vitro MIC testing for echinocandins on the isolated C. tropicalis using the CLSI (formerly NCCLS) M27-A2 standard methods.3 This method has been proven to be reproducible and reliable in the study of MIC trends and patterns of antifungal medications.4 MICs of caspofungin, micafungin and anidulafungin were 4.0, 8.0 and 1.0 mg/L, respectively. This is the first documented case of C. tropicalis infection clinically resistant to caspofungin. This suggests that all Candida species are capable of developing resistance to echinocandins. The CLSI has established an echinocandin MIC of >2 mg/L to identify ‘non-susceptible’ Candida species.5 Our isolated strain’s caspofungin MIC is consistent with this breakpoint. We also observed cross-resistance of the isolated species to micafungin. This pattern of cross-resistance is similar to the observations made by Mougdal et al.6 for Candida parapsilosis. This may suggest a similar mechanism of resistance of Candida species to echinocandins, specifically caspofungin and micafungin.

Four mechanisms of reduced susceptibility to caspofungin have been suggested: (i) fks1 gene mutation; (ii) efflux-based mechanism; (iii) Sbe2p overexpression; and (iv) paradoxical or eagle effect.1,7 Only the fks1 gene mutation, however, is proven to cause clinical failure with caspofungin therapy.1 Further investigation of the fks1 gene of our isolated strain would help support Candida species’ similarity of mechanism for echinocandin resistance.

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References


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Detection of blaVIM-2 carbapenemase in Pseudomonas aeruginosa in Ireland

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