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Letters to Editor

Fatal Case of Candidemia due to *Candida glabrata*

Sir,

The incidence of *Candida* species in blood stream infections (BSI) has increased worldwide in the last three decades. Although *Candida albicans* has been the most common isolate from BSI worldwide, candidemia due to non-*albicans Candida* such as *Candida tropicalis*, *Candida parapsilosis, Candida glabrata* and *Candida krusei* has been steadily increasing in different parts of the world. *C. glabrata* has been found to be highly resistant to fluconazole while *C. krusei* is intrinsically resistant to the drug.

A 69-year-old male patient was admitted in our hospital (a University Teaching Hospital in Chennai) in May 2009; with complain of progressive, painless dysphagia for solid foods for the past 4 weeks. The patient had a history of diabetes mellitus for the past 3 years. An upper gastrointestinal (GI) endoscopy was performed, which revealed a growth in the lower third of the esophagus. A diagnosis of carcinoma esophagus (lower third) was made, which was confirmed by histopathologic examination of the biopsy material. Trans-hiatal esophagectomy with gastric pull through cervical anastomosis was performed. Post-operatively, the patient was administered cefepime (2 g intravenous [IV] BD) and metronidazole (500 mg IV BD) through peripheral IV line. The patient was symptomatically better. 7 days after the surgery, he developed a low grade continuous fever. The total leucocyte count (TLC) was 31,790/cu mm. Blood sample was collected from the patient after all aseptic precautions and sent for culture. Blood culture was done using the automated blood culture system (VersaTREK). Initial growth in the blood culture bottle revealed yeast cells on gram stain. A preliminary diagnosis of candidemia was made and the patient was started on fluconazole (400 mg/day IV). However, the patient expired within 24 h of starting fluconazole therapy. Fungal culture on Sabouraud dextrose agar followed by various phenotypic tests like sugar assimilation and fermentation and growth on tetrazolium reduction medium identified the organism as *C. glabrata*. The isolate was sensitive to amphotericin B but resistant to fluconazole by disk diffusion method which was performed following CLSI (Clinical and Laboratory Standards Institute) guidelines.[1]

C. glabrata has emerged as an important pathogen worldwide. An 8-year-old study from Michigan, USA found *C. glabrata* to be responsible for 17% of all episodes of fungemia.[2] Some studies from India have also reported an increasing incidence of *C. glabrata* in blood isolates.[3] Although *C. glabrata* is not intrinsically resistant to azoles, it acquires resistance rapidly. There are several mechanisms for the development of resistance to the azole group of drugs in *C. glabrata*. Increased expression of an adenosine triphosphate (ATP)-binding cassette transporter gene has been found to play an important role in the acquisition of resistance to azole antifungals in *C. glabrata*.[4] "Cross resistance" between fluconazole and the extended spectrum triazoles (voriconazole, itraconazole and posaconazole) has been described among isolates of *C. glabrata* and is associated with increased expression of the genes (CgCDR1 and CgCDR2) encoding the *Candida* drug resistance (CDR) efflux pumps.[5] Another reason for rapid development of resistance to fluconazole in *C. glabrata* is its haploid state in contrast to diploid *C. albicans*, where mutations in both the copies may be necessary for expression of resistance.[6]

In India, fluconazole is more widely used than other antifungals for treatment of candidemia because it is significantly less expensive and is available in both IV administered and oral formulations with high bioavailability. However, the emergence of fluconazole resistant pathogens like *C. glabrata* has made it necessary for physicians to rethink regarding the empirical use of fluconazole in candidemia cases.

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