CORRESPONDENCE

Increasing Non-Albicans Candida in Hematological Patients with Fluconazole Prophylaxis: A Case Series

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Dear Editor

Candida species are opportunistic yeasts capable of causing life threatening infections in immune-suppressed patients. Neutropenic patients are particularly susceptible to these opportunistic organisms. Antifungal prophylaxis is an essential part of management patients undergoing chemotherapy for haematological malignancies and bone marrow transplantation [1]. This has led to alteration in epidemiology of invasive mycoses with rise of non-albicans candida (NAC) infections [2]. Here we present four cases where neutropenic patients on azole prophylaxis developed non-albicans candidiasis.

Case Reports

Case 1 A 62 year old patient of multiple myeloma underwent a successful induction therapy with Bortezomib, dexamethasone and Thalidomide. After a complete remission, he developed nadir of neutropenia on day +3 and neutrophil engraftment was noted on day +9 (ANC > 500/cumm). Since the start of his conditioning regimen, he was on fluconazole prophylaxis; (200 mg i.v.twice daily). On day +13, he developed dysphagia and nausea. Examination showed extensive oral candidiasis. Since the patient was on fluconazole prophylaxis, this was stopped and amphotericin B was started. Oral swab was sent for fungal elements. Gram stain and KOH mount showed budding yeast

cells. Isolate was identified as *C.famata* on the basis of colour on TTC (Triphenyl tetrazolium chloride) medium and microscopic morphological features of the growth obtained through slide cultures on corn meal agar. Antifungal susceptibility testing (AFT) was done by disk diffusion method as per CLSI guideline against fluconazole, voriconazole, amphotericin B, ketoconazole [3]. It was susceptible only to ketoconazole. Amphotericin was stopped and patient was put on ketoconazole (200 mg BD) and his symptoms resolved completely over next one week.

Case 2 A 52 year old male was investigated for pancytopenia and splenomegaly. Bone marrow examination confirmed Hairy Cell Leukemia and patient was commenced on cladribine. Because of severe neutropenia fluconazole prophylaxis (200 mg B.D twice daily) was used. Recovery of neutropaenia was complicated by NAC septicemia, identified as *C. guilliermondii* (by Vitek 2C) and was sensitive to Amphotericin B, caspofungin and micafungin. Patient was managed by intravenous amphotericin B. A repeat Blood culture taken after 2 weeks was negative.

Case 3 A 14 years old male, was diagnosed to have severe aplastic anaemia and was admitted for allogeneic bone marrow transplantation. Conditioning regimen used was fludarabine with cyclophosphamide. Antifungal prophylaxis was initially fluconazole (200 mg twice a day PO) till the day 0 when it was changed to posaconazole (200 mg thrice a day PO). His blood culture was sent on day +1 due to a spike of temperature and this grew *C parapsilosis*. It was sensitive to fluconazole, voriconazole, amphotericin B, flucytocine, caspofungin, and micafungin (Vitek2C). Sensitivity to posaconazole was not determined. Patient was shifted on amphotericin B and consequent blood cultures were negative for *Candida* species.

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Case 4 A 40 year old male was diagnosed as a case of acute myeloid leukemia and received inj. daunorubicin, inj.cytarabine and inj etoposide as induction therapy. He was on prophylactic fluconazole (200 mg twice a day PO). During therapy patient had fever for which blood culture was sent. It grew NAC identified as *C parapsilosis*. This was sensitive to fluconazole, voriconazole, flucytocine, amphotericin B,caspofungin and micafungin(Vitek 2C).He was then treated with amphotericin B to which he responded.

Non-albicans nosocomial candidiasis is now becoming very significant clinically. Here we have reported four cases where patients undergoing treatment for haematological malignancies and haematopoietic stem cell transplantation, developed breakthrough of NAC infection while on azole prophylaxis as per IDSA guidelines. Of the four isolates obtained, *C. parapsilosis* was isolated in two cases.in a background of fluconazole prophylaxis.

The other two isolates in our series, *C. guilliermondii* and *C. famata* are rare (0.73% and 0.2–2% of isolates respectively) [4, 5]. They have been reported to be resistant to one or more antifungal agents as was also seen in our cases. It is interesting that the *C. famata* infection in one of the four cases described, occurred after recovery from neutropenia and the isolate was resistant to all antifungal agents tested except ketoconazole, which is rarely used these days for haematological patients as an empirical agent.

Routine testing and identification of *Candida* isolates to the species level followed by their antifungal susceptibility testing must be available in all centres where patients with haematological malignancies and bone marrow transplantation are being managed. This helps in knowing the

prevalence of various species and their sensitivity pattern. This will aid in initiating empirical antifungal treatment while awaiting sensitivity results. In cases where breakthrough NAC infection is documented in a background of prophylactic antifungal drug, switching over to the broad spectrum antifungal agent (based on sensitivity profile of NAC isolates of the centre) should be an immediate measure and followed by use of appropriate antifungal agent based on sensitivity profile of the particular isolate. Given that delays in appropriate antifungal therapy are associated with increased mortality, early empirical and preemptive therapy should also help reduce invasive candidiasis -associated mortality.

Compliance with Ethical Standards

Conflict of interest None.

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