Breakthrough Fungemia due to *Hansenula anomala* in a Leukemic Patient Successfully Treated with Amphotericin B

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Sir,

During the last years many yeasts and yeast-like organisms previously considered as saprophytes have been reported to cause systemic infections, especially after bone marrow transplantation or with acute leukemia. There are 23 cases of Hansenula spp infections described up to date; 19 were fungemias, in 17 cases associated with catheter infection, but only 2 described within the last 7 years [1-4]. We describe breakthrough Hansenula anomala fungemia despite prevention with fluconazole in a leukemic female during reinduction chemotherapy and neutropenia.

A 46-year-old female with acute myelogenous leukemia (AML) was admitted with a relapse of AML received chemotherapy with VP-16 120 mg/m2 days 1-5 and mitoxantrone 12 mg/m2 days 1-3. On the 1st day of antineoplastic chemotherapy a central venous (jugular) catheter was inserted. On day 3 of chemotherapy, the patient had a fever of 38.5 °C and received empirically ciprofloxacin, piperacillin (for therapy) and fluconazole 400 mg/day intravenously (as a prophylaxis). On day 6 of the therapy the patient was afebrile, but on day 10 a fever of 39 °C again appeared and the therapy was modified to ceftazidime, netilmicine and fluconazole intravenously. No pathogen was isolated until day 10. On the same day three blood cultures were drawn and 2 days later they showed positivity for *H. anomala* in all three cultures obtained through a peripheral vein susceptible to fluconazole, amphotericin B and miconazole. The catheter could not be removed because of severe thrombocytopenia and bleeding on from the oral cavity (5 thrombocytes/ml). The patient was also neutropenic on day 5, and on the day of fungemia (day 12 of antibiotic therapy) she had 50 neutrophils/ml and was neutropenic on the next 10 days (less than 500 neutrophils/ml). Intravenous amphotericin B in a daily dose of 1 mg/kg was given but 2 and 5 days later blood cultures were again positive for *H. anomala*. This organism was identified with the Vitek Junior system and confirmed microscopically. After 5 cultures were positive for yeasts after the administration of three thrombocyte concentrates the catheter was extracted and replaced with a new jugular catheter despite deep thrombopenia (5/mm3) and the risk of bleeding. Surprisingly, the catheter tip was negative for both fungi and bacteria. On day 9 of fungemia, despite persisting neutropenia the patient was afebrile. There was no evidence of a complication of the fungemia (CT scan of CNS, ultrasound of liver, ophthalmoscopy negative, echocardiography negative). On day 10 of fungemia, antibiotics were
stopped, and amphotericin B continued until day 25 of fungemia (total dose 1,725 g). On the same day the patient was discharged from hospital. 2 and 4 months later she had no evidence of fungal infections.

We have never observed this organism either as a pathogen or colonizer in our cancer centre. Over the preceding 6 years all isolates from sputum, swabs and blood cultures were reviewed. We had 44 Candida spp, 1 Malassezia spp, 1 Rhodotorula spp, 3 Torulopsis spp, 3 Blastoschizomyces spp, 1 Trichosporon spp and 2 Fusarium spp fungemias, but we never observed Hansenula in our patients.

The source of fungemia in the patient is unknown. The catheter is a possible origin despite negative catheter tip cultivation (the catheter was left for 7 consecutive days after the first fungemic episode and amphotericin B may have sterilized it, because severe trombocytopenia did not enable us to extract the catheter immediately. Risk factors of our patient were neutropenia, previous therapy with a combination of broad spectrum antibiotics, catheter insertion, cytotoxic chemotherapy and neoplastic disease. The fungemia appeared despite 8 previous days of intravenous fluconazole (in a dose of 400 mg daily), which is surprising because Hansenula spp is generally well-susceptible to azoles [3] and cases of Hansenula spp fungemia successfully treated with fluconazole have been reported in the literature [4]. Surprisingly, the outcome despite profound and long-lasting neutropenia was favorable; however, the mortality in leukemic patients with a single positive blood culture is 40-60% and with three and more blood cultures 70-80% [1-2].

References

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Kunova/Spanik/Kollar/Trupl/Krcmery