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LETTER TO THE EDITOR

Reply to the letter to the editor "chronic disseminated candidiasis" by Kenneth Rolston

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Dear Editor,

We would like to thank Kenneth Rolston for his comments regarding our recent *Supportive Care in Cancer* article on chronic disseminated candidiasis (CDC) in patients with hematological malignancies on the behalf of SEIFEM (Sorveglianza Epidemiologica Infezioni Fungine in Ematologia) group [1].

We acknowledge the small sample size (N = 20) and the retrospective nature of the study, which is probably not enough capable to lead to significant modifications of the CDC treatment recommendations. However, we would like to underline some aspects.

First, the guidelines of the Infectious Diseases Society of America (IDSA) strongly recommend the first line therapy of CDC with lipid formulation amphotericin B (AmB) 3–5 mg/kg daily [2]. Our data suggest that high-dose (HD) liposomal AmB (5 mg/kg daily) is the better choice for the treatment of CDC. This is likely due to the fungicide action of HD liposomal AmB in the liver and spleen derived from better tissue concentrations (target of liposomal formulation: reticuloendothelial system) than that of triazoles and echinocandins [3]. In addition, the 5 mg/kg daily dosage for liposomal AmB may be useful for less susceptible species, such as *Candida glabrata* and *Candida krusei* [2]. On the other hand, in our series, the majority of patients were receiving triazoles prophylaxis and thus had an increased risk of developing infection with a fluconazole-resistant organism [2]. Moreover, according to the IDSA guidelines, fluconazole (6 mg/kg daily) should be administered only for maintenance therapy [2].

Second, 13/20 (65%) patients received diagnosis of probable CDC according to standard criteria, i.e., an alkaline phosphatase increase, hepatic and/or splenic nodules with typical bull's eye aspect (seen at imaging tools), and blood cultures positive for *Candida* spp. (no polymicrobic sepsis occurred in our series) [4]. Such patients had negative serum galactomannan monitoring and negative thorax radiological assessments; three cases had a serum β-D-glucan assay >80 pg/ml (270, 520, and 370 pg/ml, respectively). Altogether, it is very unlikely that these findings may represent infections due to other organisms, particularly molds. According to the policy of the SEIFEM group, when clinically indicated, we performed liver biopsy using a Menghini-type automatic fine-cutting needle (1.2 mm, 18G) under color ultrasound guidance, as already reported [5, 6]. In fact, the remaining seven patients underwent a mini-invasive procedure that was well tolerated with no discomfort and provided reliable information regarding liver histology, leading to the definitive diagnosis of CDC.

Third, both cases no. 11 and no. 20 died early as a result of CDC (before the definitive microbiological results from blood samples); they were receiving empirical antifungal treatment, respectively, with fluconazole and itraconazole.

Finally, no liposomal AmB-related toxicity of grade ≥3, according to the Common Terminology Criteria for Adverse Events (CTCAE), occurred in our series [7].

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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