Why Should We Monitor (1-3)- β -D-Glucan Levels during Invasive Candidiasis? Just Ask Your Ophthalmologist!

Gennaro De Pascale,^a Brunella Posteraro,^b Salvatore Lucio Cutuli,^a Anselmo Caricato,^a Domenico Lepore,^c Mario Tumbarello,^d Mariano Alberto Pennisi,^a Maurizio Sanguinetti,^e Massimo Antonelli^a

Department of Intensive Care and Anesthesiology, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy^a; Institute of Hygiene, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy^b; Department of Ophthalmology, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy^c; Institute of Infectious Diseases, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy^d; Institute of Microbiology, Catholic University of the Sacred Heart, Agostino Gemelli Hospital, Rome, Italy^e

We read with great interest the article by Sims et al. published in a recent issue of the *Journal of Clinical Microbiology* (1), in which the authors established the usefulness of (1-3)- β -D-glucan (BG) serum measurement as a prognostic marker of treatment outcome, by correlating initial and final BG levels with the therapeutic responses in patients with proven invasive candidiasis (IC). Remarkably, a positive (decrease) or negative (increase) slope in BG levels correlated, respectively, with the success or the failure of antifungal treatment. Unfortunately, few patients with hard-to-treat fungal infections (i.e., endophthalmitis, endocarditis, meningitis, osteomyelitis) were studied (1).

We agree with the authors in that baseline and consecutive serum BG determinations may be helpful in monitoring the response to treatment during IC, particularly for critically ill septic patients in whom the rapid clearance of fungal pathogen from the bloodstream is regarded as a major determinant of clinical outcome. In this context, we previously demonstrated that a single positive BG value in medical patients admitted to the intensive care unit (ICU) with sepsis and expected to stay for more than 5 days preceded a culture-documented detection of candidemia by 1 to 3 days (2), thereby resulting in a cost-effective timely diagnosis and prompt treatment strategy (3). Apart from the contribution of BG to early and accurate IC diagnosis (4, 5), we are yet conscious that continued BG monitoring in patients with candidemia could enable physicians to carefully follow the clinical course of this infection and its deep-seated complications.

Herein, we report three cases of candidemic patients admitted to our ICU (Table 1) who developed metastatic ocular candidiasis (OC) 11 to 35 days from the initial IC diagnosis (BG levels were >500 pg/ml), at which time the patients were started on anidulafungin and BG level measurements were per-

formed three times weekly. Central venous catheters were promptly removed. Echocardiographic and funduscopic examinations, performed within few days of the IC diagnosis, were negative. After 7 days of treatment, BG levels did not decrease despite fungal clearance from blood cultures and improvement of severe sepsis/septic shock symptoms. Finally, new search for metastatic foci and fungal infection sources, including endocarditis, septic venous thrombosis, or contaminated device revealed only the presence of OC, i.e., chorioretinitis in two patients and endophthalmitis in the remaining one (Table 1). Anidulafungin was stopped and liposomal amphotericin was initiated in all the three patients.

Ocular involvement is a relatively frequent complication of *Candida* bloodstream infection (6). However, the optimal evaluation timing is not well known and, particularly in critically ill sedated patients, the complete absence of symptoms might be a pitfall for physicians. In our experience, a sustained high BG level could be used as a surrogate marker of residual fungal burden and then facilitate the finding of metastatic hidden foci.

ACKNOWLEDGMENTS

This study did not receive any funding. We declare no conflict of interest relevant to this article.

We were involved in patient care, data analysis, and writing the article.

REFERENCES

1. Sims CR, Jaijakul S, Mohr J, Rodriguez J, Finkelman M, Ostrosky-Zeichner L. 2012. Correlation of clinical outcomes with β -glucan levels in patients with invasive candidiasis. *J. Clin. Microbiol.* 50:2104–2106.
2. Posteraro B, De Pascale G, Tumbarello M, Torelli R, Pennisi MA, Bello G, Maviglia R, Fadda G, Sanguinetti M, Antonelli M. 2011. Early diagnosis of candidemia in intensive care unit patients with sepsis: a prospective comparison of (1 $\rightarrow$ 3)- β -D-glucan assay, *Candida* score, and colonization index. *Crit. Care* 15:R249.
3. Eggimann P, Marchetti O. 2011. Is (1 $\rightarrow$ 3)- β -D-glucan the missing link from bedside assessment to pre-emptive therapy of invasive candidiasis? *Crit. Care* 15:1017.
4. Eggimann P, Bille J, Marchetti O. 2011. Diagnosis of invasive candidiasis in the ICU. *Ann. Intensive Care* 1:37. doi:10.1186/2110-5820-1-37.

TABLE 1 Clinical and microbiological characteristics of 3 patients with OC following candidemia^a

Patient	Sex	Age (yr)	Comorbidity(ies)	Source of infection	Time (days) to OC diagnosis	Outcome
1	M	45	Malnutrition	Esophagitis	35	Dead
2	F	71	COPD, CAD	Intra-abdominal infection	11	Alive
3	F	78	None	CVC	15	Alive

^a Abbreviations: OC, ocular candidiasis; M, male; F, female; BG, (1-3)- β -D-glucan; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; CVC, central venous catheter. The isolate in each case was *C. albicans*. The BG value at candidemia diagnosis for each patient was >500 pg/ml.

Address correspondence to Gennaro De Pascale, gennaro.depascale@email.it.

For the author reply, see doi:10.1128/JCM.03258-12.

Copyright © 2013, American Society for Microbiology. All Rights Reserved.

doi:10.1128/JCM.03090-12

5. Cornely OA, Bassetti M, Calandra T, Garbino J, Kullberg BJ, Lortholary O, Meersseman W, Akova M, Arendrup MC, Arikan-Akdogan S, Bille J, Castagnola E, Cuenca-Estrella M, Donnelly JP, Groll AH, Herbrecht R, Hope WW, Jensen HE, Lass-Flörl C, Petrakos G, Richardson MD, Roilides E, Verweij PE, Viscoli C, Ullmann AJ. 2012. ESCMID guideline for the diagnosis and management of *Candida* diseases: non-neutropenic adult patients. Clin. Microbiol. Infect. 18(Suppl 7):19–37.
6. Nagao M, Saito T, Doi S, Hotta G, Yamamoto M, Matsumura Y, Matsushima A, Ito Y, Takakura S, Ichiyama S. 2012. Clinical characteristics and risk factors of ocular candidiasis. Diagn. Microbiol. Infect. Dis. 73:149–152.