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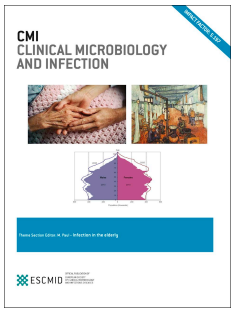

Diagnosing fungal infections in hematology patients - Another case of less is more in the clinical setting?

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Diagnosing fungal infections in hematology patients - Another case of less is more in the clinical setting? REVISION 1

Invasive fungal diseases (IFD) are a major cause of morbidity and mortality in immunocompromised patients, with invasive pulmonary aspergillosis accounting for 30–50% among patients with hematologic malignancies [1]. Early diagnosis is crucial in identifying and treating patients with IFD, and hence reducing costs and avoiding unnecessary toxic treatment in patients not suffering from mycoses [1]. Currently, the golden standard for diagnosis of IFD are direct microscopic examination and culture [2], however, both methods suffer from low sensitivity. The European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group (EORTC/MSG) developed a classification of the likelihood of an IFD [3], where diagnosis rests on a combination of clinical and host factors, and microbiologic criteria. This approach is relatively straightforward as including various fungal antigen tests improves diagnosis and lowers the turnaround time. The galactomannan ELISA test (GM) is recommended as a diagnostic marker for serum and bronchoalveolar lavages (BAL) [3]. GM is a polysaccharide of the cell-wall of *Aspergillus* species, which is shedded into serum and other body fluids during invasive aspergillosis (IA). GM concentrations, defined as optical density (OD) values, may be detected in body fluids by a double-sandwich EIA. However, reported sensitivity and specificity of serum GM ranged between 0% and 100% and 38% and 98%, respectively [4]. BAL GM appears to have improved diagnostic performance by corresponding sensitivity and specificity within a range of 57% and 100% and 89% and 99%, respectively [5]. In the clinical real life setting, the GM test is either implemented as a screening or targeted diagnostic tool. However, there exist several open questions related to the release of fungal GM and the infection sites and test performance in the clinical setting [6]. This variable performance seems to be multifactorial in origin and covers GM shedding depending on the stage of fungal growth (e.g. swollen conidia and hyphae), release of GM from the infection into the human blood system, binding of GM in the human body, host factors being present (e.g. location and degree of fungal diseases, antifungal and antibacterial treatment), methodological factors, and determination of a positive assay result (single or sequential positivity).

In the light of the high mortality associated with IFD, particularly among critically ill patients, a number of guidelines have focused on empirical and prophylactic antifungal treatment. Accordingly, the use of antifungals has increased from 4.6% to 48.5% in some settings [1]. Yet, little was previously known on whether antifungal treatment influences the accuracy of diagnostic tests. One great challenge in the field is the shortcoming in current techniques of diagnosing IFDs.

In this issue of CMI, Vena and colleagues [7] report findings of a single centre study to determine if GM testing in high-risk hematology patients receiving prophylaxis with micafungin influences the accuracy of GM testing. In this trial, the authors came to the conclusion, that serum GM surveillance of asymptomatic patients receiving prophylaxis with micafungin is unnecessary, because of either negative or false-positive results. Serum GM screening was done twice a week and positivity was interpreted as an OD index of ≥ 0.7 or ≥ 0.5 being present in one or two consecutive samples, respectively. Asymptomatic and afebrile patients underwent screening, whereby the presence of neutropenia with fever under broad-spectrum antibiotics, clinical or radiological features suggestive of IFD and positive cultures from respiratory specimens defined the diagnostic GM approach. 149 patients with 208 high-risk episodes were evaluated and IFD was defined according to