A combined screening strategy for invasive fungal infections in high risk hematology patients: Early computed thoracic tomograpy and serum 1,3-β-D- glucan

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INTRODUCTION

The aim of this study is to investigate the performance of early computed tomography (CT) combined with serum 1,3-beta-D-glucan (BDG) detection as a screenning strategy in high risk hematology patients.

PATIENTS AND METHODS

Patients who had undergone chemotherapy for acute myelogenous leukaemia (AML), acute lymphocytic leukaemia (ALL), or allogenic stem cell transplantation (ASCT) with an expected neutropenia period longer than 7 days were included in the study.

Galactomannan (GM) (Platelia Aspergillus ELISA; Bio-Rad Laboratories) were performed twice weekly based on the manufacturers' instructions from the day of an absolute neutrophil count of < 500/mm^3 until recovery of neutropenia or diagnosis of invasive fungal infection. as a part of routine care. Concurrent serum samples were collected for 1,3-beta-D- glucan (BDG) (Fungitell; Associates of Cape Cod, East Falmouth, MA, USA) and stored at -80˚ C until tested.

Thoracic CT (multislice CT 16-section MDCT scanners) was performed in case of:

- GM antgenemia > 0.5
- Persistent fever for 72-96 hours unresponding to broad spectrum antibacterail therapy

In patients with radiologic evidence of pulmonary invasive aspergillosis, but negative GM, the serum samples were re-tested by a modified methodology which was previously proven to have an increased sensitivity [Mennink-Kersten et al. J Clin Microbiol 2008].

Invasive fungal diseases (IFDs) were catogorized based on definitions of the European Organization for Research and Treatment of Cancer and Mycoses Study Group (regardless of BDG results [De Pauw, et al. Clin Infect Dis 2008].

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RESULTS

A total of 75 neutropenic episodes (NE) in 64 patients were prospectively followed between February 2012 and January 2013. Median age of the patients were 41 years (range, 18-69 years), and 34 of them were female. The underlying hematological disease was AML in 38 patients, ALL in 24 patients, biphenotypic leukemia in 1 patient, and aplastic anemia in 1 patient. 7 out of 24 patients with ALL, 5 out of 38 patients with AML, and 1 patient with aplastic anemia underwent ASCT. Neutropenia was complicated with fever in 71 out of 75 episodes.

IFDs were detected in 15 patients (Probable Invasive Aspergillosis in 11, possible IFI in 1, sinusitis in 1, and fungemia in 2 patients.).

❖**The sensitivity of BDG was 53.5% (95%CI 34.2-71.9), specificity was 76% (95%CI 70.8-80.9), positive predictive value (PPV) was 26.3%, and negative predictive value was (NPV) 73.6%.**

❖**BDG was above commercially recommended cutoff in 7 (53.3%) out of 13 patients with IA while GM index obtained by standard methodology was above 0.7 in 4 (30.7%) out of 13.**

❖ **BDG was above 80 pg/mL at an average of one week before the blood cultures were available in patients with fungemia (Blastoschizomyces capitatus fungemia in 1 and Non-albicans candidemia in 1)**

❖ **While GM index obtained by standard methodology was positive in 3 (33.3%) out of 9 patients receiving mold active prophylaxis or empirical antifungal therapy, BDG was >80 pg/ml in 6 (66.6%) out of 9.**

❖ **CT was triggered by persistent fever in all patients. Detection of biomarker positivity and radiologic findings of IA was synchronous in all but one patient.**

❖ **By use of modified GM detection methodolgy, the category of IFDs was improved from possible IFD to probable IA in eighy patients , and by use of BDG the category of IFD was improved from possible IFDto probable IFD in six patients**

CONCLUSIONS

➢**Early thoracic CT combined with serum BDG detection can recognize patients with invasive aspergillosis and fungemia properly**

➢ **While BDG was found to be significantly usefull in the early diagnosis of fungemia, this advantage was not significant in patients with IA**