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False Positivity for *Aspergillus* Antigenemia with Amoxicillin-Clavulonic Acid

Invasive aspergillosis is one of the serious problems in patients with hematological malignancies. Early diagnosis is very important because of the high mortality. Noninvasive tests, including screening of *Aspergillus* galactomannan (GM) antigen, (1→3)-β-D-glucan, and *Aspergillus* DNA, have been studied for early diagnosis to improve the treatment. Although the optimal method has not been clear, among those tests, the double-sandwich enzyme-linked immunosorbent assay for GM (Platelia *Aspergillus*) was found to be highly sensitive and specific (1, 2). In spite of this finding, false positivity is an important issue. There are several reports of false-positive reactions in patients receiving piperacillin-tazobactam (6, 7), and recent false-positive results were reported for patients receiving amoxicillin-clavulonic acid (AMC) (3, 4).

We want to report a similar case from a cohort of 58 patients with a high risk of febrile neutropenia and underlying hematological malignancies. The patient was a 20-year-old female receiving induction chemotherapy with idarubicin and cytarabine for acute myeloblastic leukemia. She had no evidence of fungal infection clinically or on two consecutive computed tomographies of the thorax during her stay in the wards. However, the serum GM optical density index rose from 0.1 to 4.0 and 4 days later to 9.0. At that period, she was having a diarrhea attack and receiving sulbactam-ampicillin (SAM) for gingival abscess, and so the GM positivity was thought to be related to diarrhea. Five days after SAM was stopped, the GM level dropped to 4.2 and then to 0.5. Due to the recurrence of the abscess, at this time the patient was put on AMC, and on the ninth day the GM level began to rise again, being 3.8 at the highest point and remaining high for 7 days after AMC was stopped. This time, there was no other confounding factor, such as diarrhea.

Amoxicillin and piperacillin are semisynthetic derivates of ampicillin that are obtained from the genus *Penicillium*. False positivity of the GM antigen has been published for *Penicillium chrysogenum* and *Penicillium digitatum* (5). The cell wall structure of *Penicillium* could be a possible cause of false-positive Platelia *Aspergillus* test results in patients receiving *Penicillium*-derived antibiotics.

In conclusion, we suggest that positive Platelia *Aspergillus* test results belonging to patients who don't have evidence of fungal infection clinically should be evaluated carefully, especially for the antibiotics used during the serological screening period. It should be kept in mind that even after discontinuation of the antibiotics, positivity for GM can be seen, depending on the half-life of the drug.

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Authors' Reply

We thank Dr. Metan and colleagues for their interest in our paper.

We do not suggest a role of diarrhea as a possible cause of false-positive Platelia *Aspergillus* test results in immunocompromised hosts, as we did not observe any case of transient GM antigenemia related to chemotherapy-induced mucositis or diarrhea in a cohort of a 109 high-risk neutropenic patients with hematological malignancies.

The possibility of false-positive Platelia *Aspergillus* test results should be considered when interpreting an increase of GM antigenemia in immunocompromised hosts at risk of invasive aspergillosis (IA) who are receiving semisynthetic penicillins.

A major problem is how to manage patients with a diagnosis of probable IA made during piperacillin-tazobactam (TZP) and AMC treatment (1).

We did not discontinue itraconazole prophylaxis in our patient following the onset of serum GM reactivity, and we agree with Maertens et al. that patients with a diagnosis of probable IA supported only by positive results of GM antigenemia with-

out any other microbiological or radiological criteria should not be enrolled in clinical trials with antifungal drugs if they are receiving TZP and AMC treatment (2).

In conclusion, as a golden rule, a critical interpretation of laboratory data, a thorough clinical evaluation, and a careful review of concomitant treatments are mandatory to avoid unnecessary antifungal treatment in patients at risk of IA.

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