Platelia Aspergillus Assay and Potential Cross-Reaction

Str—I read with interest 2 articles in the 15 March 2004 issue of Clinical Infectious Diseases. Both Adam et al. [1] and Viscoli et al. [2] reported their findings of “false-positive” results obtained with the Platelia Aspergillus ELISA test (Bio-Rad) among patients receiving piperacillin-tazobactam. Investigation revealed that these patients did not have any invasive fungal diseases.

The Platelia Aspergillus assay detects galactomannan (GM), a complex sugar, which is found in the Aspergillus cell wall. A positive reaction to the assay could be a sign of a possible Aspergillus infection. However, GM is a polysaccharide that is also found in many food products and is also present in other fungi. These other sources of GM may also give positive results with the Platelia Aspergillus test. GM is a normal by-product of the penicillin fermentation process. It is a noninfectious, nonpyrogenic carbohydrate.

As noted by Viscoli et al. [2, p. 915], “…cross-reactions of the monoclonal antibody (Mab) EB-A2, used in this test, have been described with other organisms (such as Fusarium oxysporum, Rhodotorula rubra, Trichophyton rubrum, Trichophyton interdigititis, Penicillium chrysogenum, Penicillium digitatum, Paecilomyces variotii, and Alternaria species) and also with infant milk formulas, cyclophosphamide, and food.” Piperacillin-tazobactam is manufactured in sterile manufacturing facilities and is subjected to rigorous sterility controls prior to its release to the market. Wyeth conducted laboratory testing of piperacillin-tazobactam product. The product is sterile and free of Aspergillus organisms. It is not “contaminated” with Aspergillus organisms or Aspergillus GM.

Because the Platelia Aspergillus test kit detects GM, not Aspergillus as its name implies, there can be a positive reaction to any GM, regardless of source. Therefore, the reaction is better characterized as either a positive reaction to GM or a “cross-reaction” by the test. It is not evidence of “contamination” of the sample being tested. Wyeth has taken steps to notify clinicians of this “cross-reaction” through a letter to health care providers, mailed in December 2003/January 2004, and through a modification of the Laboratory Interactions section of its worldwide product directional circular.

Acknowledgment

Potential conflict of interest. D.H.W. is an employee of Wyeth Pharmaceuticals.

David H. Wu
Global Medical Affairs, Wyeth Pharmaceuticals, Collegeville, Pennsylvania

References

Reply to Wu

Sir—We read with interest Dr. Wu’s comments [1] about our article [2] on the relationship between false-positive results of the Platelia Aspergillus ELISA (Bio-Rad) and treatment with piperacillin-tazobactam. Careful investigation clearly showed an association between the false-positive reaction and administration of piperacillin-tazobactam, and no other explanation was found. We never doubted that piperacillin-tazobactam is a sterile product and certainly not contaminated with Aspergillus organisms. This is important and reassuring, both for patients and for clinicians. On the other hand, we never used the term “contamination” in our article [2].

We agree with Wu [1] that the molecule responsible for the cross-reaction of the Platelia Aspergillus test is so far of uncertain origin and that it does not necessarily originate from Aspergillus species. For this reason, we expect that Wyeth Pharmaceuticals will be able to provide the scientific community with an explanation for the phenomenon, including the molecular characterization and origin of this “extraordinary” molecule, very soon.

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Marco Machetti and Claudio Viscoli
Infectious Disease Unit, National Institute for Cancer Research, University of Genova, Italy

Reference

Reply to Penack et al. and Wu

Sir—in their letter, Penack et al. questioned the reliability of the association between false-positive galactomannan (GM) antigenemia results obtained with use of