## Use of Galactomannan Enzyme Immunoassay for Diagnosis of Invasive Aspergillosis in a Tertiary-Care Center over a 12-Month Period

Invasive pulmonary disease caused by Aspergillus species is an increasing concern for patients who are immunosuppressed, especially patients with neutropenia or hematologic malignancies (6). Since invasive aspergillosis can be difficult to diagnose, tests have been developed to combat this problem, including the Platelia galactomannan enzyme immunoassay (Bio-Rad). Although the test is approved by the FDA for use with patients with neutropenia and those undergoing stem cell transplantation, controversy about the test's utilization exists. Although initial results were promising, various sensitivities and specificities (29 to 99%) have been reported recently in prospective studies (1–5, 7–9). To evaluate the utilization and value of this test with our patient population (a hematopoietic stem cell transplant center), we reviewed all galactomannan tests performed in 2005, with correlation of clinical history and pathology results.

Two hundred thirty-four tests were performed on 86 patients in 2005 at University of North Carolina Hospitals. Twentyeight patients (33%) had multiple tests performed, while the remainder had just one test performed. Of the 86 patients, 58 (67%) had hematologic malignancies, 35 (41%) had undergone bone marrow transplantation, 4 (5%) had received lung transplantation, and 5 (6%) had received heart transplantation. Review of pathology results revealed that 73 (85%) had no findings of invasive aspergillosis, 10 (12%) had no pathological specimens, and 3 (3%) had biopsy-proven invasive aspergillosis. Two patients with biopsy-proven invasive aspergillosis had multiple negative galactomannan tests: (i) an acuteleukemia patient with a heel skin punch biopsy demonstrating invasive aspergillosis had two negative galactomannan tests, 18 and 4 days prior to the biopsy, and (ii) an acute-myelogenousleukemia patient with a left lower lobe wedge biopsy showing invasive aspergillosis in 2003 had 19 negative galactomannan tests in 2005. The second patient was treated with antifungal therapy in the intervening time period.

Four patients had a total of six positive galactomannan test results, with only one of the patients having positive pathological correlation. This was an acute-myelogenous-leukemia patient undergoing chemotherapy. She had a chest computed tomography scan consistent with a left lower lobe aspergilloma and a confirmatory lung wedge biopsy. The other three patients with positive galactomannan test results all had negative pathology for *Aspergillus* infection: (i) an acute-lymphocytic-leukemia patient with a history of *Aspergillus* infection had one negative galactomannan test result followed by a positive result, (ii) a heart transplant recipient in 1996 with subsequent development of non-small cell lung carcinoma had one positive galactomannan test result, and (iii) a sarcoidosis patient with a history of *Aspergillus* pneumonia had two positive galactomannan test results.

At our institution, the galactomannan test is used mostly by hematologists in the setting of hematologic malignancies. Thirty-three percent of patients had multiple serial tests, and 67% of patients had only one test, reflecting variability in how the test is utilized. Further review of pathology specimens revealed that of the nine patients with biopsy-proven aspergillosis between 1 July 2004 and 31 December 2005, six patients did not receive a galactomannan test, two patients had multiple negative galactomannan tests (although one patient had been treated), and one patient was galactomannan positive. Thus, the utilization and correlation with clinical, serologic, and pathological parameters are highly variable in this limited study. Larger studies are required to further evaluate this correlation and the utility of this assay.

## REFERENCES

- Herbrecht, R., V. Letscher-Bru, C. Oprea, et al. 2002. Aspergillus galactomannan detection in the diagnosis of invasive aspergillosis in cancer patients. J. Clin. Oncol. 20:1898–1906.
- Machetti, M., M. Feasi, N. Mordini, et al. 1998. Comparison of an enzyme immunoassay and a latex agglutination system for the diagnosis of invasive aspergillosis in bone marrow transplant recipients. Bone Marrow Transplant. 21:917–921.
- Maertens, J., J. Van Eldere, J. Verhaegen, E. Verbeken, J. Verschakelen, and M. Boogaerts. 2002. Use of circulating galactomannan screening for early diagnosis of invasive aspergillosis in allogeneic stem cell transplant recipients. J. Infect. Dis. 186:1297–1306.
- Maertens, J., J. Verhaegen, H. Demuynck, et al. 1999. Autopsy-controlled prospective evaluation of serial screening for circulating galactomannan by a sandwich enzyme-linked immunosorbent assay for hematological patients at risk for invasive aspergillosis. J. Clin. Microbiol. 37:3223–3228.
- Maertens, J., J. Verhaegen, K. Lagrou, J. Van Eldere, and M. Boogaerts. 2001. Screening for circulating galactomannan as a noninvasive diagnostic tool for invasive aspergillosis in prolonged neutropenic patients and stem cell transplantation recipients: a prospective validation. Blood 97:1604–1610.
- Marr, K. A., R. A. Carter, F. Crippa, A. Wald, and L. Corey. 2002. Epidemiology and outcome of mould infections in hematopoietic stem cell transplant recipients. Clin. Infect. Dis. 34:909–917.
- Pinel, C., H. Fricker-Hidalgo, B. Lebeau, et al. 2003. Detection of circulating Aspergillus fumigatus galactomannan: value and limits of the Platelia test for diagnosing invasive aspergillosis. J. Clin. Microbiol. 41:2184–2186.
- Siemann, M., M. Koch-Dorfler, and M. Gaude. 1998. False-positive results in premature infants with the Platelia Aspergillus sandwich enzyme-linked immunosorbent assay. Mycoses 41:373–377.
- Williamson, E. C., D. A. Oliver, E. M. Johnson, A. B. Foot, D. I. Marks, and D. W. Warnock. 2000. Aspergillus antigen testing in bone marrow transplant recipients. J. Clin. Pathol. 53:362–366.

Daniel C. Zedek Melissa B. Miller\*

Department of Pathology and Laboratory Medicine University of North Carolina School of Medicine Chapel Hill, NC 27599

\*Phone: (919) 966-3723 Fax: (919) 966-0486

E-mail: mbmiller@unch.unc.edu