Galactomannan Testing for Early Diagnosis of *Exserohilum rostratum* Infection

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Exserohilum rostratum is the most common pathogen in the current U.S. outbreak of fungal central nervous system infection, septic arthritis, and localized spinal or paraspinal infections (1). Rapid laboratory diagnosis is urgently needed but is unfortunately still limited. Only 30% of the 372 case patient specimens sent to the Centers for Disease Control and Prevention (CDC) had PCR evidence supportive of fungal infection (1, 2). The β -D-glucan assay, which can detect (1,3)- β -D-glucan, a major cell wall component of many fungi, was useful in culture-independent diagnosis of three patients who were potentially exposed to contaminated methylprednisolone and presented with findings suggestive of fungal central nervous system infection (3). The assay, however, has not been approved by the U.S. Food and Drug Administration (FDA) for use on cerebrospinal fluid (CSF) samples.

Galactomannan is a major constituent of *Aspergillus* cell walls that is released during growth and can be detected by an FDA-approved immunoassay (4). Positive serum galactomannan antigen has also been reported during invasive infections by other fungi, such as *Penicillium*, *Alternaria*, *Paecilomyces*, *Histoplasma*, *Geotrichum*, *Fusarium*, and *Cryptococcus* species (5–10). We present a case of *Exserohilum rostratum* infection in which the serum galactomannan assay facilitated early diagnosis. A 44-year-old male with acute lymphoblastic leukemia who underwent allogeneic stem cell transplantation developed necrotic lesions in the nose and maxillary sinus. Biopsy showed angioinvasive brown-pigmented septate hyphae, and the culture was identified morphologically and by intergenic transcribed spacer (ITS) region and 28S ribosomal DNA sequences as *Exserohilum rostratum*. Treatment with intravenous amphotericin B deoxycholate at 1.5 mg/kg of body weight/day resulted in clinical improvement, and recovery followed engraftment. The serum galactomannan test was positive at presentation, thus driving early detection of invasive fungal disease. Galactomannan levels declined slowly under treatment (Table 1) but remained positive after neutrophil recovery. At the time of serum sample collection, the patient did not receive antibiotics, such as piperacillin-tazobactam, amoxicillin-clavulanate, or gluconate-containing Plasma-Lyte solutions, that could have caused false positivity in the galactomannan assay (11, 12).

The clinical isolate was tested *in vitro* for galactomannan content. Fresh inocula of 10^4 spores per ml were grown overnight at 30°C in YPD broth medium (yeast extract-peptone-dextrose, 2:2:2 g/liter) on a rotary shaker. Fungal suspensions in phosphate-buffered saline (PBS) were extracted by centrifugation ($2,000 \times g$) followed by filtration (0.2 μ m pore size). The filtrates were tested for galactomannan (Platelia *Aspergillus* antigen [Ag] kit; Bio-Rad Laboratories, Inc., Hercules, CA, USA) after appropriate dilution with saline. The *Exserohilum rostratum* isolate yielded a positive test, with a galactomannan content comparable to that of an *Aspergillus fumigatus* positive control (Table 1). Testing galactomannan in serum and CSF is recommended for the diagnosis of

TABLE 1 Galactomannan levels in serum and fungal extracts

Sample	Galactomannan ODI ^a for sample with:	
	No dilution	10^{-3} dilution
Serum		
Upon diagnosis	2.25	
After 2 wk of treatment	1.5	
After 3 wk of treatment	0.95	
4 wk following neutrophil recovery	0.52	
Fungal extract		
<i>Exserohilum rostratum</i> (our case)	5.08	2.01
<i>Aspergillus fumigatus</i> (ATCC 64026)	5.02	1.85

^a ODI, optical density index.

invasive aspergillosis (13, 14). Although our observation is based on a single case, it suggests that the widely available galactomannan assay, applied to CSF, warrants evaluation as an aid in the early detection of *Exserohilum rostratum* infection in the current epidemic.

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