biomnis
YOUR PARTNER IN PATHOLOGY

Focus

Aspergillus Galactomannan Antigen Testing

Invasive fungal infections are a major cause of morbidity and mortality among severely immunocompromised patients. The frequency and severity of such infections has risen steadily over the last few decades. Invasive aspergillosis (IA) is a severe infection which occurs in patients with prolonged neutropenia, following transplantation or who have received aggressive immunosuppressive treatments.

IA has an extremely high mortality rate of 50-80% due in part to the rapid progression of the infection and partly due to the difficulties of diagnosis leading to late recognition of the presence of infection in many cases. Approximately 30% of cases remain undiagnosed and untreated at death.

Traditional Diagnosis of IA

Definitive diagnosis of IA requires histopathological evidence of deep-tissue invasion or a positive culture. However, this evidence is often difficult to obtain due to the critically ill nature of the patient and the fact that severe thrombocytopenia often precludes the use of invasive procedures to obtain a quality specimen. The sensitivity of culture in this setting is also low, reportedly ranging from 30% to 60% for bronchoalveolar lavage fluid. Accordingly, the diagnosis is often based on nonspecific clinical symptoms (fever, cough, chest pain, dyspnoea) in conjunction with radiological evidence from CT scan and diagnosis is often not established until the infection becomes overwhelming.

Galactomannan Enzyme Immunoassay

The advent of biomarker tests such as the galactomannan enzyme immunoassay offers a potential adjunct of diagnosis of IA. Galactomannan is a polysaccharide component of the Aspergillus cell wall that is released from growing Aspergillus hyphae. The Aspergillus enzyme immunoassay utilizes a monoclonal antibody in a double-sandwich assay for detection of galactomannan. Results of the test are interpreted based on the optical density (OD) ratio of the sample divided by a threshold control referred to as the OD index. The test received FDA clearance for use in adult immunocompromised patients using a low index to define positivity after results of a prospective study found that an OD index of 0.5 resulted in improved sensitivity and earlier indication of infection compared with prior recommendations. Serum galactomannan can often be detected a mean of 7 to 14 days before other diagnostic signs of IA become apparent and monitoring of galactomannan can potentially allow initiation of preemptive antifungal therapy before life-threatening infection occurs.

Interpretation of Results/Test Limitations

A positive result in the galactomannan antigen assay supports a diagnosis of invasive aspergillosis. Positive results need to be interpreted in conjunction with other clinical and diagnostic findings. A negative result does not rule out IA. Repeat testing is recommended if the result is negative but IA is suspected. Patients who are at risk of IA (e.g. patients who have a prolonged period of neutropenia) should have a baseline serum tested and should be monitored twice weekly for increasing galactomannan antigen levels. Galactomanan levels may be useful in the assessment of therapeutic response. Antigen levels decline in response to antifungal therapy.

False positive results are reported to occur at rates of 8-14% with this assay. For all positive results it is recommended that a new aliquot of the same specimen be repeated as well as collection of a new specimen from the patient for repeat testing. Two or more consecutive positive results should be obtained from separately drawn specimens before the patient is considered to have a positive Aspergillus antigen test. Numerous foods (pasta, rice etc.) contain galactomannan and consumption may be associated with false positive results. Other genera of fungi such as Penicillium and Paecilomyces may also show cross-reactivity with the assay. There are reports in the literature of positive galactomannan test results in patients receiving piperacillin/tazobactam; therefore results in these patients should be interpreted with caution and confirmed by other diagnostic methods.

The concomitant use of anti-fungal therapy in some patients with IA may result in reduced sensitivity of the galactomannan assay. The assay may also exhibit reduced sensitivity in patients with chronic granulomatous disease and Job's Syndrome. The performance of the assay has not been evaluated with neonate serum specimens or for use with plasma or other specimen types such as urine or cerebrospinal fluid. False-positive galactomannan results are possible in patients receiving PLASMA-LYTE for intravenous hydration or if PLASMA-LYTE is used for bronchoalveolar lavage. Specimens containing Histoplasma antigen may cross-react in the Aspergillus galactomannan assay.

EIA Test Performance Characteristics

In clinical studies submitted for the Food and Drug Administration (FDA)-approval process, the sensitivity of the test was reported to be 81% for proven/provable invasive aspergillosis and the specificity was 89%. The positive and negative predictive values were reported as 68% and 96% respectively, based on an average prevalence of 14% in the study population. In a low-prevalence population (5%) the positive predictive value decreases to 31%; the negative predictive value remains at 96%.

Test Information

Please find details below regarding Aspergillus Galactomannan Antigen Testing which may be ordered through your local laboratory or directly with Biomnis Ireland:

Galactomannan (Aspergillus Antigen)
Sample Requirements: 3 mL Serum + 4°C
Turnaround time: 5 working days

Contact Us

For more information about this test or any of our other tests or services contact Biomnis Ireland at:

Phone: (01) 295 8545
Email: sales@biomnis.ie
Web: www.biomnis.ie