Invasive Fungal Disease (IFD)

Surveillance Fungal Culture Yield in Invasive Fungal Disease Management

Discussion:
Invasive Fungal Disease is difficult to diagnose, especially in its early stages, and new serological tests have been developed to overcome some of the deficiencies of existing tests. The utilization of “Gold Standard” diagnostic reference data is required in the evaluation of the clinical performance of new diagnostic tests. As a “Gold Standard” for the diagnosis of Invasive Fungal disease (IFD), fungal culture has suffered much criticism as being relatively insensitive. With an insensitive “Gold Standard,” new, higher sensitivity tests are at risk of excess apparent false positives relative to the standard.

Surveillance culture has been suggested as a useful tool to assess risk of IFD. Recently, Youngster et al., published the results of a large single center study of the diagnostic performance of fungal surveillance culture (FSC) in pediatric hematopoietic stem cell transplant (HSCT) patients. As a reference standard, proven and probable cases of IFD were determined using the revised guidelines of the European Organization for Research and Treatment of Cancer-Mycosis Study Group. A total of 5,618 FSCs from 360 individual HSCT patients were analyzed. A single positive FSC was observed with 232 patients (64.4%); 30.3% of stool samples were positive; and 30 patients (8.3%) met the definition for IFD. Of the 232 patients with a positive FSC 17, (7.9% [sic]) developed an IFD. Interestingly, of the 128 patients with a negative FSC, 13 (10.1%) developed an IFD. The rate of IFD was 0.127 (95% CI, 0.041 – 0.121) and 0.089 (95% CI, 0.052 – 0.13) per 1,000 days in the FSC-positive and FSC-negative populations, respectively. Among patients with a positive FSC, there was no significant difference between those who received a change in antifungals relative to those who did not. The authors noted that nares and throat cultures added little data of clinical value and there was a low concordance between the fungal species detected by FSC and the organisms responsible for the IFD cases. The cost of a FSC at their institution was $80 and the total FSC expenditure during the study period was $449,000. They analyzed survey data from 40 HSCT transplant centers, which revealed that 40% practiced weekly post-transplant FSC and that the respondents felt the FSC results were of little value. The study conclusions include a call for wider evaluation of newer strategies for assessing the likelihood of IFD, including routine use serum fungal markers.
Recent Publications on Serum BG and Related Matters:
Chen, M. et al. Pulmonary fungus ball caused by *Penicillium capsulatum* in a patient with type 2 diabetes: a case report. BMC Infectious Diseases 2013, 13:496-500. This case report describes the clinical investigation and therapy of a diabetic Chinese garden worker who was determined to have an upper left lobe pulmonary fungus ball. The organism was determined to be *Penicillium capsulatum* based upon culture from a biopsy specimen. A serum beta-glucan test revealed a BG burden of 459 pg/mL. The patient was cured by a combination of surgery (lobectomy) and sequential fluconazole (400 mg/day, 90 days) and caspofungin (70 mg/day, 14 days) treatment.

Esteves, F. et al. (1→3)-β-D-Glucan in association with lactate dehydrogenase as biomarkers of *Pneumocystis* pneumonia (PcP) in HIV-infected patients. Eur. J Clin. Microbiol. Infect Dis.. 2014 DOI 10.1007/s10096-014-2054-6. This study evaluated the (PcP) in HIV-infected patients. A cohort of PcP HIV-positive patients (N=100) and healthy controls (N=50) were compared. PcP was established by examination of pulmonary specimens with anti-*Pneumocystis* immunofluorescence microscopy and PCR. (PPV/NPV), and positive/negative likelihood ratios (PLR/NLR) were 91.3 %, 61.3 %, 85.1 %, 79.2 %, 2.359, and 0.142, respectively, for the BG kit assay, and 91.3 %, 35.5 %, 75.9 %, 64.7 %, 1.415, and 0.245, respectively, for the LDH test. Combining the test results using a BG cutoff of 400 pg/mL and a LDH cutoff of 350 U/L gave a 92.8 % sensitivity, 83.9 % specificity, 92.8 % PPV, 83.9 % NPV, 5.764 PLR and 0.086 nLR (P<0.001). The authors concluded that BG level is a reliable indicator of PcP and the its combination with LDH data is a promising alternative.

Hoarau, G. et al. Detection of (1→3)-β-D-Glucan in situ in a *Candida albicans* brain granuloma. J Infect. 2013; 67: 622-4. This case report describes the contribution of (1→3)-β-D-Glucan (BG) to the diagnosis of a *Candida albicans* brain granuloma in a pediatric patient. A left frontal mass was observed in the 2 year old child. Biopsy and CSF culture were negative. Histopathological analysis of section stained with haematoxylin-eosin-safran and periodic acid Schiff showed fungal pseudomycelia and blastoconidia. BG analysis of serum and CSF were negative. A 3 mm³ biopsy specimen homogenate (BG-free suspending solution) supernatant was tested for both BG and mannan. Both were positive at levels exceeding 500 pg/mL. With observations suggestive of a Candida infection, PCR was performed and *C. albicans* was identified.

Edathodou, J. et al. Invasive fungal infection due to *Triadelphia pulvinata* in a patient with acute myeloid leukemia. J Clin Microbiol. 2013 Oct;51(10):3426-9. This case report describes a post-transplant fungal infection in a patient treated for acute myelogenous leukemia. After more than 4 months, the patient relapsed and was readmitted. Imaging and fungal growth from peripheral blood indicated a fungal infection. Results of serial testing for serum galactomannan and (1→3)-β-D-Glucan (BG) were negative for the former and initially negative and then positive for the latter. Laboratory investigation of the isolate revealed that it was *Triadelphia pulvinata*, a dematiaceous soil fungus. The supernatant of RPMI-culture was negative for galactomannan and strongly positive for BG (>500 pg/mL). The RPMI control was negative. The authors note that this is the first reported case of invasive fungal disease caused by this organism.

**Discussion References:**