Topic:

Invasive Fungal Disease (IFD)

Diagnostic inaccuracy consequences; Increased morbidity/mortality and costs.

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Discussion:

Inadequate diagnosis and treatment of invasive fungal disease is observed to lead to both increasing morbidity and mortality as well as the associated higher costs of treating IFD patients[1, 2]. Most such studies, studies have focused upon Candida and *Aspergillus* infections as they account for approximately 85 – 90% of nosocomial IFD[3]. Hospital-acquired IFD accounts for the majority of cases, but community acquired IFD has been found to be substantial, with one US study concluding that nearly a third of candidemia was community acquired[4]. The high mortality rates of IFD have led to increased levels of prophylaxis and empirical therapy for patients with the appropriate host and clinical factors. However, the efficacy of near-universal prophylaxis is still unclear in various populations. There was no significant difference in the invasive aspergillosis (IA) prevalence in prophylaxis versus non-prophylaxis in a recent meta-analysis of lung transplant patients, although fewer IA cases occurred in the cohort with prophylaxis[5]. In addition, the choice of drugs used for prophylaxis is important due to cost impact and a variable efficacy spectrum with different genera, as is indicated in a recent study of fluconazole versus voriconazole in a stem cell transplant population[6]. Over-treatment is a concern. In a recent single center study, 117 of 690 hematological oncology patients received systemic antifungal therapy and of the 117, only 29% met consensus criteria for possible invasive fungal infection[7].

Blood-borne fungal antigen surveillance is increasingly recommended as a method to improve early recognition of invasive fungal disease so as to achieve the benefits of both early, appropriate therapy. In addition, it may help to reduce the costs, adverse events, and potential resistance emergence associated with widespread prophylaxis and inappropriate antifungal therapy[8, 9, 10, 11, 12]. Fungitell® is a FDA-cleared *in vitro* diagnostic specific for the measurement of serum (1→3)-β-D-Glucan as an adjunct to the diagnosis of invasive fungal disease.

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Recent Publications on Serum BG and Related Matters:

Damiani, C. *et al.* Combined Quantification of Pulmonary *Pneumocystis jirovecii* DNA and Serum (1→3)-β-D-Glucan for Differential Diagnosis of *Pneumocystis* Pneumonia and Pneumocystis Colonization. J. Clin. Micro. 2013; 51: 3380-3388. This study retrospectively evaluated the diagnostic effectiveness of combined bronchoalveolar lavage (BAL) fluid quantitative PCR (qPCR), and serum (1→3)-β-D-glucan (BG) in patients with either *Pneumocystis* pneumonia (PCP) (N=17) or *Pneumocystis* colonization (N=29). PCP was defined both clinically and with microscopy of BAL fluid. BAL *Pneumocystis* DNA copy numbers in the PCP and colonization cohorts were 1.3×10^7 and 3.4×10^3 per mL, respectively. 100% sensitivity and specificity for PCP were achieved at a lower cutoff of 1.6×10^3 and 2×10^4 copies/mL respectively. 14/46 patients were found to be in the qPCR indeterminate zone. A serum BG cutoff of 100 pg/mL correctly assigned these patients to the PCP (N=4) or colonization (N=10) cohorts.

Lobo ML, Esteves F, de Sousa B, Cardoso F, Cushion MT, Antunes F, Matos O. Therapeutic potential of caspofungin combined with trimethoprim-sulfamethoxazole for pneumocystis pneumonia: a pilot study in mice. PLoS One. 2013 Aug 5;8(8):e70619. doi: 10.1371/journal.pone.0070619. Print 2013. Recent data have shown that echinocandin class antifungal drugs are potent in eliminating the cyst form of *Pneumocystis* sp. in animal models of models of *Pneumocystis* pneumonia. In addition, a few case reports have described the application of echinocandin drugs to human cases of PCP in salvage therapy applications. This study evaluated the effect of the first line anti-pneumocystis medication, trimethoprim-sulfamethoxazole (TMP) in a mouse model of PCP. The results showed that while caspofungin, an echinocandin, was not effective in eliminating *Pneumocystis*, its addition to a TMP regimen was more effective than TMP alone. In addition to qPCR and BAL fluid organism burden evaluation, serum (1→3)-β-D-glucan (BG) was evaluated. Serum BG levels were observed to decline markedly in the treatment groups where therapy was effective.

Mosquera RA, Estrada L, Clements RM, Jon CK. Early diagnosis and treatment of invasive pulmonary aspergillosis in a patient with cystic fibrosis. BMJ Case Rep. 2013 Nov 18;2013. pii: bcr2013201360. doi: 10.1136/bcr-2013-201360. This report describes a case of invasive pulmonary aspergillosis in a male pediatric cystic fibrosis patient. Clinical suspicion of pulmonary fungal infection was based upon imaging findings and non-responsiveness to antibiotic therapy. Voriconazole therapy was begun empirically. Subsequently, the patient was found to be both BG and galactomannan positive. After three months of hospitalization, the patient was discharged but with continuing voriconazole therapy and improving respiratory function.

Chen M, Houbraken J, Pan W, Zhang C, Peng H, Wu L, Xu D, Xiao Y, Wang Z, Liao W. Pulmonary fungus ball caused by *Penicillium capsulatum* in a patient with type 2 diabetes: a case report and literature review. BMC Infect Dis. 2013 Oct 23;13(1):496. [Epub ahead of print]. The report describes a case of a female diabetic patient presenting with fever, cough, yellow sputum, and fatigue. She was unresponsive to a 14 day course of cefoxitin. Imaging showed a cavitary lesion in the left lung containing a gravity dependent mass. A glucan test was positive at 459 pg/mL. Septate hyphal elements were identified in specimens retrieved from the mass. Subsequent identification procedures revealed that this was pulmonary infection with a rare organism, *Penicillium capsulatum*. This case adds to the clinically isolated species of *Penicillium* (now *Talaromyces*) that are seen to contribute to positive serum burdens of (1→3)-β-D-glucan.

Discussion References:

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