Diagnostic performance of Aspergillus galactomannan antigen and Real-Time PCR detection among children with hematological malignancies

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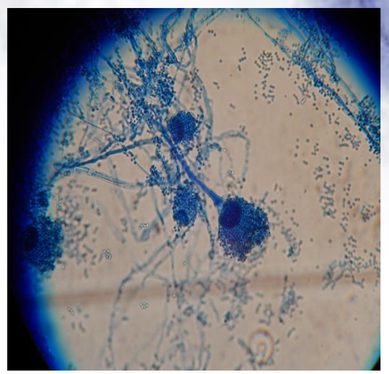
Background

One of the major fatal causes in immunosuppressed patients is the invasive fungal infection by Aspergillus. Invasive aspergillosis (IA) is accepted as the second most common fungal infection requiring hospitalization. IA infections are associated with high rates of morbidity and mortality in transplant recipients, hematologic patients or patients with other malignancies receiving chemotherapy. The early diagnosis and timely antifungal treatment of IA is of great importance for high-risk patients. The diagnosis of IA remains a challenge all over the world given that traditional blood cultures are rarely positive. Serological detection of galactomannan (GM) is included as a criterion of IA diagnosis by the EORTC/MSG. However, detection of Aspergillus DNA has not been yet included due to a lack of standardization and validation in clinical trials. The study concerns the comparative evaluation of GM-antigen detection and Aspergillus DNA detection, as massive screening methods among patients at high-risk of invasive aspergillosis.

Material/Methods

The study includes 224 pediatric patients with hematological malignancies and neutropenia. The measurement was made using the GM immunoenzymatic method Platelia™ Aspergillus (Bio-Rad, Hercules, CA). The detection of Aspergillus DNA in serum or BAL was measured with MycAssay Aspergillus real-time PCR (Myconostica Ltd, UK). Two or more consecutive samples per patient were examined (serum and BAL). Samples with a cut-off index of ≥0.5 in serum and ≥1.0 in bronchoalveolar lavage (BAL), respectively, were considered positive.



Aspergillus fumigatus

Results

Thirteen from 224 patients were found positive by both methods. Eight children were found positive for Aspergillus GM (5 patients) or DNA (3 patients). The results are shown in the Table. Results' agreement (GM+/PCR+ and GM-/PCR-) was found in 216 patients and 353 samples (96,4 % of patients and 95,4 % of samples). Respectively, disagreement existed only in 8 patients (17 samples), in which the positive result in any of the two methods was evaluated as true positive, in conjunction to the clinical and radiological findings. All children with positive results received antifungal therapy, while a child with GM+/PCR+ deceased.

Results	Serum	BAL	CSF	Number of samples	Number of patients
GM+/PCR+	16	7	2	25	13
GM+/PCR-	11	1	-	12	5
GM-/PCR+	4	1	-	5	3
GM-/PCR-	308	16	4	328	203
Total	339	25	6	370	224

Conclusions

Recent techniques such as GM-antigen and PCR-Aspergillus DNA are important diagnostic tools in cases of consecutive samples (at least two per week). The addition of PCR to GM monitoring in high-risk pediatric patients with hematological malignancies provides greater diagnostic accuracy in invasive aspergillosis. Further studies are needed to assess the test of serum or BAL samples and/or their combination.

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