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INVASIVE ASPERGILLOSIS IN CHILDREN WITH ONCOHEMATOLOGICAL DISEASES IN SAINT-PETERSBURG, RUSSIA

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Objectives

Invasive aspergillosis (IA) is a severe opportunistic infection with high mortality. Publications about IA in children are limited.

We analyzed the risk factors, aetiology, clinical signs and symptoms, and results of treatment of IA in children with oncohematological diseases in St. Petersburg, Russia.

Methods

The prospective study was conducted during the period of 2002-2012 y.y. The criteria EORTC / MSG 2008 was used.

Results

During the study period 567 patients with IA were included. The mean age of patients was 36 years (range 1-76), male – 53%, female – 47%. Children were 21%.

Children with IA: males - 54%, females - 46%. Age of patients - from 1 to 17 years (median – 10±5 years).
Main underlying conditions in children with IA were oncohematological malignancies - 95%.

The most frequently baseline haematologic malignancy were acute myeloid leukemia, acute lymphoblastic leukemia, and Hodgkin's disease (table 1).

Table 1.
Haematologic malignancies in patients with IA

Haematological malignancies (ICD-10)	Children %	Adults %
Acute lymphoblastic leukemia	44	17
Acute myeloid leukemia	27	35
Aplastic anemia	7	1
Oncologycal diseases’	6	1
Chronic myeloid leukemia	6	7
Acute leukemia unspecified	5	3
Hodgkin's lymphoma	4	8
Myelodysplastic syndrome	1	5
Chronic lymphocytic leukemia	3	5
Multiple myeloma	0	4
Non-Hodgkin's lymphoma	0	13
Eosinophilic leukemia	0	1

Results

Risk factors for IA in children with oncohematological malignancies were: cytostatic chemotherapy (92%), agranulocytosis (90%), lymphocytopenia (65%), the use of corticosteroids (75%), and allo-BMT (43%).

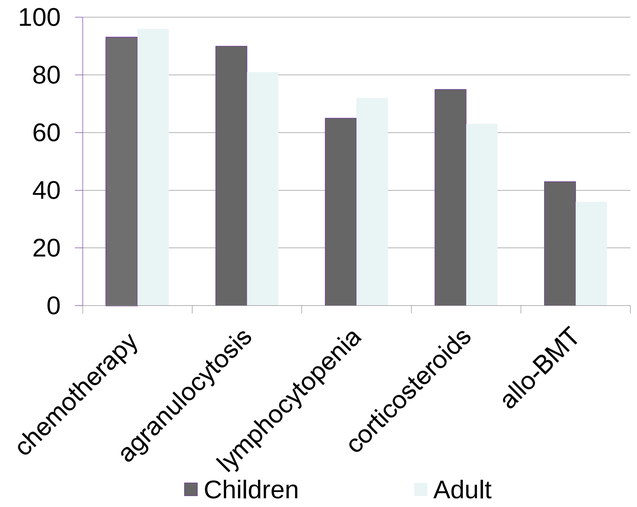

Fig.1. Risk factors for IA in children with oncohematological malignancies.

The main sites of IA in children with oncohematological diseases were lungs - 90%, sinuses - 10% and CNS – 8%. More then two organs were affected in 12% of patients. In adult group we diagnosed pulmonary aspergillosis (98%), sinusitis (4%), and CNS (4%).

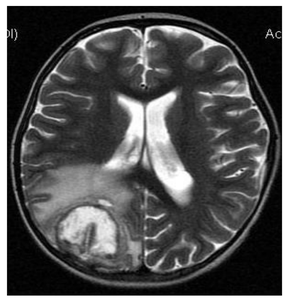

Fig.2. Patients with IA CNS. Child 4 years.

On CT scan we revealed infiltrative lesions (56%), nodular (68%), ground-*glass* (26%), and specific signs of lung damage ("halo" and) is rarely detected (11% and 3%). GM in serum was positive in 77% vs. 84% of specimens.

Results

The aetiology of IA in children: *A. fumigatus* - 55%, *A. niger* - 30%, *A. flavus* - 15%, A*. terreus* – 15%. In adults: *A. fumigatus* - 45%, *A. niger* - 35%, *A. flavus* -17%, *A. ochraceus* - 2%*, A. versicolor* - 1%.

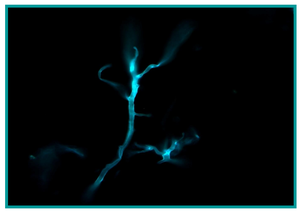

Fig.3. *A.fumigatus* in BAL.

All children with IA received antifungal therapy - voriconazole (57%), amphotericin B deoxycholate (43%), itraconazole (24%), caspofungin (17%), liposomal amphotericin B (13%), posaconazole (4%), amphotericin B lipid complex (6%). Combination therapy was used for 20% of patients (voriconazole+caspofungin, amphotericin B+caspofungin). Duration of treatment was 2-300 days (median - 39). Surgery was used in 5% of patients. Overall survival at 12 week was 71%.

We used multifactory analysis by Statistic 6.1 for Windows 7. Positive prognostic factors of the 12th week survival were: antifungal treatment with voriconazole (p=0,06) and caspofungin (p=0,02), combination antifungal therapy (p=0,03) and secondary prophylaxis (p=0,01).

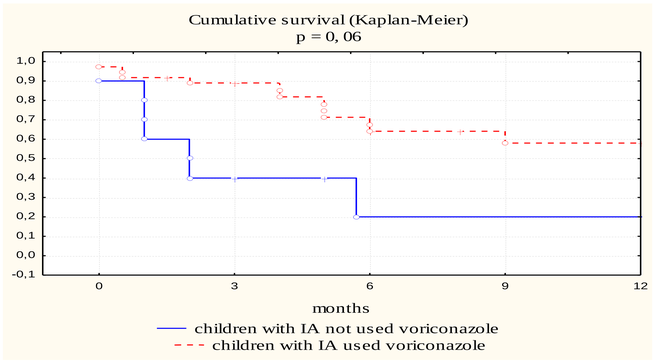

Fig.4. 12th week survival and treatment with voriconazole.

Conclusions

The main underlying diseases in children with IA were acute lymphoblastic leukemia and acute myeloid leukemia (71%). The main aetiology agent was *A. fumigatus* (55%). Voriconazole was used in 57% of patients. Twelve weeks overall survival was 71%. Positive prognostic factors of the 12 weeks survival were: voriconazole and caspofungin use, combination antifungal therapy and secondary antifungal prophylaxis.

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