Features of invasive aspergillosis in B-cell lymphoma patients: risk factors, diagnostics, treatment and survival.

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Objectives

To study invasive aspergillosis (IA) in B-cell lymphoma patients after cytostatic chemotherapy (CCT) and autologous stem cell transplantation (ASCT).

Methods

The prospective study included 813 B-cell lymphoma patients: Hodgkin lymphoma (HL) – 363, 16-65 years (median – 33), and non-Hodgkin lymphoma (NHL) – 450, 19-74 years (median – 50). For the IA diagnosis criteria EORTS/MSG 2008 were used.

Results

Frequency of IA in patients with B-cell lymphoma was 4,98% (HL – 5,6%; NHL – 4,5%, p=0,49), after ASCT – 2,85% (HL – 2,35%; NHL – 3,33%, p≥0,05), during induction and relapse therapy – 4,09% vs 7,14% (p=0,08) accordingly. In patients with relapse of NHL frequency of IA was 10,25%, during induction therapy – 2,88% (p=0,004). The main etiology agents were *A.fumigatus* (41%), *A.niger* (39%), and *A.flavus* (14%) (Fig. 1)

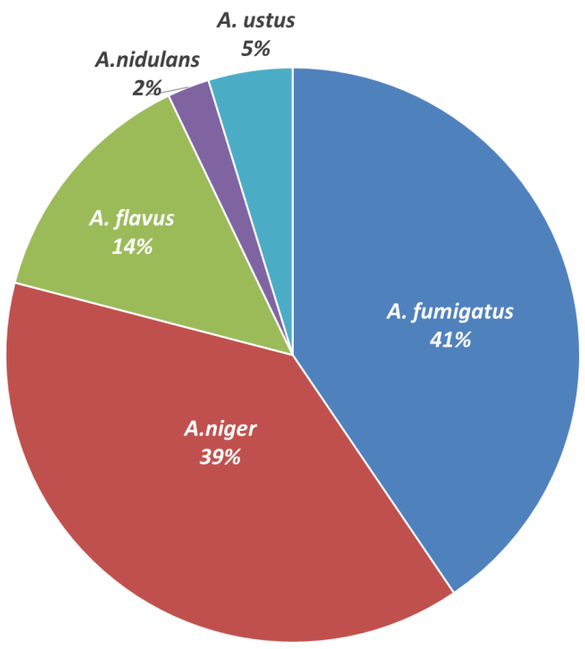


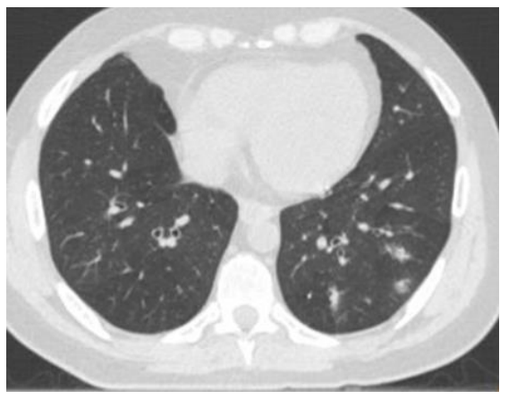
Fig.1 Etiological agents

Risk factors for IA were: relapse of lymphoma (p=0,005), B-symptoms (p=0,035) and radiation therapy in anamnesis (p=0,041), profound neutropenia (p=0,000), concurrent lung (p=0,007) and renal pathology (p=0,03). In patients with HL additional risk factor was viral infection (p=0,002), in patients with NHL – ≥2 lines of CCT in anamnesis (p=0,032).

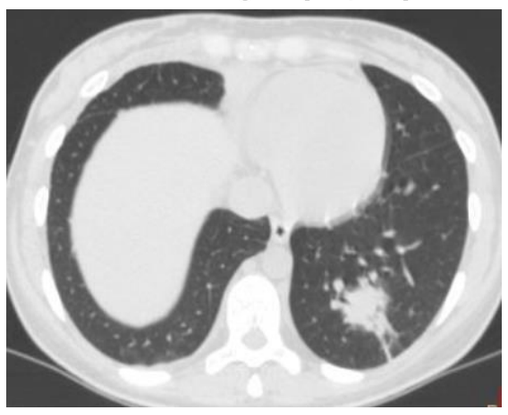
The lungs were involved in 100% cases, ≥2 organs involvement was in 4,5% NHL patients. Clinical symptoms of IA were nonspecific: fever 68%, cough 48%, dyspnea 32,5%, hemoptysis 4,7%, and chest pain 4%.

Chest CT scan sings of IA were nonspecific: focal changes 63,5%, infiltrates 58,7% and "ground-glass opacity" 23%; bilateral lung damage – 62,7% (Fig. 2).

Galactomannan test was positive in BAL fluid and serum in 83,6% cases. The presence of septated mycelium in BAL was observed at microscopy in 15,5% patients. *Aspergillus* spp. culture was obtained in 34,7% patients (HL – 20,4%; NHL – 46,3%, p=0,004).



Focal changes **(63,5%)**



Infiltrates (58,7**%)**

Fig.2 CT-signs of invasive aspergillosis

"Probable" IA was diagnosed in 92,9%, "proven" – in 7,1% of cases. The main antifungal drug was voriconazole – 79%. In patients with IA the 12-weeks overall survival (OS) was 84,9% (HL – 88,1%; NHL – 82,1%).

The use of bronchoscopy and voriconazole improved 12-weeks OS (88,1% vs 64,7%, p=0,011; 92,6% vs 71,1%, p=0,004, accordingly) and 1-year OS (78,9% vs 52,9%, p=0,010; 82,7% vs 62,2%, p=0,010, accordingly).

IA did not influence on 2- and 4-year OS, 1-,2-3-year progressive-free survival (PFS) and 1-,2-,2,5- year relapse-free survival (RFS) in patients with induction chemotherapy.

Furthermore IA did not influence on 2-year OS, 1-,2-year PFS and 1-,2-year RFS in patients with relapsed or refractory B-cell lymphoma (p>0,05).

Conclusions

Frequency of IA in patients with B-cell lymphoma was 4,98% (HL – 5,6%; NHL – 4,5%), in patients with relapse of NHL - 10,25%. Risk factors for IA were relapse of lymphoma (p=0,005), B-symptoms and radiation therapy in anamnesis (p=0,035 and p=0,041), profound neutropenia (p=0,000), concurrent lung and renal pathology (p=0,007 and p=0,03). Etiology agents were *A.fumigatus* (41%), *A.niger* (39%), *A.flavus* (14%). Clinical and CT-signs were nonspecific. The main antifungal drug was voriconazole – 79%. Overall 12-weeks survival in patients with IA was 84,9%. IA did not influence on OS, PFS and RFS survival of patients with B-cell lymphoma, who receive induction and anti-relapse cytostatic chemotherapy.

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