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 EORTC/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 – 2.65% (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).

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).

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).

"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.