Clinical and immunological features of invasive aspergillosis in patients with multiple myeloma

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Background: Invasive aspergillosis (IA) often occurs in hematological patients with immunodeficiency after cytostatic therapy or allo-HSCT. Immunological features of IA in patients with multiple myeloma are not well understood.
Material/methods: Prospective study in 1998-2015 yy. We used criteria EORTS/MSG, 2008 for the diagnosis of IA. We observed 46 adult patients with proven (4%) and probable (96%) IA. Group I included 22 patients with multiple myeloma (MM), median age was 56 years (range – 41- 65), females - 64%. Group II: 24 patients with acute lymphoblastic leukemia (ALL), median age – 43 years (range 21 -68), median 43, females – 44%.

Results: We found that common risk factors before IA development were detected less frequently in patients with MM as compared to ALL, including prolonged neutropenia 45% vs 92% (p = 0,01), and lymphocytopenia 27% vs 67% (p = 0,02).

In both groups, the primary sites of infection were lungs 100 vs 96%. Probable IA was diagnosed in 96% patients, proven – 4%. The main pathogens were A. niger (64% vs 29%), A. fumigatus (18% vs 57%) and A. flavus (9% vs 14%). We identified significant differences of immunological parameters in MM patients compared to ALL. MM patients were less likely to have decrease in the absolute number of CD4 + (0,51 (0,40 + 0,73) * 10⁹/l vs 0,31 (0,07 + 0, 72) * 10⁹/l), p = 0,04; B-cells CD20 + number (0,20 (0,10 + 0,25) * 10⁹/l vs 0,05 (0,02 + 0,16) * 10⁹/l), p = 0,04; decrease of the induced production of cytokines TNF-α (380 (356 + 497) pg/ml vs 164 (95 + 440) pg/ml), p = 0,02; IFN-γ (755 (615 + 1067) pg/ml vs 128 (70 + 795) PG/ml), p = 0,01; IL-6 (696 (669 ÷ 720) pg/ml vs 374 (242 ÷ 635) pg/ml), p = 0,01. The immunoglobulin A production and neutrophils killer activity were significantly higher in MM patients compared with ALL (p=0,08 and p=0,001, respectively). Overall survival rate in twelve weeks was 100% vs 83%, (p = 0,04). Positive prognostic factor of 12-weeks survival was voriconazole use as initial therapy (p = 0,02).

Conclusions: Significant differences in multiple myeloma patients with invasive aspergillosis were less expressed immunological changes, including prolonged neutropenia, lymphocytopenia, decrease in the absolute number of CD4 +, B-cells, and decrease of the induced production of cytokines compared to ALL-patients. Twelve week overall survival was 100%. Positive prognostic factor of 12th week survival was initial treatment with voriconazole.