

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

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Introduction

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.

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% ($p = 0,02$) (Fig.1).

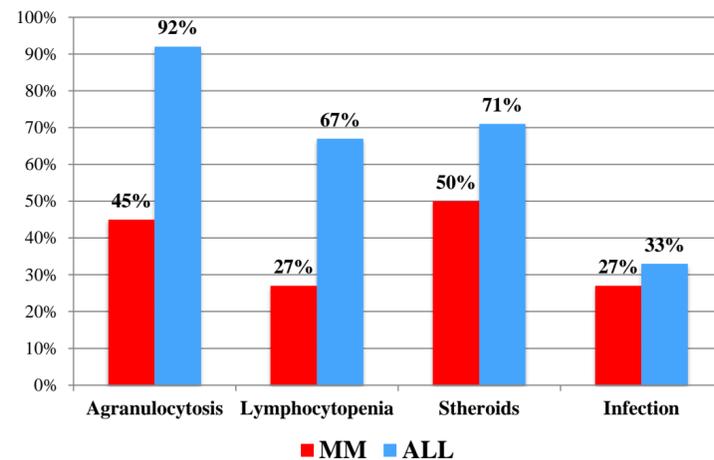


Fig. 1. The main risk factors of IA.

In both groups, the primary sites of infection were lungs 100 vs 96% (Fig.2).



Fig. 2. IA with lung involvement in MM patient.

Probable IA was diagnosed in 96% patients, proven – 4%.

The main pathogens were *A. niger* (58% vs 22%), *A. fumigatus* (28% vs 67%) and *A. flavus* (7% vs 11%) (Fig.3).

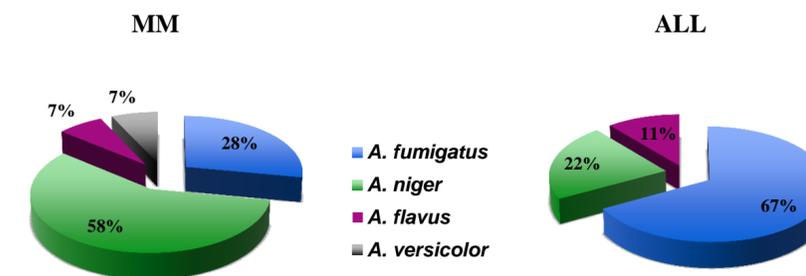


Fig. 3. Etiological agents.

We identified significant differences of immunological parameters in MM patients compared to ALL. MM patients were less decreased in the absolute number of CD4 + ($0,51 (0,40 \div 0,73) \cdot 10^9/l$ vs $0,31 (0,07 \div 0,72) \cdot 10^9/l$), $p=0,04$; B-cells ($0,20 (0,10 \div 0,25) \cdot 10^9/l$ vs $0,05 (0,02 \div 0,16) \cdot 10^9/l$), $p=0,04$; decrease of the induced production of cytokines TNF- α ($380 (356 \div 497)$ pg/ml vs $164 (95 \div 440)$ pg/ml), $p=0,02$; IFN- γ ($755 (615 \div 1067)$ pg/ml vs $128 (70 \div 795)$ PG/ml), $p=0,01$; IL-6 ($696 (669 \div 720)$ pg/ml vs $374 (242 \div 635)$ pg/ml), $p=0,01$ (Fig.4).

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).

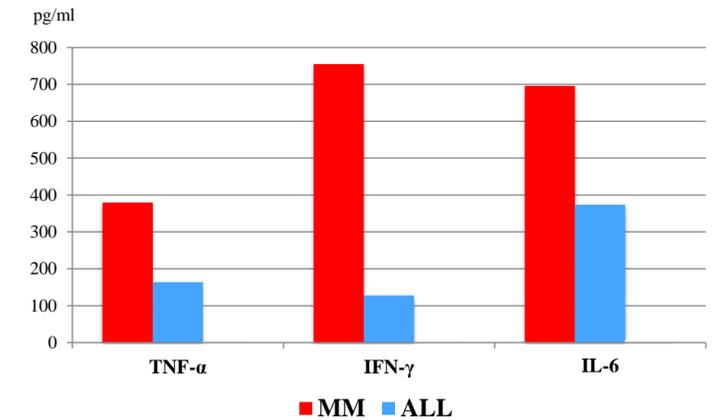


Fig. 4. Immunological parameters in MM and ALL patients.

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.