

Immunological features of invasive aspergillosis in hematological patients after allogeneic hematopoietic stem cells transplantation

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Abstract

Invasive aspergillosis (IA) is a major complication in patients after allogeneic hematopoietic stem cells transplantation (allo-HSCT). The immunological features in these patients are not well understood.

Objectives

Investigation of the immunological features of invasive aspergillosis in hematological patients after allo-HSCT.

Methods

We studied immunological parameters in 16 hematological patients with IA developed after allo-HSCT. For the diagnosis of IA criteria EORTS/MSG, 2008 was used.

Lymphocyte subsets were determined by immunocytochemical method with using monoclonal antibody («DAKO»).

Levels of immunoglobulins in the serum were estimated by nephelometric method for protein analyzer «Turbox plus».

Blood cell supernatants were tested for IFN-g and IL-10 by using an ELISA test («Cytokine», Russia).

Immunological parameters were evaluated in the first 2-4 weeks of IA diagnosis. Patients were followed for 3-6 months.

Results

100% of patients had probable IA (EORTS/MSG, 2008). Lung involvement was observed in 94% of cases, central nervous system - 6%. In 25% of cases IA was confirmed by culture. Aetiologic agents were: *A.fumigatus*, *A.niger*, *A.nidulans*.

Underlying diseases were: acute myeloid leukemia - 38%, acute lymphoblastic leukemia - 25%, chronic myeloid leukemia - 13%, lymphoma - 12%, chronic lymphocytic leukemia - 6% and myelodysplastic syndrome - 6% (Fig.1).

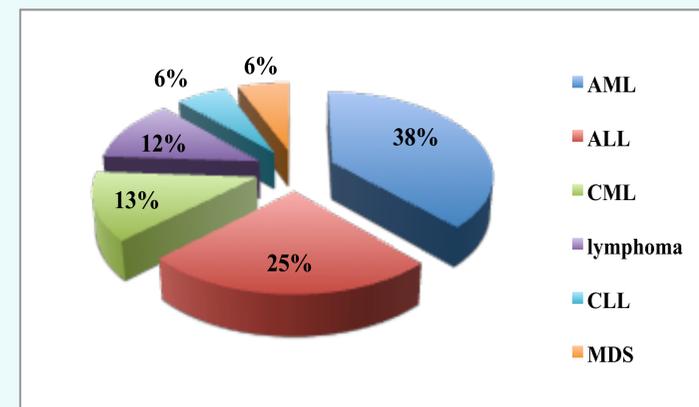


Fig.1. Underlying diseases in patients with IA

56% of patients after allo-HSCT have unrelated donors, HLA-matched donors - 31% and HLA-mismatched donors – 13% (Fig.2).

All patients received immunosuppressive therapy (cyclophosphamide, tacrolimus, methotrexate). Graft versus host disease was observed in 94%.

Results

IA was diagnosed between 18 and 270 days after HSCT (median – 33 days). At the time of diagnosis of IA in 18% of patients viral infection were detected. 12 weeks overall survival was 81%.

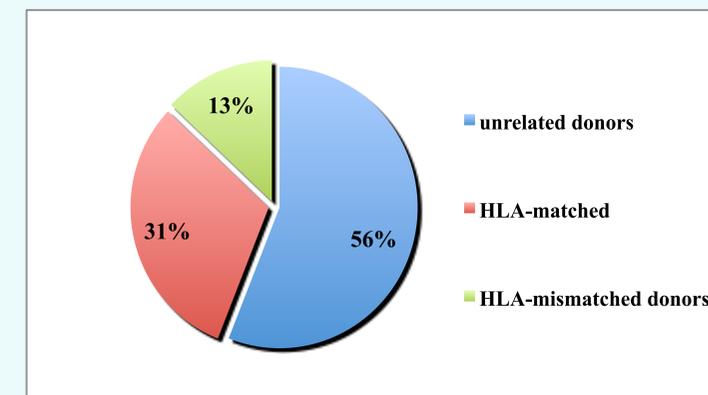


Fig.2. Types of donors

We identified significant immunological defects in all patients: lymphocytopenia ($<1,0 \times 10^9/L$) was revealed in 44%, reduction in the absolute number of T-helper CD4+ ($<0,680 \times 10^9/L$) – 82%, natural killer cells CD16+ ($<0,200 \times 10^9/L$) - 62%. Counts of cytotoxic T-cells CD8+ were increased ($>0,700 \times 10^9/L$) along with low production of IL-10 in 87%. Low number of lymphocytes with activation markers - receptors for IL-2 (CD25+) was found in 62%. (Fig. 3).

Humoral immune response was decreased: reduced the number of B-cells (CD20+) - 68 % of patients, IgG (<7.0 g/l) and IgM (<0.4 g/l) - 63%. (Fig.3, 4).

Results



Fig.3. Number of lymphocytes is expressed as percentage of healthy peoples levels

75% of patients have decline of the killing activity of neutrophils, 56% - decrease of IFN-g production (<500 pg/ml) (Fig.4).

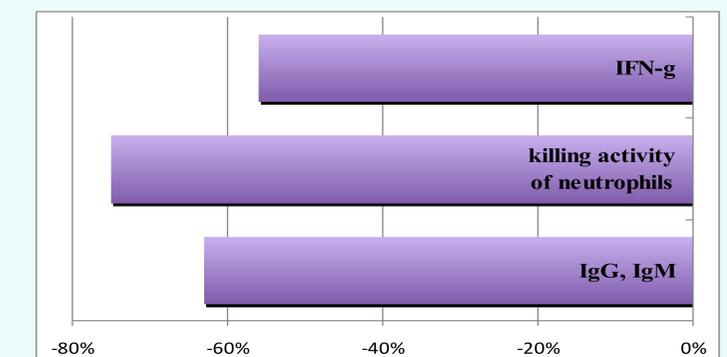


Fig.4. Values of the functional activity of cells is expressed as percentage of healthy peoples levels

Conclusions

Hematological patients after allo-HSCT with invasive aspergillosis have significant disorders of the immune response.

