To study the prognostic value of immunological parameters in hematological patients with invasive aspergillosis.

Methods

We observed 48 hematological patients with invasive aspergillosis (IA) after cytostatic chemotherapy. The median age of patients was 46 years (range 18-78), males - 20%.

Group I: 36 patients, who had complete remission IA during the 12-month observation period and antifungal therapy was stopped.

Group II: 12 patients with the fatal outcome of IA.

For the diagnosis of IA criteria EORTC/MSG, 2008 were used. Immunological parameters were evaluated within 1-4 weeks after IA diagnosis, median - 14 days.

Lymphocyte subsets were determined by immunocytochemical method with using monoclonal antibody («DAKO»). Immunoglobulins levels in serum were estimated by nephelometric method for protein analyzer «Turbox plus».

Blood cell supernatants were tested for IFN-γ, IL-6, IL-10, IL-17, TNF-α, G-CSF by using an ELISA test («Cytokine», Russia). Phagocytic and killing activity of neutrophils were assessed by using C. albicans strain.

Receiver operating characteristic (ROC) analysis was performed to determine prediction rules for clinical outcome invasive aspergillosis.

Underlying diseases were: acute myeloid or lymphoblastic leukemia - 52%, chronic leukemia - 13%, lymphoma - 23%, aplastic anemia - 4%, myelodysplastic syndrome and multiple myeloma – 2% each, other – 4% (Fig. 1).

Significant immunological defects in patients with fatal outcomes were: decline the absolute number of CD8+ cells 0.25 (0.20-0.48) vs 0.50 (0.30-0.93)×10⁹/L, CD20+ cells 0.05 (0.02-0.07) vs 0.15 (0.05-0.20)×10⁹/L, and CD16+ cells 0.06 (0.03-0.10) vs 0.15 (0.09-0.26)×10⁹/L; (p<0.05) (Fig. 2).

IA was diagnosed between 5 and 50 days since last course of cytostatic therapy (median – 30).

The main sites of infection were lungs — 97%, CNS - 3%.

According to EORTC/MSG, 2008 diagnostic criteria, probable IA had 96%, proven - 4%. All patients received antifungal therapy (voriconazole, caspofungin, itraconazole and others).

Overall survival rate in 12-weeks was 91%.

Low production of IFN-γ (94 (63-229) vs 590 (240-866) pg/ml, p=0.003), TNF-α (104 (7-177) vs 388 (253-463) pg/ml, p=0.001), IL-6 (54 (14-361) vs 476 (98-619) pg/ml, p=0.04), and IL-17 (17 (5-37) vs 66 (23-170) pg/ml, p=0.03).

Neutrophils number and killer activity and immunoglobulin levels did not differ between groups.

Conclusions

TNF-α serum level may be used as a prognostic marker for 12-weeks survival. TNF-α cut off < 215 pg/ml at baseline predicts adverse outcome IA with high probability (sensitivity - 82% and specificity - 83%, (p=0.03), and AUC of the ROC was 0.795 (Fig. 3).