

P1264

Paper Poster Session VI

Fungal epidemiology

Prognostic value of TNF-alpha serum level in haematological patients with invasive aspergillosis

O. Shadrivova¹, E. Frolova¹, L. Filippova¹, A. Uchevatkina¹, T. Bogomolova¹, A. Volkova², M. Popova², L. Zubarovskaya², N. Vasilyeva¹, B. Afanasyev², N. Klimko¹

¹North-Western State Medical University named after I.I.Mechnikov, Saint-Petersburg, Russia

²R.Gorbacheva Memorial Institute of Children Hematology and Transplantation I. Pavlov State Medical University, Saint-Petersburg, Russia

Objectives: To study the prognostic value of immunological parameters in hematological patients with invasive aspergillosis (IA).

Methods:

We observed 48 hematological patients with IA after cytostatic chemotherapy (acute myelo- or lymphoblastic leukemia - 52%, chronic leukemia – 13%, lymphoma – 23%, aplastic anemia – 4%, myelodysplastic syndrome and multiple myeloma – 2% each, other – 4%). The median age of patients was 46 years (range 18-78), males – 20 %. We investigated immunological parameters in 36 patients, who had complete remission IA during the 12-month observation period and antifungal therapy was stopped, and 12 patients with the fatal outcome of IA. For the diagnosis of IA criteria EORTS/MSG 2008 were used. Immunological parameters were evaluated within 1-4 weeks after IA diagnosis, median - 14 days. Lymphocyte subsets, neutrophil killer activity, immunoglobulin levels, production of IFN- γ , IL-6, IL-10, IL-17, TNF- α , G-CSF were examined. Receiver operating characteristic (ROC) analysis was performed to determine prediction rules for clinical outcome invasive aspergillosis.

Results: In 48 patients proven IA had 4%, probable - 96%. The main sites of infection were lungs — 97%, CNS - 3%. All patients received antifungal therapy. Overall survival rate in 12-weeks was 91%. 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, p=0,03), CD20+ cells (0,05 (0,02±0,07) vs 0,15 (0,05±0,20) × 10⁹/L, p=0,02), CD16+ cells (0,06 (0,03±0,10) vs 0,15 (0,09±0,26) × 10⁹/L, p=0,01), 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, ?=0,001), IL-6 (54 (14±361) vs 476 (98±619) pg/ml, ?=0,04), and IL-17 (17 (5±37) vs 66 (23±170) pg/ml, ?=0,03). Neutrophils number and killer activity and immunoglobulin levels did not differ between groups.

TNF- α serum level may be used as a prognostic marker for 12-weeks survival. TNF- α cut off < 215pg/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.

Conclusion: We identified significant immunological defects in the patients with a fatal outcome as compared with a favorable outcome of IA. Low TNF- α serum level < 215pg/ml after initiation of treatment may be early predictor of mortality in invasive aspergillosis.