PROGNOSTIC FACTORS IN MULTIPLE MYELOMA

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Multiple myeloma(MM) is a malignant hemopaty with heterogeneous clinical symptoms, patient development being influenced by many clinical, biological, molecular and cytogenetic factors. Median survival of patients is between a few months after diagnosis and over 10 years, with a median of about 4 years. Patients with reduced survival should be identified and monitored more closely for specific therapy to receive, perhaps even individualized in the future. The main objective of our study is to identify and analyze as many prognostic factors in patients with multiple myeloma.

The thesis is divided into two parts: a general part and a special part. In general part are the current issues in the specific literature on multiple myeloma and information on the influence of prognostic factors on survival of patients. The special part is personal research.

Material and methods: In this study we analyzed prognostic factors in a number of 111 patients who were diagnosed within the Hematology Department of the Medical Clinic no.1 of the County Clinical Emergency Hospital Targu-Mures during 1996-2012. At first, we analyzed the factors related to the host: age, male gender and performance status. Then we investigated factors related to tumor mass and intrinsic malignancy: creatinine value, hemoglobin value, platelet count, the calcium value, the percentage of plasma cells in the bone marrow, the β2-microglobulin value, MM type, the stage of disease, the albumin value and lactate dehydrogenase. Also on a group of 16 patients we analyzed the prognostic value of CD56 expression. We analyzed the influence of complications on patient evolution: infections and acute renal failure. Each prognostic factor was separately studied and it was correlated with other studied prognostic factors. We also investigated their influence on the response to therapy.

The used statistical tests were: Fisher's exact test, dispersion analysis, Kaplan Meier curves, log-rank test, Gehan-Breslow-Wilcoxon test and proportional hazard regression. Data were statistically analyzed using Graph Pad Prism 5 software and IBM SPSS version 20.0.

Results: The mean age was 64 years with a range between 38 and 88 years. The patients often secreted immunoglobulin G (63.06% of cases) and were in the stage III of disease (76.57% of cases). Median survival of analyzed group was 18 months and median survival without relapse of disease was 13 months. In our study the median survival of patients was adversely influenced by the values at diagnosis of the following factors: the age over 60 years, ECOG status ≥ 3, the creatinine above 2 mg/dl, hemoglobin level below 10 g/dl,

number of 150.000/mmc platelets, calcium value above the normal range, more than 40% plasma cells in the bone marrow, the albumin less than 3.5 g/dl, LDH supernormal values, advanced stage of disease, of MM IgA type or MM with light chains.(p <0.050) Regarding β2-microglobulin and ISS stage, they also significantly influenced the patient survival.(p <0.050) Patients with negative CD56 expression had indefinite survival, and those with positive CD56 expression had a median survival of 42 months.(p > 0.050) Acute renal failure has significantly influenced the survival, the patients with this complication having lower survival.(p<0.050) The patients, who completely responded to therapy, had a significantly better survival compared to those with partial response and those without therapeutic response.(p<0.050) The factors, which have independent prognostic value on survival, are: the age, the performance status, the number of plasma cells in the bone marrow, the LDH, albumin, creatinine, β2-microglobulin and ISS disease stage. Free time progression disease was adversely influenced by the low performance status, the calcium above the upper limit of normal, the bone marrow plasma cell infiltration than 40%, the supernormal value of LDH and by MM IgA.

The value at diagnosis of the following factors: the amount of albumin, the creatinine, hemoglobin level, performance status, bone marrow plasma cell infiltration, advanced stage of disease and β2–microglobulin had a negative statistically significant influence on the overall and complete response to therapy.

Patients older than 60 years had the following negative prognostic factors: the increased bone marrow plasma cell infiltrate, the poor performance status, the low serum albumin and the advanced stage of disease.The patients having a large numbers of plasma cells at diagnosis, with a low albumin and creatinine level, showed low haemoglobin, low advanced disease and low platelet level. In case of the patients with low haemoglobin and platelet there were high marrow plasma cell infiltration, low albumin and advanced stage of disease. In our study the patients with increased β2-microglobulin level had low performance status, low albumin, creatinine and calcium increased value. CD56 negative patients had an increased β2-microglobulin and creatinine level in a large percentage of cases.

Conclusions: Increased values of creatinine, β2-microglobulin, bone marrow plasma cell infiltrate, advanced disease, poor performance status and low albumin and hemoglobin are negative prognostic factors in development of multiple myeloma patients, adversely affecting response rates to therapy and reducing patient survival.

Adversely influence on survival of patients with multiple myeloma have the following studied factors: age, type MM IgA and MM light chains, decreased platelet count, elevated serum calcium and lactate dehydrogenase, lack of complete response and acute renal failure.

Key words: multiple myeloma, survival, prognostic factors, response to therapy.