

ZAP-70 PROGNOSTIC FACTOR IN B-CHRONIC LYMPHOCYTIC LEUKEMIA

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Background: ZAP-70 is a protein tyrosine kinase who belongs to the Syk -ZAP-70 protein tyrosine kinase family and is normally expressed on T and natural killer cells, having an important role in initiation of T cell signaling. ZAP -70 has a role in growth signal receptor cells on the surface immunoglobulin of malignant B lymphocytes and its measurement can serve as a surrogate marker for mutational status of immunoglobulin heavy chain gene. This protein has important prognostic value in B-cell chronic lymphocytic leukemia.

Methods: We studied 30 patients with B-cell chronic lymphocytic leukemia, who were diagnosed and treated in the Medical Clinic I, who were analyzed by flow cytometry for ZAP-70 expression. Using Kaplan-Mayer curve we calculated the survival of these patients and we made correlations with other prognostic factors: age, sex, hemoglobin value, lymphocytes count, platelets count, serum LDH of diagnosis, and Binet stage of disease.

Results: Of the 30 patients in which ZAP-70

expression was detected, we had 22 (73.3%) patients with ZAP-70 negative, lower than 20%, and 8 (26.6%) patients with ZAP- 70 positive, greater than 20%. Median survival was 60 months for the patients with ZAP-70 positive and indefinitely for the patients ZAP-70 negative. (Log-rank test p=0, 04) ZAP-70 positive patients had more frequent at diagnosis, lymphocytes count more than 30.000/mm³, hemoglobin value below than 12 g / dL, advanced stage of disease, Binet C, and marrow infiltration with lymphocytes more than 80%, statistically significant data. In the group with ZAP-70 positive patients, we obtained the percentage of complete remission rate lower than ZAP-70 negative patients. Percentage of partial remission was slightly higher in ZAP-70 positive subgroup, but overall remission (CR + PR) was higher in the ZAP-70 negative group. With the Fisher Exact test we checked the correlations but we obtained not statistically significant data. Number of patients who needed treatment was 10 (33,3%), nine(40,9%) patients in ZAP-70 negative group and one(12,5%) patient in ZAP-70 positive group.(p=0, 40). Most patients (75%) who had ZAP-70 positive, had also CD 38 positive.

Conclusions: ZAP-70 determined by flow cytometry is a significant predictive factor in both progression and survival in patients with chronic lymphocytic leukemia.