THE VALUE OF THE ALL CHILDREN' PROGNOSIS ACCORDING TO THE METAPHASES TYPE

Corina NAGY[1]

[1],,Babes-Bolyai" University Cluj-Napoca, Faculty of Biology

INTRODUCTION

The cancer disease's genetics allow us to obtain some fundamental knowledge in the study of the biology of tumors. The chromosomal abnormalities, the rearrangements of chromosomes, the deletions, the aberrations constitute a study object by means of which new information on the genes involved in cancer can be obtained and their involvement in oncogenesis.

The nowadays tendencies in pedriatic oncology have in view the supervision of the oncologic disease at its debut by the help of the most advanced hematologic, immunologic and cytogenetic techniques, the purpose being the diagnosis establishment and the decision towards a treatment adequate to the malignant disease which will finally lead to the patient's survival.

In this study we examined a group of children diagnosed with acute leukemia living in Bihor county and in the surrounded areas.

MATERIALS AND THE METHOD

During 1997-2003 in the cytogenetic laboratory of The Clinical Hospital of Children from Oradea a karyotype analysis was made to 26 patients susceptible of lymphoid leukemia (ALL) following clinical and hematological findings.

The children came from the oncology hospital-section of The Clinical Hospital of Children, Oradea and of The Pedriatic Clinic U.M.F. Timişoara. The patients are 1 to 15 years old. The majority of the cases were investigated before the introduction of the therapy.

The biological substance used was the lymphocyte culture from the hematogene bone marrow and the peripheral blood.

In order to prepare the bone marrow samples we used the direct method of 24 h and 48 h cell-culture in the RPMI 1640 culture medium, the Giemsa-banding with tripsininisary and the karyotyping according to Denver scheme.

The investigated patients are classified in three categories according to the chromosomal differences. By the presence or the absence of an abnormal clone and by the proportion of abnormal cells, they can be classified into:

- normal = NN, all the metaphases are cytogenetically normal;
- -normal/abnormal = NA, cells with or without chromosomal abnormalities in the same time;
- -abnormal = AA, all the cells are cytogenetically abnormal.

In order to value the ALL-patients prognosis we used the survival and the remission curve by means of Kaplan Meier method (13). The survival curves have a decreasing fragmented line form because the cumulative survival is mentioned actually in the decease moment and remains between the successive deceases. The graphic reaches to zero only if the longest survivor patient has died, but if he is still alive, the survival curve is plotted from the last decease until the final part of the research.

A point with a special value in the survival curve plots the median survival.

The median survival represents the moment in which the survival percentage reaches 50%. If more than a half of patients are cured, there is no such point on the survival curve and the median is indefinite (13). I plotted the remission and the survival curves of the ALL patients with NN, NA and AA metaphases.

In this graphics analysis there can be noticed a cumulative survival of 33% and a cumulative remission of 35% for the patients showing normal metaphases and a median duration of survival and remission of 36, respectively 20 months. Those with normal and abnormal metaphases show almost the same percentage as the first group, that is a cumulative survival of 31% and a cumulative remission of 21% with a median duration of remission of 24 months, while the median duration of survival outruns the previous group's value, that being of 63 months.

For the ALL group of patients showing only abnormal metaphases, the situation is more dramatic, because all the patients have died until the end of interval of time. The median duration of remission and survival is of 7, respectively, 13 months from their registering moment.

The patients with abnormal metaphases have the gloomiest prognosis.

The general analysis of these groups using these criteria is to the advantage of the groups with normal metaphases, but optimistic results can be obtained also for those with mixed metaphases. The first mentioned group has the most survivors, and the second has a median duration of survival showing a favorable prognosis.

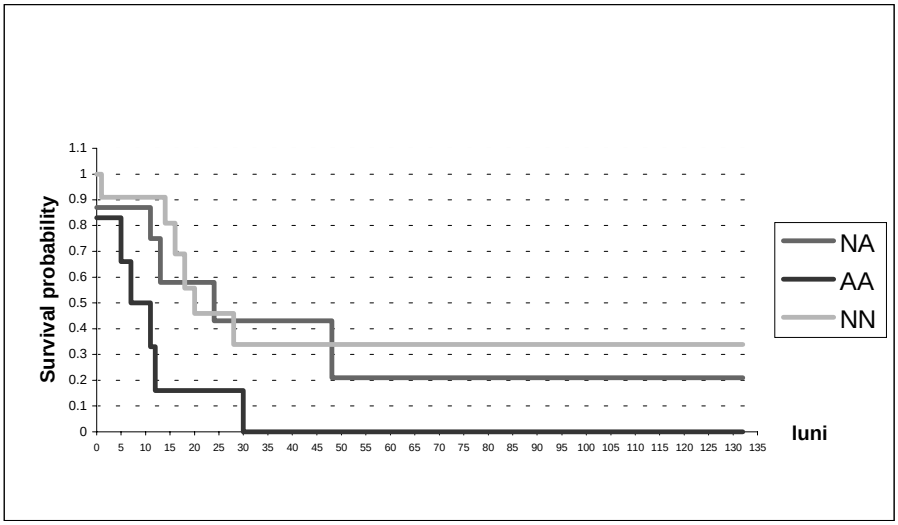

Fig. 1 Remission curves of patients from subgroups with NA, AA, NN karyotipe

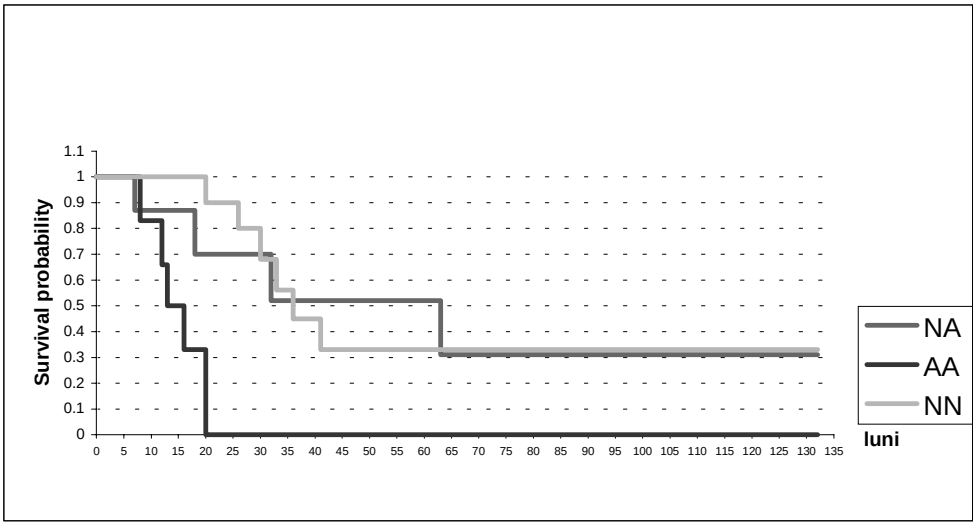

Fig. 2 Survival curves of patients from subgroups with NA, AA and NN karyotype

CONCLUSIONS

The duration of the survival of the ALL children with an NN karyotype (normal cells) and an NA karyotype (normal/abnormal) has a prognosis superior to those with an AA karyotype (abnormal metaphases).

The patients whose karyotype has only abnormal metaphases (AA) are included in the pseudodiploids category, having specific translocations and/or structural abnormalities, features that establish an inauspicious evolution of the disease.

We obtained a cumulative survival of 33% and a cumulative remission of 35% for the children with a NN karyotype (normal metaphases); those with mixed NA metaphases have a cumulative survival of 31%

and a cumulative remission of 45%. These results emphasize the advantage of these groups in comparison with those with a AA karyotype whose cumulative survival is zero at the end of the studied duration.

The longest median duration of remission and survival can be noticed at the mixed metaphases NA group, with a median remission of 24 months and a survival of 63, followed by the group with normal metaphases, NN, whose median duration of survival is 36 months and a median remission of 20 months.

For a better statistic analysis we need to spread this study in other counties and geographic areas.

This research and mostly the introduction of the cytogenetic analysis in the pedriatic oncology prove the utility and the broadening of new perspectives in leukemia's study, in order to approach the ethiology and the treatment of the cancer disease.

BIBLIOGRAPHY

An International System for Human Cytogenetic Nomenclature (ISCN) 1987. Cytogenetic Cell Genetic 21: 309, 1987.

Bain BJ, Leukemia Diagnosis: A Guide to the FAB Classification. Gower Medical Publishing, London, 1990.

Balogh E, Olah E, Kovacs I. Pronostic value of chromosome aberation in childhood acute lymphoid leukemia. Acta Pediatrica Hungarica, 30, 1990.

Bleyer WA. Acute lymphoblastic leukemia in children, advances and prospectus. Cancer 65:689, 1990.

Bleyer WA. University of Texas M.D. Anderson Cancer Center, Division of Pediatrics, Houston 77030, USA. The U.S. pediatric cancer clinical trials programmes: international implications and the way forward,Review,23 refs.European Journal of Cancer, 33,9:1439-47, 1997.

Bunin GR. Feuer EJ. Witman PA. Meadows AT. Increasing incidence of childhood cancer: report of 20 years experience from the greater Delaware Valley Pediatric Tumor Registry.Paediatric & Perinatal Epidemiology, 10,3:319-38, 1996.

Dos Santos Silva I. Cancer Epidemiology-Principles and Methods. International Agency for Research on Cancer Lyon, France, 1-11, 57-87, 277-305,1999.

Greaves MF, Colman SM, Beard ME, et al. Geographical disrtibution of acute lymphoblastic leukemia subtypes: second report of the collaborative group study. Leukemia ,7:27,1993.

Fourth International Workshop on chromosomes in Leukemia. A prospective study of acute non-lymphoblastic leukemia 1982 (IV. IWCL).

Cancer Genetics Cytogenetic, 11:249, 1984.

Greaves MF, Pegram SM, Chan LC Collaborative group study of the epidemiology of acute lymphoblastic leukemia subtypes. Background and first report. Leukemia Res,9:715,1995.

Heim S, Mitelman F. Cytogenetic analisys in the diagnosis of acute leukemia . Cancer supplement ,70, 6: 1701-1708, 1992.

ISHCN: An International System for Human Cytogenetic Nomenclature. Cytogenetic Cell Genetic 21:309, 1978

Isabel dos Santos Silva. Cancer Epidemiology. Principles and Methods. International Agency for Research on Cancer, Lion, France, 48-70:266-275. 1999.

Kaspers G.J.L., smets L.A., Pieters R., Van Zantwijk C.H., Veerman A.J.P. Farorable prognosis of hyperdiploid common acute lymfoblastic leukemia may be explained by sensitivity to antimetabolites and other drugs : results of an in vitro study – Blood , 85, 3:751-756, 1995.

Katano N, Tsurusawa H, Hiroto T, Horikashi Y, Mimaya J, Iwai T, Kaneko Y, Tsuji Y, Fujimoto T. Cytogenetic abnormality and prognosis in childhood acut myeloblastic leukemia . Children's Cancer and Leukemia Study Group . Rinsho Ketsueki (Japan), 38,8:647-656,1997.

Kowalczyk R, Grossi M, Sandberg AA: Cytogenetic findings in childhood acute lymphoblastic leukemia. Cancer Genetics Cytogenetics, 15: 47, 1985.

Mitelman F. Catalog of Chromosome Aberration in Cancer.5th Ed.New York, Wiley-Liss,1994.

Morphologic, Imunologic and Cytogenetic (MIC) Working Classification of the Acute Lymphoblastic Leukemias. First MIC Cooperative Group (I.MIC). Cancer Genetics Cytogenetics 23:189, 1986.

Morphologic, Imunologic and Cytogenetic (MIC) Working Classification of the Acute Myeloid Leukemias. Second MIC Cooperative Group (II.MIC). British Journal Haematology 6:487, 1988.

Oshimura M, Freeman AI, Sandberg AA. Chromosome and causation of human cancer and leukemia.XXVI. Banding studies in acute lymphoblastic leukemia (ALL). Cancer 40:1161, 1977.

Ross JA. Severson RK. Pollock BH. Robison LL. Childhood cancer in the United States. A geographical analysis of cases from the Pediatric Cooperative Clinical Trials groups. Cancer. 77,1:201-7, 1996 .

Rowley JD, Testa JR. Chromosome abnormalities in malignant hematologic diseases.Adr. Cancer Resarce, 36;103-110,1982.

Secker-Walker LM. The prognostic implications of chromosomal findings in acute leukemia. Cancer Genetics Cytogenetics 11:233, 1984.

Second MIC Cooperative Study Group. Morphologic, imunologic,and cytogenetic (MIC) Working classification breakpoint in acute myeloid leukemias. Cancer Genetics Cytogenetics,30:1-15,1988.