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Clinical and Epidemiological Observations on Acute Lymphoblastic Leukemia Subtypes at the Sheba Medical Center, Israel

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A. Introduction

Childhood lymphoproliferative disorders have multifactorial etiologies, in which environmental and genetic factors play a major role in determining the age distribution, clinical presentation, and course of the disease. Most of the data, however, are indirect. The gradual appearance of the 3–5 years age peak of common ALL in developed countries and its absence in developing countries and the marked decrease in the incidence of alpha heavy chain disease in Israel are two examples of changes in patterns of disease that can be attributed to environmental factors.

As Israel is a relatively small country with a heterogeneous population, good medical facilities, and central cancer registry, it lends itself for such studies. Furthermore, the Gaza Strip is an ideal region for such studies as marked improvement in socioeconomic status has occurred there during the past decade. Most probably related to these socioeconomic changes is a decrease in the frequency of Burkitt's lymphoma with a concomitant rise in acute leukemia [1].

The present communication is a summary of our experience of acute lymphoblastic leukemia (ALL) subtypes between 1978 and 1981 – a period when cell markers were routinely performed in our center [2].

B. Patient Characteristics and Results

Fifty-two patients will ALL were diagnosed and treated in our center and 49 of them could be classified. Thirty were Arabs from the Gaza Strip and 19 were Jews; 42 were children below the age of 16 and seven were adults. The markers used to classify the patients and the distribution into subtypes are presented in Table 1. In both ethnic groups 30% of the patiens were T-cell ALL and two-thirds had poor risk clinical criteria [3]. The subdivision of the cases according to number of risk factors is given in Table 2.

Table 1. Immunological subtypes of the ALL patients

T-cell		
Definite	13	E^+; mediastinal mass 7/13
Probable	3	E^-; mediastinal mass 3/3; high ADA
	16	
Non-B, Non-T		
Common ALL	10	E^-; sIg^-; $CALLA^+$
Pre-B	4	E^-; sIg^-; cIg^+
Null	5	E^-; sIg^-; cIg^-; $CALLA^-$
Partially characterized	14	E^-; sIg^-
	33	

Table 2. Distribution of patients according to risk factors

Risk factors[a]	0	1	2	3	4
No. of patients	17	9	12	10	1

[a] 1, WBC $> 50 \times 10^9$/liter; 2, Age $< 2 > 10$ years; 3, Mediastinal tumor; 4, T-cell ALL; 5, CNS leukemia

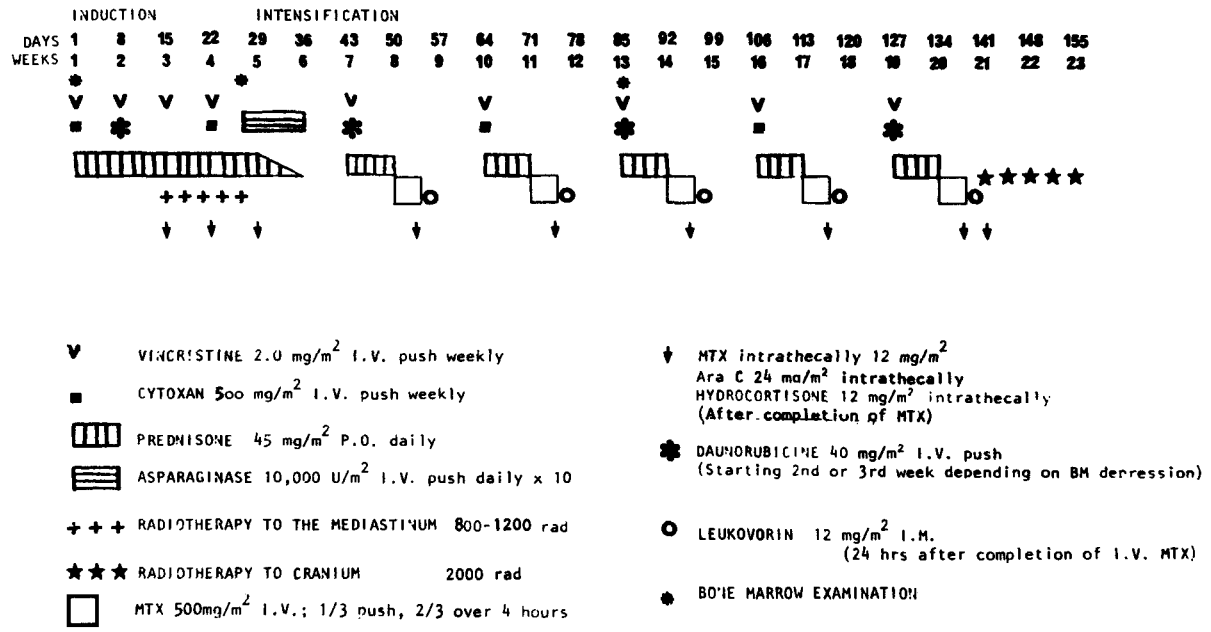

Fig. 1. Treatment protocol for high-risk and other types of ALL and generalized lymphosarcoma

Since 1975, we have used, in addition to the standard immunological markers, adenosine deaminase (ADA) levels as a marker of T-cell ALL [4, 5]. In the present series of patients significant differences in the ADA activity between T-cell ALL and non-B, non-T ALL were confirmed: 44.8 ± 6.3 vs 24.3 ± 3.2 μmol/h per 10^8 cells; $P < 0.0005$. However, the activity of the second purine metabolism enzyme, nucleoside phosphorylase (NP), was not found to differ between the two groups [6].

Our previous observation that Arab children with acute leukemia succumbed within 2 years [3], and the fact that the frequency of acute leukemia among them rose, prompted us to set up a more aggressive protocol for the treatment of poor-risk patients. The details of this protocol are given in Fig. 1. Sixteen children with high-risk leukemia were treated by this protocol – all attained a complete remission, but four relapsed and died of their disease during the 1st year and one died of an unrelated cause. Eleven patients have been in continuous complete remission for 8–55 months. When we analyzed our high-risk patients according to various prognostic factors such as ethnic group, age, initial white cell count, mediastinal tumor, T-cell markers, it was found that out of the seven patients with high ADA four died, while none of the eight patients with ADA levels below the mean of the group (40 μmol/h per 10^8 cells) died of the disease. So it seems from our preliminary data that ADA is an independent risk factor and should be studied in a larger group of high-risk ALL patients [7].

C. Conclusions

Our experience from the Sheba Medical Center would indicate the following: a decrease in the incidence of Burkitt's lymphoma and the increase in ALL in the Gaza Strip Arab children seen in the past decade is most likely due to the socioeconomic development in the Gaza Strip. The present incidence of ALL in this area is about 4 in 100,000 which is similar to that reported from developed countries. Moreover, in this population the minimal estimate of the frequency of T-cell ALL is 30%, which is significantly higher than in Western populations but similar to the observed frequencies in American blacks [8]. However, while in the American blacks the high frequency of T-cell ALL is relative as there is a low incidence of non-T, non-B ALL in the Gaza Strip Arabs, the incidence of ALL is similar to developed countries and so it seems that there is an absolute increase in T-cell ALL.

A similar incidence of T-cell ALL was found in Jews but as we have no country-wide data, no epidemiological conclusions

can be drawn at the present time on the frequency of T-cell ALL in the Jewish population. Such an epidemiological study is ongoing.

As most of our patients are in the high-risk category, we had to introduce an aggressive and intensive chemotherapy protocol. Using this protocol 60% of our patients are in remission – results as good as seen in low-risk cases [3]. ADA activity appears to be an independent risk factor so it would be of great importance to obtain additional data on other populations.

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