Medical Journal of the
Islamic Republic of Iran

Volume 2
Number 4
Zemestan 1367
Jamadiolawwal 1408
Winter 1988

IMMUNOLOGICAL PHENOTYPING OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN UNIVERSITY AFFILIATED HOSPITALS: A PRELIMINARY REPORT ON 50 PATIENTS

S.Z. TABEI, M.D.,* AND Z.AMIRGHOFRAN, M.S.**

From the Depatment of Pathology, Shiraz University of Medical Sciences, School of Medicine, Shiraz, Islamic Republic of Iran, and the Tarbiat Modarres University**, Tehran, Islamic Republic of Iran.*

ABSTRACT

The peripheral blood and bone marrow samples from 50 patients with ALL were investigated by indirect immunofluorescent technique. The most common type of ALL was common-ALL (82%) and the least common was T-ALL (2%). Other subtypes of ALL were unclassified by our technique (8%), B-ALL (4%), and pre B-ALL (4%). The correlation between immunophenotype, clinical condition and hematological profile is discussed.

MJIRI, Vol. 2, No. 4, 259-261, 1988

INTRODUCTION

After skin cancer, leukemias and lymphomas are the most common malignancies in the southern parts of Iran.[1] Among the leukemia group, the incidence of the lymphocytic type isslightly higher than the granulocytic type and acute lymphoblastic leukemia (ALL) is the most common type of malignancies in children.[2,3]

Recent advances in immunology have led to important insights into lymphocyte differentiation and the cellular origin of ALL. Now, it is well recognized that the identification of the lymphoblast's surface markers, or immunological phenotyping of ALL has provided important information in the diagnosis, prognosis and treatment of these patients.[4,5]

The purpose of this study is to report the immunological subtypes in 50 patients obtained from hospitals in Shiraz from November, 1987 to June, 1988. Also we have provided some information about morphology of the blast cells, sex, age, symptoms, and clinical findings of the patients.

MATERIALS AND METHODS

Peripheral blood and bone marrow samples from 50 patients with clinically and hematologically verified acute lymphoblastic leukemia were obtained from hospitals in Shiraz. The samples were analysed by indirect immunofluorescent technique, using specific monoclonal antibodies that define cell surface antigens. The monoclonal antibodies used were anti HLA-DR, Anti-B lymphocyte antigen, anti-T lymphocyte antigen, antimyelo/monocytic antigen and anti-cALLA. These were combined with more traditional cell markers such as surface membrane immunoglobulins (SmIg), and sheep erythrocyte receptors on T lymphocytes, and also cytochemical stains such as PAS and Sudan black B.[6,7]

RESULTS

The data from this study show that common-ALL is the most common phenotype of ALL at the present time in this area. About 82% of all cases and 88.6% of childhood-ALL are classified as common-ALL. 8% of cases were unclassified, 4% were B-ALL, 4% were pre B-ALL and 2% were of T-cell origin. The relative incidence of immunological subtypes of ALL are presented in Table I.

79.2% of all cases were morphologically L2 type, 10.4% were L1 type, 6.2% were L3 type, and 4.2% were acute unclassified leukemia (AUL).

The majority of patients with C-ALL (84.6%) were

Table I. The relative incidence of immunological subtypes of ALL.

Phenotype	Subtype	No. patients	Percent
CALLA$^+$, Dr$^+$, B.Ag$^+$, SmI.g$^-$, T.Ag$^-$, ER$^-$, myelo/monocytic Ag$^-$ CALLA$^+$, Dr$^+$, B.Ag$^-$, SmI.g$^-$, T.Ag$^-$, ER$^-$, myelo/monocytic Ag$^-$.	Common- ALL	41	82
CALLA$^-$, Dr$^+$, B.Ag$^+$, SmI.g$^-$, T.Ag$^-$, ER$^-$, myelo/monocytic Ag$^-$	Pre B-ALL	2	4
CALLA$^-$, Dr$^+$, B.Ag$^+$, SmI.g$^+$, T.Ag$^-$, ER$^-$, myelo/monocytic Ag$^-$	B-ALL	2	4
CALLA$^-$, Dr$^-$, B.Ag$^-$, SmI.g$^-$, T.Ag$^+$, ER$^+$, myelo/monocytic Ag$^-$	T-ALL	1	2
CALLA$^-$, Dr$^-$, B.Ag$^-$, SmI.g$^-$, ER$^-$, myelo/monocytic Ag$^-$	Unclassified	4	8
Total		50	100

cALLA: Common acute lymphoblastic leukemia antigen; Ag: Antigen; SmI.g: surface membrane immunoglobulin; ER: E-Rossette;

reported to have the L2 morphologic form, whereas only 10.2% had the L1 type, and 2.5% the L3 type. One case of C-ALL was morphologically L3 type.

The majority of patients with C-ALL (88.6%) were aged 1-12 years. 66% of all cases and 65.8% of patients with C-ALL were male. With cytochemical staining all cases were Sudan black-B negative, and about 51% of all cases and 51.2% of C-ALL were PAS-positive. All cases of B-ALL were PAS negative.

As summarized in Table II, an analysis of clinical data recorded in 50 patients shows that fever and pallor are the most common symptoms; and splenomegaly (70.8%), hepatomegaly (66%) and lymphadenopathy (60.4%), are the most common clinical findings.

About 7.1% of all patients and 5.8% of C-ALL cases had mediastinal mass, and none of the patients whose charts were available had a testicular mass. A study of the patients' charts showed that CNS involvement was found in 40% of all cases and in 40% of C-ALL cases. The range of WBC count was from 1100/mm^3 to 370, 000/mm^3, and about 18.7% of cases had WBC counts above 50,000/mm^3. WBC counts in all cases of the unclassified group were above 80,000/mm^3.

DISCUSSION

The common classification of ALL is based on the FAB system, which defines three categories of ALL with regard to the morphology of the blast cells. This classification has a limited value for significant diagnosis, prognosis, and treatment of patients with ALL. Even cytochemical stainings are not very valuable.[8,10]

The most useful method of classification of subtypes of ALL depends on cell membrane markers. In this method we can divide ALL into 4 subtypes. First, common-ALL, which is the largest group and the blast cells in this category are cALLA-positive. Second, B-ALL, in which cells are of mature B-cell origin and have surface membrane immunogloblins. Third, T-ALL, in which cells are of T-cell origin, and the fourth group, Null-ALL or unclassified in which cells are SmIg, E.Rosette, and cALLA-negative.[2,11] Recent advances in monoclonal antibody production and gene rearrangement have indicated that all cases of Null-ALL are of B-cell origin.[12-15] Thus new classifications of ALL have been suggested. In our study we had five groups of patients. Three groups were patients with

Table II. Clinical presentations of ALL.

Clinical Findings	Total %	C-ALL %
Mediastinal mass	7.1	5.8
Lymphadenopathy	60.4	57.5
Splenomegaly	70.8	70
Hepatomegaly	66	64.1
CNS Involvement	40	40
WBC> 50,000/mm^3	18.7	12.8
Platelet < 50,000/mm^3	34.7	42.5
Hb < 8g/dL	60.9	63.1

C-ALL, B-ALL and T-ALL, which we could recognize easily by monoclonal antibodies against cALLA, B-Ag, and T-Ag. However we had some difficulties with other groups: 8% of cases were negative for all of the monoclonal antibodies which we used, so we called them an unclassified group. Also, in 4% of cases, cALLA and SmIg were negative but B antigen was positive. We could not classify them as B-ALL (because of absence of SmIg) and C-ALL (because of absence of cALLA), so we classified them as pre-B-ALL. Our study shows that common-ALL is the most common type of ALL, and T-ALL is the least common especially in children. Only one of 50 patients had T-ALL (2%).

In contrast with foreign reports, the majority of patients with C-ALL (84.6%) were reported to have the L2 morphologic form, whereas only 10.2% had the L1 type.[2,11] Although all cases of ALL were Sudan black-B negative, about half of all the cases and 51.2% of the C-ALL group were PAS-positive. This matter shows that these stainings are not very significant for the diagnosis of ALL. In comparison with foreign reports with a high incidence of mediastinal mass in patients with ALL, only about 7.1% of all patients had mediastinal mass in this study. This may be because of the very low incidence of T-ALL in this area, as mediastinal mass is very common in T-ALL.[2]

ACKNOWLEDGEMENT

We would like to thank the Mostazafan Foundation for providing monoclonal antibodies and Zahra Shahmanesh for typing the manuscript.

REFERENCES

1. Iranian Cancer Society Reports, Fars Province Cancer Registry. 1978-1981.
2. Theil E, Thier Felder: Recent results in cancer research. Leukemia, 102: 128-33, 1984.
3. Nelson Textbook of Pediatrics, Philadelphia, W.B. Saunders, 1085-1087, 1987.
4. Foon K A, Todd R F: Immunological classification of leukemia and lymphoma. Blood 68: 1-31, 1986.
5. Fisleder A J, Lucas F V, et al: Immunophenotypic characterization of acute leukemia by immunocytology. J Clin Pathol 81: 611-7, 1984.
6. Rose N: Manual of Clinical Laboratory Immunology. 219-22, 1986.
7. Civin C I, Daltito K L, Karen V: Flow cytometric analysis of human bone marrow. Normal B lymphocyte development. Blood 70: 1316-24, 1987.
8. Harrison's Principles of Internal Medicine, New York. McGraw-Hill 1542-8, 1987.
9. Hoelzar, Gale RP: Acute lymphoblastic leukemia in adults. Recent progress, future directions. Semin Hematol 24: 27-39, 1987.
10. Marrer A M, Rivera G K: Controversies in the management of childhood acute lymphoblastic leukemia. Semin Hematol 24: 12-26, 1987.
11. Wintrobe: Clinical Hematology. Philadelphia, W.B. Saunders, 1493-513, 1981.
12. Fugger L, Paltz P, Ryder L: Immunological reclassification of 22 children with a former diagnosis of non-T, non-B-ALL. Eur J Haematol 39: 369-75, 1987.
13. Adrianson H, Bartram C R, Vandongen J: T-cell receptor CD3 complex during early T-cell differentiation, analysis of immature T-cell actue lymphoblastic leukemia (T-All) at DNA, RNA and cell membrane level. J Immunol 138: 1260-9, 1987.
14. Nadler L M, Korsmeyer SJ, Anderson KC, Boyd AW, Slaughenhoupt B, Park E, et al: B cell origin of non-T cell acute lymphoblastic leukemia. A model for discrete stages of neoplastic and normal pre-B cell differentiation. J Clin Invest 74 (2): 332-40, 1984.
15. Korsmeyer SJ, Arnold A, Bakhshi A, Ravetch JV, Siebenlist U, Hieter PA, et al: Immunoglobulin gene rearrangement and cell surface antigen expression in actue lymphoblastic leukemias of T cell and B cell precursor origins. J Clin Invest 71(2): 301-13, 1983.