THE CD 10 MARKER IN THE INVESTIGATION OF ACUTE LYMPHOBLASTIC LEUKAEMIA

Lt Col HARSH KUMAR*, Lt Col RAJAT KUMAR†,
Lt Col R RANGA RAO‡, Maj Gen JR BHARDWAJ, vsm**

ABSTRACT

Immunophenotyping of leukaemias is presently well established. It is invaluable for proper case management [1]. The most useful information on the management of cases of Acute Lymphocytic Leukaemia (ALL) is provided by the detection of the CD 10 marker on the leukaemic cell. The CD 10 positive ALL has since long been associated with a favourable prognosis as compared to the CD 10 negative ALL [1,2]. As immunophenotyping is resource intensive, the monoclonal antibodies (MO ABS), are not in widespread use in our country. The expenses involved make this procedure prohibitive in most institutions. For this reason, a limited panel of MO ABS has been used in this study, with a special emphasis on the CD 10 marker. A total of 25 cases of ALL were studied. 17 cases were found to be positive for the CD 10 marker (68%). These cases were associated with a favourable prognosis as compared to the CD 10 negative group. Although, the diagnosis of ALL and leukaemias in general, is essentially based on the study of Romanowsky stained smears [3,4], the additional information provided by the cell surface marker study results in better case management [1].

MJAFI 2002; 58 : 27-29

KEY WORDS : Common ALL Antigen; Immunophenotyping; Surface markers.

Introduction

Advances in the study of white blood cell markers have led to greater understanding of the leukaemic cell. These surface markers can be precisely defined using monoclonal antibodies enabling a more accurate classification of leukaemias [1,5]. A vast panel of monoclonal antibodies are presently available, however, their major utility lies in the classification of acute lymphoblastic leukaemias. They can be broadly placed in B cell group, T cell group, non B non T cell group and the null cell group [1].

In 1975, the common ALL antigen (CALLA) or the CD 10 marker was discovered and was found to be positive in majority of cases of ALL. These cases were termed non B non T cell ALL. Further studies showed that most of these cases of ALL are malignancies of precursor B cell, and these precursor B cell ALLs were found to have a favourable prognosis [1,6,7].

Material and Methods

25 cases of ALL were studied. They were diagnosed on the criteria laid by the French-American-British (FAB) Cooperative study group [3,4]. In addition to study of Romanowsky stained blood films, cell surface marker study was carried out on blood and bone marrow smears using the alkaline phosphatase anti-alkaline phosphates (APAAP) technique [8,9]. Apart from CD 10, a limited panel of surface markers for B cells (CD 19, CD20) and T cells (CD2, CD7) were also used.

A positive reaction was seen as a cell having a red staining of an intensity greater than that seen in the background (Fig-1). The criterion for surface marker positivity was its expression in at least 20% of the leukaemic blast cells [10]. The patients were treated using standard chemotherapeutic regimens, till both haematological and clinical remission was achieved and then the cases were consolidated accordingly and followed up. The final outcome of the cases was correlated with CD 10 positivity.

Results

There were a total of 25 cases of ALL. These included 15 children and 10 adults. Out of these, 14 cases were FAB L1 subtype and 11 FAB L2 subtype. CD 10 positivity was seen in 17 (68%) out of the 25 cases of ALL. These 17 cases comprised 12 childhood ALLs and 5 adult ALLs.

As per the FAB classification, the childhood ALL (n=15) were

Fig. 1 : APAAP staining of leukaemic cell with MO ABS. A positive reaction is seen as red staining around the cell.

*Classified Specialist (Pathology), Transfusion Centre (Eastern Command), Calcutta, †Classified Specialist (Medicine & Haematology), Army Hospital (R&R), New Delhi, ‡Classified Specialist (Medicine & Oncology), INHS, Ashvini, Mumbai, **Addl DGAFMS, New Delhi.

mostly of the FAB L1 subtype (n=9), while adult cases of ALL (n=10) were largely of the FAB L2 subtype (n=7).

Following chemotherapy, it was observed that CD 10 positive children achieved remission by 30-45 days, while in CD 10 positive adult ALL this period ranged from 30-96 days. In most of these cases, there was a disease free period for at least 14 months after achieving remission. The exceptions were, an infant aged 3 months who died during the induction phase of chemotherapy and a child who died of septicemia consequent to pneumonitis. These patients survived for 25 and 32 days respectively. The details are shown in Table 1 and 2.

TABLE 1

Immunophenotyping of childhood ALL and response to chemotherapy

Immunophenotype	FAB subtype		Response to chemotherapy
	L1	L2	
CD 10+ CD 19+ and/or CD 20+	8	4	Remission by 30-45 days. Two deaths. An infant on day 25 and a child on day 32. Others disease free 14 months after remission.
CD 10- CD 19+ and/or CD 20+	1	1	Remission in 36 and 111 days respectively. Relapse after 8 and 10 months respectively.
CD 10- CD 2+ and/or CD 7+	-	1	Remission after 113 days, relapse after 8 months

TABLE 2

Immunophenotype of adult ALL and response to chemotherapy

Immunophenotype	FAB subtype		Response to chemotherapy
	L1	L2	
CD 10+ CD 19+ and/or CD 20+	1	4	Remission achieved in 30-96 days. Then disease free for period for at least 14 months.
CD 10- CD 19+ and/or CD 20+	1	2	No remission in 2 cases. Third had remission in 5 wks and relapse in 3 months.
CD 10- CD 2+ and/or CD 7+	1	1	No remission

The CD 10 negative group comprised mostly adults. A low remission rate was achieved in these cases, and the relapse rate was high. It is of interest to note that in this study, all cases which were CD 10 positive, belonged to the group of precursor B cells. They were positive for CD 19 and/or CD 20 or both. The CD 10 negative cells belonged both to the precursor B ALL (n=4) and T cell ALL (n=3). The latter showed positivity with CD 2 or CD 7 or both. There were no cases of CD 10 positive T cell ALL.

Discussion

Immunophenotyping of leukaemias is well established. The major utility of this procedure lies in the classification of ALL [1]. The CALLA or the CD 10 was discovered in 1975 and was observed in majority of cases of ALL which were of the non B non T cell type. Subsequently, these cases were observed to be neoplasms of the precursor B cells. The CD 10 positive precursor neoplasms were associated with a fa-

vourable prognosis [6,7].

In this study, a total of 25 cases of ALL were studied. There were 17 cases of CD 10 positive ALL and 8 cases of CD 10 negative ALL. The overall incidence of CD 10 positivity works out to 68%. The incidence of CD 10 was somewhat higher in children (80%). Other workers have put the overall incidence of CD 10 around 70% [3,6]. A study at Tata Memorial Hospital described CD 10 positive ALL as the commonest ALL type in our country [11]. The CD 10 positive ALL has been found to have better rate of remission and a subsequent disease free period as compared to the CD 10 negative ALL [1,2,7]. Poor prognosis in CD 10 positive infantile ALL is well known [12]. CD 10 positive T-ALL fares as badly as CD 10 negative T-ALL [2,6]. The CD-10 marker therefore serves as an important tool for the management of ALL. The corollary to this is that a more aggressive chemotherapy or bone marrow transplantation can be considered.

To conclude, the laboratory diagnosis of ALL essentially rests on Romanowsky stained blood and bone marrow smears. However, the use of MO ABS forms an important aspect in defining the subtypes of ALL. The CD 10 marker has been shown to be associated with a favourable prognosis. In our country, and other third world countries, MO ABS are not in widespread use due to the high costs involved. Nevertheless, by using a limited panel of MO ABS which includes CD 10, additional data can be provided to improve patient management. The aim of this study was to highlight that even a limited panel of MO ABS can be of immense utility to identify basic subsets of ALL and as a corollary offer better patient care.

References

1. Foon KA, Todd RF. Immunologic classification of leukaemia and lymphoma. *Blood* 1986;68:1-31.
2. Vannier JP, Bene MC, Faure GC, Bastard C, Garand R, Bernard A. Investigation of CD 10 CALLA negative acute lymphoblastic leukaemia : further description of a group with a poor prognosis. *Br J Haematol* 1989;72:156-60.
3. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DAG, Gralnick HR, et al. Proposals for classification of acute leukaemias. *Br J Haematol* 1976;33:451-8.
4. Bennett JM, Catovsky D, Daniel MT, Flandrin G, Galton DAG, Gralnick HR, et al. Proposed revised criteria for the classification of acute myeloid leukaemia : A report of the French-American-British cooperative group. *Ann Intern Med* 1985;103:620-5.
5. Maheu M, Baker MA, Falk JA, Taub RN. Immunologic diagnosis and monitoring of acute myeloid leukaemias. *Am J Pathol* 1981;103:139-58.
6. Greaves MF, Janossy G, Peto J, Kay H. Immunologically defined subclasses of acute lymphoblastic leukaemia in chil-

- dren : their relationship to presentation features and prognosis. *Br J Haematol* 1981;48:179-97.
7. Boowitz MJ. Immunological marker in childhood acute lymphoblastic leukaemias. *Haematology/Oncology clinics of North America*. 1990;4:743-65.
 8. Cordell JL, Falini B, Erber WN, Glosch AK, Abdulaziz Z, Macdonald S, et al. Immunoenzymatic labeling of monoclonal antibodies using immune complexes of alkaline phosphatase, antialkaline phosphatase (APAAP Complexes). *J Histochem Cytochem* 1984;32:219-29.
 9. Erber WN, Mynheer LC. APAAP labeling of blood and bone marrow samples for phenotyping leukaemias. *Lancet* 1986;i:761-5.
 10. Hanson CA, Gajl-Peezalskak J, Parkin JL, Brunning RD. Immunophenotyping of acute leukaemia using monoclonal antibodies and the alkaline-antialkaline phosphatase technique. *Blood* 1987;70:83-9.
 11. Kamat DM, Gopal R, Advani SH, Nair CN, Kumar A, Saikia I, Nadkarni JJ, Nadkarni JS. Pattern of subtypes of acute lymphoblastic leukaemia in India. *Leukaemia Research* 1985; 9(7):927-34.
 12. Crist W, Pullen DJ, Boyett J et al. Clinical and biologic features predict a poor prognosis in acute lymphoid leukaemia in infants : A paediatric oncology group study. *Blood* 67:1-11.