ACUTE LEUKAEMIA IN CHILDREN - FRENCH-AMERICAN-BRITISH (FAB) CLASSIFICATION AND ITS RELATION TO CLINICAL FEATURES

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ABSTRACT

A retrospective study of 45 patients of acute leukaemia in children (15 years age), in relation to FAB classification, is presented. Acute lymphoblastic leukaemias (ALL)were commoner than acute myeloid leukaemias (AML), with an ALL:AML ratio of 4.63:1. Amongst ALL, Li was the most frequent type (59%), followed by L2 (35%) and L3 (5.4%), respectively. FAB types M2, M3, M4 and MS were diagnosed in 2 patients each. An analysis of clinical features in relation to FAB classification is also presented (JPMA 42: 29, 1992).

INTRODUCTION

Leukaemias are amongst the commonest cancers under fifteen years age, constituting 13-30% of all the cancers diagnosed in this age group[1,2]. In children, acute lymphoblasticleukaemia (ALL) is the most frequent form, accounting for approximately 80% of leukaemias. Acute myeloid leukaemia is the next commonest (17%), with chronic myeloid leukaemia (CML) and juvenile CML constituting the remainder[3]. Acute leukaemias are usually classified according to French- American-British (FAB) classification. ALL is classified into three types, designated L1, L2 and L3[4]. In order to differentiate between L1 and L2, ascoringsystem based on nuclear: cytoplasmic ratio, cell size, character of nuclear membrane and number of nucleoli, has been devised[5]. In L3, lymphoblasts are large and contain moderate to abundant basophilic, PAS negative cytoplasm which shows distinct vacuolation. FAB Li is the most frequent and is associated with the most livourable prognosis. L2 is less common and has a relatively poor prognosis[6]. L3 is rare and is considered by some as a haematogenous phase of Burkitt\'s lymphoma[7,8]. AML can be classified according to FAB system into seven subgroups, designated as Mi, M2, M3, M4, M5, M6 and M7. FAB Mi to M3 are peroxidase and sudan black positive. M4 and M5 can be diagnosed by strongly positive NSE with partial (M4) or complete (M5) inhibition with sodium fluoride[9]. The FAB classification system appears to have a prognostic value6. Patients with Li morphology have both a higher induction rate as well as more prolonged remission duration and survival. Patients with L2 morphology have a poor prognosis and this feature has been reported by some to function as an independent prognostic variable whereas patients with L3 disease have the worst prognosis[10]. Although the FAB classification may have prognostic usefulness, no biologic basis for the morphologic differences among these cell types have been elucidated. In this study, we have performed a retrospective analysis of 45 patients of acute leukaemias in children (<15 years) with reference to FAB classification and the presenting clinico-haematological features.

PATIENTS AND METHODS

A retrospective study of 45 leukaemic children diagnosed at Rawalpindi Medical College, during 1987

-1990, was undertaken. A detailed account of clinical features was recorded in a proforma with special emphasis on fever, pallor, bleeding from various sites, lymphadenopathy, hepatomegaly and splenomegaly. Laboratory investigations included Hb estimation by cyanmethaemo- globin method, white cell and platelet leucocyte count after staining the smear by May-Grunwald-Giemsa Stain. Bone marrow aspiration was performed at posterior superior iliac spine in most of the patients; however, in children less than twoyears age, marrowwas aspirated from tibia, below the tibial tuberosity. The smears were stained by May-Grunwald-Giemsa stain, periodic acid schiff stain (Sigma) and myelo-peroxidase stain (Sigma). When PAS and peroxidase were negative, a smear was also stained with naphthyl acetate esterase (NAE) stain. For diagnosis and classification of acute leukaemias, FAB classification was followed. In case of ALL, scoring was performed on the basis of nuclear: cytoplasmic ratio, cell size, outline of nuclear membrane and prominence and number of nucleoli. A score of 0 to + 2 led to the diagnosis of Li whereas a score of-i to -4 established L2. L3 was diagnosed when blast cells were large and contained moderate to abundant vacuolated PAS negative cytoplasm.

RESULTS

In a total of 160 patients of various types of leukaemia diagnosed at pathology department of Rawal-pindi Medical College, from 1987 to 1990, 47 (29.4%) were children (<15 years of age). Among these children 45 manifested acute leukaemias, whereas 2 had juvenile CML The breakup of patients of acute leukaemias is given in Table I, which also shows sex distribution of various subtypes. Acute lymphoblastic leukaemias were more common (82%) as compared to acute myeloid leukaemias (i8%). Amongst ML, Li was the commonest subtype (59%) followed by L2 (35%) and L3 (5.4%) respectively. FAB subtypes M2, M3, M4 and MS were diagnosed in 2 patients each.

Age distribution

In ALL-Li, 4i% of patients were between i and 4 years of age and 50% between 6 and 14 years. In L2 patients, 30% were between i and 3 years and 70% between 5 and i4 years. The age representation of the remaining FAB subtypes is given in Table I.

TABLE I. Age distribution in various FAB subtypes of acute leukaemias.

Age	L1	L2	L3	M2	M3	M4	M5	Total
6-9 months	-	-	-	-	-	-	1	1
1 year	-	-	-	-	-	-	1	1
1-2 years	2	2	-	-	-	1	-	5
2-3 "	3	2	-	-	-	-	-	5
3-4 "	4	-	-	-	-	-	-	4
4-5 "	1	-	-	-	1	-	-	2
5-6 "	1	3	1	1	-	1	-	7
6-8 "	4	-	1	-	1	-	-	6
8-10 "	3	1	-	-	-	-	-	4
10-12 "	2	4	-	1	-	-	-	7
12-14 "	2	1	-	-	-	-	-	3

Sex distribution (Table II)

TABLE II. Acute leukaemias according to FAB classification and sex representation.

	ALL N=37			AML N=8				
	L1	L2	L3	M2	M3	M4	M5	Total
Males	9	8	2	1	2	1	2	25
Females	13	5	-	1	-	1	-	20
Total	22	13	2	2	2	2	2	45

L1 was commoner in females (M:F ratio 1:1.44), whereas L2 was more common in males (M:F ratio 1.6:1).

TABLE III. Presenting clinical features in ALL (L1 and L2) and AML patients.

Clinical features	L1 %	L2 %	AML %
Fever	100	100	100
Pallor	100	100	100
Bleeding gums	73	27	88
Ecchymoses	53	16	75
petechiae	16	16	25
Epistaxis	16	5	37
Lymphadenopathy	100	100	50
Hepatomegaly	68	75	75
Splenomegaly	90	91	100

Clinical features (Table III) Fever and pallor were invariably observed as presenting features in all the types of leukaemia. Bleeding manifestations, especially bleeding from gums and ecchymoses, were more frequent in Li as compared to L2 subtype. Both the patients of M3 manifested severe forms of bleeding; one of them died of cerebral haemorrhage before the treatment could be started.

Laboratory Investigations

Hb concentration: Mean values of fib level were 5.6 G/dl(+1.43 S.D.) in Li, 5.5 G/dl (±132 S.D.) in L2 and 6.0 G/dl (± 1.42 S.D) in AML patients. White cell count: Amongst the 22 Li cases, 9 showed white cell count below4.Ox 109/1, 5 between 4.1 x 109/1 and 11.0x 109/1 and8 between i2.5x 109/1 and 25.5 x 10~/1. in a total of 13 L2 cases, 4 had a white cell count below 4.0 x 109/1, 6 between 4.1 and 8.0 x i09/I and3 between 11.5x109/1 and 18.8x109/1. In AML (8 patients), only one showed a TLC less than 4.0x 109/1, two between 4.1x 109/1 and 8.Ox 109/1 and the remaining 5 between 12.0x 109/1 and 40x 109/1. Platelet count (Table IV): Variable degree of thrombocytopenia was invariably present. Itwas more severe in AML patients. The degree of thrombocytopenia correlated with bleeding manifestations.

DISCUSSION

FAB classification of acute leukaemias is now widely accepted. In children, acute lymphoblastic leukaemia (80%) is commoner than acute myeloid leukaemia[3]. In ALL patients, Li is the commonest, followed by L2 and L3, respectively. Zafar reported a series of 80 patients of ALL in children in Karachi; 55% of them had Li and 40% L2 subtype[11]. Alvi et al a study of 36 children having ALL, have observed Li in 92% and L2 in 8%[9]. In both these series L3 was not observed. In other childhood series, the incidence of L1 has ranged between 71% and 85%, whereas L2 was from 14% to 25%[12-14]. In the present series, ALL: AML ratio was 4.63:1. In ALL, Li was the commonest subtype (59.5%), followed by L2 (35.i%) and L3 (5.4%) respectively. These results are in agreement with those presented by Zafar[11]. L1 was more common in females, whereas L2 was commoner in males. In a total of 8 patients of AML, two had M2, two M3, two M4 and two MS. Both the patients of MS were under 1 year of age. Whereas FAB classification system itself has prognostic implications[6], there are certain additional features which have been shown to act as prognostic indicators in various types of acute leukaemias. The age at diagnosis and initial leucocyte count have been the two most reliable indicators of prognosis, both for remission rate and survival[14]. The relationship between the initial count and prognosis is linear; the patients with a high count have a worse prognosis[14,15]. An age less than two years and more than ten years, at diagnosis, is an indicator of a relatively poor prognosis[10]. In Miller's series, good prognosis or low risk patients were between 3 and 7 years of age[14]. In the present series, 24% of Li and L2 patients were below three years, 30% between 3 and 7 years and the remaining 46% more than 10 years of age. Therefore, only 30% of our patients corresponded to the good prognosis group of Miller's series. Further, in our patients, the initial leucocyte count was less than 10.0 x 10^9/1 in 64% of L1 and 45% of L2 patients. In this series, patients of ALL invariably presented with fever, pallor and lymphadenopathy. Bleeding manifestations were more common in AML than in ALL. Amongst the ALL patients, bleeding from gums and ecchymoses were more frequent in Li as compared to L2. Splenomegaly was equally frequent in Li (90%) and L2 (91%) subtypes, whereas hepatomegaly was slightly more frequent in L2 (75%) than in Li (68%). In AML, fever, pallor and splenomegaly were invariable; hepatomegaly was observed in 75% and lymphadenopathy in 50% of patients. Bleeding manifestations were slightly more frequent as compared to ALL patients. Both the patients of AML-M3 showed severe bleeding manifestations; one of them presented with intracerebral haemorrhage and died before the treatment could be started.

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