Acute Leukemia at King Hussein Medical Center: A Retrospective Review

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ABSTRACT

Objective: To describe certain characteristics of acute leukemia regarding age, gender, cytomorphology and immunophenotype at King Hussein Medical Center.

Methods: A retrospective review of bone marrow aspirate and/or biopsy reports was conducted at Princess Iman Research and Laboratory Sciences Center at King Hussein Medical Center during the period between Jan 2004 and Dec 2008. A total of 226 patients were studied regarding: age, gender, and cytomorphologic and immunophenotypic diagnosis. The age was categorized into two groups (≤14 years as children group and >14 years as adult group). Descriptive analysis using frequencies was used to describe the study variables. This study was conducted to study and analyze acute leukemia cases in children and adults in King Hussein Medical Center over the past five years.

Results: One hundred thirty-eight (61%) cases were males and 88 (39%) were females. Their ages ranged between three months and 80 years. A total of 102 (45%) patients were children ≤ 14 years old and 124 (55%) patients were > 14 years old. Acute lymphoblastic leukemia constituted 75% of all childhood leukemias, the majority (83%) were of B-cell phenotype mainly CD10+ve Precursor B-cell Acute lymphoblastic leukemia (74%); only 17% of the childhood acute lymphoblastic leukemia was of T-cell phenotype. Acute myeloid leukemia constituted 80% of all adult leukemias; most of the cases were of the French-American-British M2 morphological subtype (34%).

Conclusion: Distribution and patterns of acute leukemia differs between children and adults. While CD10+ve Precursor B-cell acute lymphoblastic leukemia was predominant in children, acute myeloid leukemia M2 was prevalent in adults.

Key words: Acute lymphoblastic leukemia, Acute myeloid leukemia, Bone marrow aspirate

Introduction

Acute leukemia is a malignant proliferation and accumulation of immature lympho-hematopoietic cells.[1] It represents a very aggressive, malignant transformation of an early hematologic precursor. The malignant clone is arrested in an immature, blast form, proliferates abnormally, and no longer has the ability to undergo maturation. In contrast, chronic leukemias are characterized by resistance to apoptosis and by accumulation of nonfunctional mature cells.[2] Leukemia is the most common childhood cancer.[3] Acute lymphoblastic (also

termed lymphocytic or lymphoid) leukemia (ALL) is the most common pediatric cancer, accounting for 30% of all pediatric malignancies.[4,5]

According to the National Cancer Institute, the age-adjusted overall incidence of ALL in the United States was 1.6 per 100,000 (1.8 in males and 1.4 in females). The incidence is higher in whites than in blacks. After an initial peak in children younger than five years of age (8.3 per 100,000), the incidence decreases continuously. It increases again above the age of 65 to a second peak in the age group above 85 years (2.0 per 100,000). The incidence of acute myeloid leukemia (AML) is relatively constant during childhood, with slight peaks in the first two years of life and in late adolescence.[1]

Both ALL and AML are heterogeneous diseases that comprise different biologic subtypes.[6-8] Classification of the phenotype of the blast cells in acute leukemia requires morphologic and cytochemical evaluations, immunophenotyping, cytogenetic, and molecular genetic studies. However, morphology remains the mean by which acute leukemia is initially detected and, together with cytochemical reactions, is the major tool in distinguishing between ALL and AML.[1,9]

This study was conducted to study and analyze acute leukemia cases in children and adults at King Hussein Medical Center over the past five years.

Methods

A retrospective review of bone marrow aspirate and/or biopsy reports was conducted at Princess Iman Research and Laboratory Sciences Center at King Hussein Medical Center during the period between January 2004 and December 2008. A total of 226 patients were studied regarding age, gender, cytomorphologic and immunophenotypic diagnosis. The patients were categorized into two groups according to age (≤14 children and >14 adults). Bone marrow aspirate smears were stained with May-Grunwald-Giemsa stain and immuno-phenotypic analysis using flowcytometry was done. Both of these tests are prerequisites for classification of acute leukemia by WHO criteria. Bone marrow biopsies of at least 1cm length with immuno-histochemical studies were also included for diagnosis in the majority of cases. The following markers were studied: CD34, HLA-DR, TdT as Hematopoietic precursors; CD13, CD33, MPO, CD117 as Myeloid precursors; CD14, CD11c, CD11b, CD64, CD68 as Monocytic lineage markers; Ab to HbA, Glycophorin A as Erythroid lineage markers; CD41, CD61 as Megakaryoblastic Lineage markers; CD19, CD20, CD22, CD79a, CD10 as B cell Lineage markers and CD2, CD3, CD7 as T cell Lineage markers. Marrow blast count of 20% was sufficient for acute leukemia diagnosis. The French-American-British (FAB) classification was used to classify AML, while the World Health Organization (WHO) classification was used to classify ALL.

Results

A total of 226 bone marrow aspirate and biopsy reports were studied, 138 (%61) were males and 88 (39%) were females. Their ages ranged between three months to 80 years. A total of 102 (45%) cases were children (age ≤ 14 years) and 124 (55%) were above 14 years.

Table I shows, the age and gender distribution of ALL and AML among the study group. ALL cases constituted 75% of patients in the children's group and 20% of the patients in the adults group. ALL occurred in 47% of males, however 80% of those above 14 years had AML and females constituted 58%.

Table II presents the age distribution of ALL immunophenotypic diagnosis among the study group. CD10+ve precursor B-cell ALL constituted 74%, however CD10-ve precursor B ALL were 9% of the children's group. Among the adults 64% had CD10+ve precursor B-cell ALL and 12% had CD10-ve precursor B ALL. Precursor T ALL was more in among the adult group (24% vs. 17%).

Table III illustrates the age distribution of AML FAB classification among the study group. AML FAB M1 was the commonest (28%), while M0 and M5 were 4% respectively among those ≤ 14 years. AML FAB M2 constituted 34% and M0 were 6% in those > 14 years. In both age groups, AML FAB M6 was not reported.

Discussion

Leukemia accounts for 300,000 new cases each year (2.8% of all new cancer cases) worldwide.[10] Unlike leukemia in adults, childhood leukemia is acute in the vast majority of cases.[1] Our study showed that ALL is the most common childhood leukemia, representing about 75% of acute leukemia, whereas it comprises only 20% of adult acute leukemia. AML accounts for 80% of all cases of adulthood acute leukemia as shown in Table I.

Table I. Age and sex distribution of ALL and AML

Variables	Number of bone marrow samples	Number of ALL cases (%)	Number of AML cases (%)
Age group			
≤ 14 years	102	77 (75)	25 (25)
>14 years	124	25 (20)	99(80)
Gender			
Males	138	65 (47)	73 (53)
Females	88	37 (42)	51 (58)

Table II. Age distribution of ALL immunophenotypic diagnosis

Age group	Number of ALL cases	CD10+ve precursor B ALL n (%)	CD10-ve precursor B ALL n (%)	Precursor T ALL n (%)
≤ 14 years	77	57 (74)	7 (9)	13 (17)
>14 years	25	16 (64)	3 (12)	6 (24)

Table III. Age distribution of AML FAB classification

Age group	No. of AML cases	M0 No. (%)	M1 No. (%)	M2 No. (%)	M3 No. (%)	M4 No. (%)	M5 No. (%)	M6 No. (%)	M7 No. (%)
≤ 14 years	25	1	7	6	2	5	1	0	3
		4	28	24	8	20	4	0	12
>14 years	99	6	15	34	17	18	8	0	1
		6	15	34	17	18	8	0	1

This is supported by a study from El Salvador and Mexico city between 1996 and 2000, which reported that the frequency rates leukemias for the Salvadoran group of 0-11 year olds were 34.2, 7.1, 0.6, 0.2, and 43.2 per million children for ALL, AML, CML, UL (unspecified leukemia), and total leukemia, respectively.[11] Al-Barazanchi et al. from Iraq found that out of sixty-four newly diagnosed ALL cases, 61% were children (age<15 years), while 39% were adults (age 15-45 years). Al-Barazanchi et al. also addressed the relation between ALL and gender, he found that males constituted 43 cases and females 21 cases with male to female ratio 2 : 1.[7] This is similar to a recent study done in the central region of Tunisia by Jmili et al. in 2004 about the epidemiologic and cytological characteristic of 193 patients with acute leukemia, who addressed the predominance of males (ratio 1.27 : 1) and reported that 72% of acute leukemia in children less than 10 years of age was of the lymphoblastic type.[12] In our study we found that males are generally affected by acute leukemia more often than females in all age groups with male to female ratio 1.76 : 1 in ALL and 1.43 : 1 in AML. Freedman et al. studied age-specific rates of leukemia by gender in Jordanian population between 1996-1998 and found that patients 10-29 years have no sex predilection, while those <10 years or ≥30 years have male predominance.[13]

The FAB Cooperative Group distinguishes three ALL groups (L1 to L3) based on morphologic criteria.[6] The WHO proposed new guidelines for the diagnosis. In addition to lowering the blast count to 20% as sufficient for an ALL diagnosis, the morphologic distinction of L1, L2, and L3 morphologies is abandoned as no longer relevant. The WHO classification of ALL divides the disease into precursor B-cell, precursor T-cell, and Burkitt-cell leuke mia. Although FAB classification system relies heavily on morphological assessment, the recent WHO International panel on ALL recommends that the FAB classification be abandoned, since the morphological classification has no clinical or prognostic relevance. It instead advocates the use of the immunophenotypic classification.[2] In our study, CD10+ve precursor B- cell ALL is by far the most common immunophenotype of ALL in all age groups, constituting 74% and 64% for childhood and adulthood ALL respectively as shown in table II. This agrees with one study from Nordic Countries in which Hjalgrim LL et al found that the incidence rate of B-cell childhood ALL is about 10 times more than T-cell ALL.[14] Hann et al. who analyzed the immunophenotype of children treated on the Medical Research Council United Kingdom ALL Trial XI (MRC UKALLXI) found that T-cell ALL constitutes only 10.7% of ALL cases.[15] An Italian study done by Consolini et al. in 1998 found that CD10 was positive in 95.6% of patients with B-lineage ALL.[16]

There are two current systems to classify AML. In

the WHO classification, the blast threshold for the diagnosis of AML is reduced from 30 to 20% blasts in the blood or marrow. In addition, patients with the clonal, recurring cytogenetic abnormalities t(8;21)(q22;q22), inv(16) (p13.1;q22), or t(16;16) (p13.1;q22) and t(15;17)(q22;q12) should be considered to have AML regardless of the blast percentage.[9] The FAB classification is also used and classifies AML into eight subtypes.[2,14] FAB M5 and M7 are more common in early childhood, whereas older children are more likely to have M0, M1, M2, M3.[6] Our study showed that FAB M1, M2, and M4 were the predominant in childhood AML, comprising 28%, 24%, 20% respectively. On the other hand, adulthood AML were mainly FAB M2 (34%), while M4 and M3 were less common constituting 18%, 17% respectively as shown in Table III.

Conclusion

Childhood and adulthood acute leukemia differ significantly in distribution. While, CD10+ve precursor B-cell ALL which has good outcome is most common in children, AML M2 is predominant in adults, which accounts for the worse prognosis of adulthood acute leukemia.

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