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Clinical Presentation and some Laboratory Findings During Four Years' Experience of AML Children

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Abstract

Acute myeloid leukemia comprises only 15% to 20% of acute leukemia in children. It remains a challenging disease with an inferior treatment outcome in comparison with acute lymphoblastic leukaemia (ALL).

This study aimed to document the clinical presentation and some lab. findings in children with Acute Myeloid Leukemia (AML) treated in the Child's Central Teaching Hospital (CCTH) in Baghdad / Iraq.

This retrospective study was conducted at CCTH in Baghdad, during the period from 1_{st} January 2009 to 31st December 2012 on 49 cases who were diagnosed as AML. Down syndrome (DS) and acute promyelocytic leukemia (APL), with undifferentiated leukemia were excluded from this study.

The average age of presentation was 5 years, and the median duration of symptoms was 4 weeks, with male (M): female (F) ratio = 1.13:1. Eleven patients not received treatment either died or lost follow-up. The most common presenting feature was fever & pallor in 100% followed by bleeding in 69%. Initial white blood cell count (WBC) > of 100×10^9/L was seen in 30.6% of patients. It can be concluded that there was slight male predominance. Most common presenting feature was fever and pallor, and the patients developed anemia (low levels of Hb%), leukocytosis (high WBC counts) and thrombocytopenia (decreased platelet counts).

Key words: AML, children, clinical presentation, Lab. Investigations

*1,2,3 Pediatric central teaching hospital/ Al-karch Health Directorate/ Ministry of Health and environment

Introduction

Acute myeloid leukemia (AML, also known as acute myelogenous leukemia) consists of a group of relatively well-defined hematopoietic neoplasms involving precursor cells committed to the myeloid line of cellular development (i.e. those giving rise to granulocytic, monocytic, erythroid or megakaryocytic elements). AML is characterized by a clonal proliferation of myeloid precursors with a reduced capacity to differentiate into more mature cellular elements. As a result, there is an accumulation of leukemic blasts or immature forms in the bone marrow, peripheral blood and occasionally in other tissues, with a variable reduction in the production of normal red blood cells, platelets and mature granulocytes [1,2]. Approximately 35% of all childhood cancers are acute leukemias, of which 15-20% is AMLs & most of others are acute (ALLs). In contrast to cure rates for ALL, those for AML have improved only moderately over the past few decades [3].

The range of presenting signs and symptoms of children with AML is exceptionally large. Patients may present with minimal symptoms or life-threatening complications due to depletion of normal bone marrow elements and organ dysfunction based on leukemic cell infiltration. Of further importance is that certain subtypes of AML have characteristic presenting signs and symptom [4].

The hallmark of acute myeloid leukemia is a reduction or absence of normal hematopoietic elements. Anemia is usually normocytic, with a reticulocyte count lower than expected for the level of the

hemoglobin. Platelet counts are usually low and generally commensurate with the degree of bleeding. WBC counts may be decreased or elevated. Numbers of mature neutrophils are usually diminished, with Auer rods are revealed in specimens of circulating blood obtained from many AML patients [5,6,7].

Patients and methods

The current retrospective study carried out in Pediatric Hemato-oncology unit in the Child's Central Teaching Hospital, Baghdad/Iraq included patients who were diagnosed during the period from 1st January 2009 to 31st December 2012 on 49 AML patients. Down syndrome and APL with undifferentiated leukaemia were excluded from this study.

The medical records of those children during the considered period were reviewed.

The patient's follow-up was taken from the record's file of the patient of the Hemato-oncology consultation clinic.

Information recording (file No., gender, residence, date of diagnosis, date of starting treatment, presenting symptoms & signs, duration of illness before diagnosis, initial finding of investigation, remission state, complications & outcome) were also collected.

For hematological investigations, venous blood samples were taken by means of disposable syringes and put in tubes containing EDTA to estimate (Hb%, WBC count and platelets counts).

The diagnosis of AML was established by clinical finding, CBC & Morphological examination of BMA only because immunophenotyping and cytogenetic studies were unavailable.

Lumber puncture for CSF cytology and cytospin were done for assessment CNS status of patients, it’s negative when there is no blast cells in CSF cytology and positive if there is identifiable blast cells.

Statistical analysis

The SPSS version 12 was used for data analysis. Chi-square test was used to identify the associations between the event free survival and studied independent variables, qualitative data were expressed as frequency and percentage, quantitative data as mean and median, P-values equal or less than 0.05 were considered significant.

Results

Results in our study showed that the age range between (0.3-13) years, with mean age at diagnosis was 5 years. Among 49 patients with AML, there were 26 (53%) males and 23 female (47%) with a male:female ratio 1.13:1. The duration of onset before diagnosis was in the range between 3 days to 6 months, and the median duration of symptoms was 4 weeks as shown in table (1).

Table (1) Age and gender distribution among AML patients

Patients characters	No.	%
Age (years)		
< 2	10	20.4
2 - 9	29	59.2
≥ 9	10	20.4
Gender		
Male	26	53
Female	23	47

Fever and pallor were observed in all of the 49 (100%) patients, followed by bleeding tendency in 34 (69%). Hepatomegaly (≥5 cm below costal margin) and splenomegaly (≥5 cm below costal margin) were recorded in 28 (57.1%) and 17 (34.7 %) patients, respectively. The number and percentage of lymphadenopathy was 14 (28.5%) followed by gone pain and Gum hypertrophy 9 (18.3%) and 2(4%) respectively, as seen in table (2).

Table (2): Clinical presentation of the studied AML patients

Clinical presentation		
Fever	49	100
Pallor	49	100
*Bleeding tendency	34	69
Hepatomegaly > 5cm	28	57.1
Splenomegaly > 5cm	17	34.7
Lymphadenopathy	14	28.5
Bone pain	9	18.3
Gum hypertrophy	2	4

***Bleeding tendency includes Petechial rash &/or ecchymosis, Gum bleeding, Epistaxis, GIT**

The initial hemoglobin reading ranged between 2.8-8g/dl, with the mean of 5.4 g/dl. The range of WBC count was between 1.3-500×10^9/L with the mean of 38.6×10^9/L. In 34 (69.4%) patients, the WBC count was below 100×10^9/L.

The platelets count ranged between 2-199×10^9/L, with the mean of 38.6×10^9/L. In 23 patients, (47%) platelets count was below 20×10^9/L.

Cytospin was negative in 26 (53%) and not done in16(32%) while it was traumatic in 7(15%) patients, as seen in table (3).

Table (3): Initial laboratory results of the studied patients

Item	No.	Percentage (%)
Hb		
<5g/dl	17	34.7
5-8 g/dl	32	65.5
WBC ($\times 10^9$/L)		
<100	34	69.5
≥100	15	30.6
Platelets ($\times 10^9$/L)		
<20	23	47
20-100	22	44.9
≥ 100	4	8.1
CNS status		
CNS negative	26	53
Not done	16	32
Traumatic	7	15

Discussion

The current study showed slight male predominance of 1.13:1 which is similar to the two studies conducted in the Pakistan by Fadoo[n] [8] and Aga Khan [9] which showed an M/F ratio of (1.87:1), and (1.3:1) respectively. The study of Khattab TM from Saudi Arabia showed slight female predominance of (0.74:1) [10].

The median age of our study was 5 years (range 0.3 year-13years) similar to Khattab TM study from Saudi Arabia of Median age of 5 years (range 0.5 year -14 years) [10]. However, they were slightly less than Fadoo [8], and Aga Khan [9], Imamura [11] findings. Median age was 8.5 years (6months – 15 years), 8 years (7 month -14.5years), 7.6 years (range 3 months-16.2 years) respectively. This might depend on the size of the sample taken and the age limits in each center.

Fever and pallor were recorded in all of the patients (100%), while other studies such as Fadoo [8], Al-Janabi [12] and Imamura [11] showed (83% and 39%), (86.44% and 85.61%), (69% and 67%) respectively, only fever was (100%) in the Aga Khan study [9], which was similar to our study, and it may attributed to uncorrected files document or it might reflect a delay in diagnosis; inadequate primary medical care results in delayed access to health professionals and in delayed recognition or misdiagnosis of the underlying symptoms of fever and/or anemia. The other relevant aspect of poor primary health care is patient vulnerability to infectious complications resulting from chronic oro-dental or cutaneous pathologies [13]. Additionally, lack of awareness of the severity of the disease and remoteness of specialist

medical care could be the other reasons for late presentation.

Bleeding tendency was presented in 34 (69%) patients which is higher than those found by Aga Khan study [9], n=13/23(56%), and Fadoo study [8] n=15/37(41%), and 37% in Pulcheri W study from Brazil [14].

Hepatomegaly and splenomegaly were recorded in 57.1% and 34.7% of our patients respectively, while in the study of Al-Janabi [12] it was n=35/59(59%) and n=35/59 (59%) respectively, but lower than AML-BFM-78 study group [15] which was 25% and 26% respectively.

Lymphadenopathy was recorded in 28.5% of our patients which is higher than n=13/59 (22%) detected in the study of Al-Janabi [12].

The median WBC count was 38.6×10^9/L, which is lower than 14.7×10^9/L in the Imamura study from Japan [11]. In our study, white blood cell count (WBC) more than 100×10^9/L was recorded in {n=15/49(30.6%)} patients, which is higher than Fadoo study [9] { n=7/37(19%)}, and Al-Janabi study [12] {n=6/59(10.17%} and Imamura study from Japan [11] {n=12/146 (8%)}, reflecting more aggressive behaviors in our AML cases or delayed onset of presentation.

All patients 49 (100%) presented with anemia with initial hemoglobin below 8g/dl, which was higher than that reported by Aga Khan [9] {n=10/23 (34.7%)} and this was probably due to delayed presentation, advanced disease at time of diagnosis and /or poor nutritional status of Iraqi children.

Initial platelets count below $<20\times10^9$/L was found in {n=23/49(47%)}, and these numbers were higher than those reported by Aga Khan [9] which was {n=9/23 (39%)}, while in the study of Al-Janabi [12] it was slightly higher {n=30/59(50.8%)} probably because of delayed and /or advanced diseases before diagnosis.

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العرض السريري وبعض النتائج المخبرية خلال أربع سنوات من الخبرة مع أطفال AML

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الخلاصة :

ابيضاض الدم النخاعي الحاد يشمل تقريبا 15٪ إلى 20٪ فقط من سرطان الدم الحاد لدى الأطفال. حيث لا يزال مرضًا صعبًا مع نتيجة علاج أقل مقارنة بسرطان الدم الليمفاوي الحاد .(ALL) **هدفت هذه الدراسة** إلى توثيق العرض السريري وبعض العوامل في الأطفال الذين يعانون من سرطان الدم النخاعي الحاد (AML) الذين عولجوا في مستشفى الطفل التعليمي المركزي (CCTH) في بغداد / العراق .أجريت هذه الدراسة في مستشفى CCTHفي بغداد ، خلال الفترة من 1 يناير 2009 إلى 31 ديسمبر 2012 حيث تم جمع 49 حالة تم تشخيصها على أنها AML. تم استبعاد متلازمة داون (DS) وابيضاض الدم النخاعي الحاد (APL) مع ابيضاض الدم غير المتمايز من هذه الدراسة .كان متوسط العمر 5 سنوات ، وكان متوسط مدة الأعراض 4 أسابيع ، مع نسبة الذكور (M):الإناث 1. 11 :1.13 = (F) مريضا لم يتلقوا العلاج ماتوا أو فقدوا المتابعة. **النتائج :** كانت الاعراض الأكثر شيوعًا هي الحمى والشحوب في 100٪ يليها النزيف في 69٪. لوحظ تعداد كريات الدم البيضاء الأولي (WBC)> 100 × 109 / لتر في 30.6٪ من المرضى. يمكن **الاستنتاج** أن هناك ارتفاع طفيف بالإصابة لدى الذكور. كانت الاعراض الأكثر شيوعًا هي الحمى والشحوب ، وقد ظهر المرضى بفقر الدم (مستويات منخفضة من الهيموغلوبين) ، زيادة عدد الكريات البيضاء (تعداد كريات الدم البيضاء المرتفعة) ونقص الصفيحات (انخفاض عدد الصفائح الدموية) .

الكلمات المفتاحية : AML , الأطفال ، الاعراض السريري ، دراسة مختبرية