

CYTOGENETIC AND MORPHOLOGICAL ANALYSIS OF DE NOVO ACUTE MYELOID LEUKEMIA IN ADULTS: A SINGLE CENTER STUDY IN JORDAN

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ABSTRACT

Acute myeloid leukemia (AML) in adults is known to be a heterogeneous disease with diverse chromosomal abnormalities. Some of these abnormalities are found with a high incidence in specific ethnic groups and in certain geographical areas. We report the results of cytogenetic studies of 35 adult Jordanian Arab patients with *de novo* AML diagnosed according to the French-American-British (FAB) criteria. Four patients did not have metaphases secondary to hypocellular bone marrow. The most common morphological subtype was M5 (55%) followed by M3 (19%). Cytogenetic abnormalities were present in 20 patients (65%); t(15;17) translocation in six patients (19%), inv(16) in four patients (13%), t(11;17) in two patients (4%), and the t(8;21) translocation was not present in any patient. Trisomy 8 was the most common numerical chromosomal abnormality [four patients (13%)].

There were variations and similarities with similar ethnic Arab populations. The most common chromosomal abnormalities were t(15;17), +8 and inv(16). Further and larger crossborder studies are needed.

Keywords: Acute myeloid leukemia (AML), Cytogenetics, Translocation, Arabs, Jordan

INTRODUCTION

Acute myeloid leukemia (AML) is a group of malignant disorders characterized by proliferation and accumulation of immature hematopoietic cells in the bone marrow and the blood. Cytogenetic findings in AML are common (50-60%) and are considered to be important prognostic and diagnostic factors [1,2].

Geographical, ethnic, and environmental influences on the clinical and biological features of AML is crucial in determining the cytogenetic and morphological features of this disease [3-8]. Reports on the cytogenetic and morphological features of AML from Arab populations are scarce [5,8,9]. Roberts *et al.* [5] reported 125 adults with AML from Saudi Arabia, where karyotypic abnormalities were seen in 104 patients (52%) and trisomy 8 being the most common abnormality. In a study from Kuwait on 45 patients with AML, chromosomal abnormalities were reported in 73%, and the most common abnormality was t(15,17) in 18% [8]. In 63 ethnic Omani patients with AML, chromosome abnormalities were present in 62%, and the most common abnormalities were t(8:21) in 11%, t(15,17) in 10% and trisomy 8 in 11% [9]. The aim of this study was to report the cytogenetic and morphological features of *de novo* AML in adult Jordanian Arabs, and to compare the results with similar ethnic Arab populations in other parts of the world.

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MATERIALS AND METHODS

The study was conducted at the King Abdullah University Hospital (KAUH), Irbid, The Hashemite Kingdom of Jordan. The KAUH is a referral hospital that serves over 1.5 million people, representing 25% of the Jordanian population [10]. Medical records of adult patients diagnosed with de novo AML were reviewed from September 2002 to April 2010. Chromosomal analysis on bone marrow aspirate was performed on 35 patients. Their age ranged from 16 to 73 years and 65% were males. Patients who had secondary AML, a previous diagnosis of myelodysplastic syndrome, or less than 16 years old were excluded. The morphological diagnosis of AML was made by a consultant hematopathologist and were based on the French-American-British (FAB) World Health Organization (WHO) criteria [11,12].

The diagnosis of AML was determined by Wright-stained bone marrow smears. Immunophenotyping of the bone marrow aspirate was performed using a panel of monoclonal antibodies (acute lymphoid and myeloid leukemia), consisting of CD11, CD14, CD15, CD33 and CD34 (myeloid markers); CD2, CD3, CD4, CD5 and CD7 (T-cell lineage markers); CD10, CD19, CD20 and CD22 (B-cell lineage markers); and cytoplasmic IgM, CD117 and TdT (pre-B-cell lineage markers).

Bone marrow aspiration samples were cultured for 24 and 48 hours without a mitogen. Conventional GTG-banding techniques were used for metaphase chromosome banding [International System for Human Cytogenetic Nomenclature (ISCN 2005-2009)] [13,14]. Cytogenetic abnormalities were identified, performed, and classified according to the ISCN 2005-2009 [13,14].

Patients were identified as having a normal karyotype only after 20 normal metaphases were analyzed. Determination of an abnormal clone required the presence of at least two metaphases with an identical structural rearrangement or an extra chromosome and/or three cells with a missing chromosome [11,13,14]. Because of the lack of facilities, we did not perform fluorescent in situ hybridization. Cytogenetic abnormalities were classified according to the type of abnormality, gain or loss of genetic material, and number of abnormalities (one, two, and three or more) [13,14]. This study was approved

by the Institutional Review Board (IRB) committee of Jordan University Hospital and King Abdullah University Hospital, Irbid, The Hashemite Kingdom of Jordan.

Statistical Analysis. An SAS version 6.2 was used for the data analysis. The chi-square test was performed, and the Yates correction was used where indicated. A p value of <0.05 was considered statistically significant.

RESULTS

Patient Data. Cytogenetic analyses were carried out on 35 consecutive adult de novo AML patients between Septembers 2002 and April 2010. Three patients did not have metaphases due to the presence hypocellular marrow with the AML and one patient had bone marrow necrosis. Thirty-one patients were included in the analysis. The median age at diagnosis was 39 years (mean 40.3 years, range 16-73 years). The male to female ratio was (65% males:35% females).

Morphological Features of Acute Myeloid Leukemia. According to the FAB classification, the morphological subtypes of AML were M5 (17 patients; 55%), M3 (six patients; 19%), M4 (four patients; 13%), M2 (three patients; 10%), and M0 (one patient; 3%). In the M5 subtype group, 12 patients were males (71%).

Cytogenetic Analysis. Cytogenetic abnormalities were observed in 20 patients (65%). Median age was 35.5 years (range 16-49 years) and male to female ratio was (60%: 40%). The most common translocation, t(15;17), was found in six patients (19%), t(11;17) (two patients; 6%), t (9;11) (one patient; 3%) and t(7;14) (one patient; 3%). The inv(16) anomaly was seen in four patients (13%), inv(11) in one (3%), inv(9) in one (3%) and inv(1) in one (3%). Trisomy 8 was the most frequent numerical chromosomal abnormality (four patients; 13%). Trisomy 22 was found in two patients (6%) and trisomy in one patient (3%). Of the losses of chromosomal material, del 7 was seen in one patient (3%) and del 11 in one patient (3%). Sole karyotype abnormalities were observed in 16/31 patients (52%) and karyotypes with combination of abnormalities were observed in 4/31 patients (13%). A few unusual abnormalities were observed in our study (Table 1).

Table 1. Analysis of the characteristics of acute myeloid leukemia patients with abnormal karyotypes.

Subject Number	Sex-Age	AML Subtype	Cytogenetic Abnormality
1	M-43	M5	22
2	M-47	M5	+8, t(9;11)(p22,q23)
3	M-34	M5	8
4	F-39	M5	t(11;17)(q23;q25)
5	M-48	M5	t(11;17)(q23;25)
6	M-44	M5	t(7;14)(q33;q32)
7	M-34	M5	8
8	F-17	M5	inv(1)(p13q32)del(7)q22;q23,del(11)(p11;q12)
9	M-16	M4	in(16)(p13;q13)/81-92 XXYY
10	F-21	M4E	inv(16)(p13;q22)
11	M-38	M4E	+8.inv(16)(p13;q23),+21
12	F-42	M4E	inv(16),+22
13	F-35	M3	t(15;17)(q22;q13)
14	F-48	M3	t(15;17)(q22;q13)
15	F-45	M3	t(15;17)(q22;q13)
16	F-19	M3	t(15;17)(q22;q13)
17	M-49	M3	t(15;17)(q22;q13)
18	M-21	M3	t(15;17)(q22;q13)

Normal karyotypes were observed in 11 patients (35%). The median age was 51 years (range 25-73 years). According to the FAB classification, nine patients had M5 and two had M2 (Table 2).

DISCUSSION

This is the first report on the cytogenetic abnormalities of *de novo* AML in adult ethnic Arabs in Jordan. The M5 anomaly was the most frequent morphological subtype. Cytogenetic abnormalities were common and observed in 65% of our patients. The most frequent balanced translocation was t(15;17) and trisomy 8 was the most common numerical chromosomal abnormality.

The median age for our patients was 39 years, which is similar to reports from other Arab populations in the region [5,8,9]. The median age in stud-

Table 2. Characteristics of acute myeloid leukemia patients with normal karyotypes.

Subject Number	Sex-Age	AML Subtype
1	F-51	M5
2	M-38	M5
3	M-63	M5
4	M-65	M5
5	M-67	M5
6	M-34	M5
7	F-34	M5
8	F-73	M5
9	M-67	M5
10	M-25	M2
11	M-49	M2

ies from western populations is in the range of 58-63 years, with the majority of patients being older than 55 years [3,15,16]. In contrast, the median age of patients at the time of diagnosis of AML tend to be younger in developing countries [5,8,9,16-19]. The explanation for the difference between age at diagnosis in patients from different geographical regions is not clear. This may be explained by the effect of ethnic, geographical and environmental factors. Similar to other studies from western countries and Arab populations there was a clear male predominance [9,15].

In this study, M5 was the most frequent morphological subtype (55%) followed by M3 (19%). In Saudi Arabia, M4 was the most common subtype (39%), in Oman it was M2 (35%) and in Kuwait it was M3 (23%) [5,8,9].

Cytogenetic abnormalities were observed in 65% of our patients, comparable to other studies from similar Arab populations (52-73%) [5,8,9], and large studies from different parts of the world (52-78%) [3,15,16]. In our study, t(15;17) was the most frequently observed balanced translocation. This was similar to that found in Kuwait [8]. Whereas in Saudi Arabia, t(8;21) was the most frequent balanced translocation [5], and t(8;21) and t(15;17) were the most frequent translocations in Oman [9]. The most frequent numerical abnormality in this study was the gain of chromosome 8 (13%), which is similar to that found in Saudi Arabia and Oman [5,9]. The inv(16) inversion was seen in 13% of our

patients, which is higher than reported in similar ethnic groups [5,8,9]. The absence of the t(8;21) translocation in our patients may be explained by the low percentage (9%) of the M2 subtype observed in this study. As with other reports, several unusual abnormalities were seen in this study.

Compared to similar reports on ethnic Arabs from the region, there were similarities and variations of the age, gender, and morphologic subtype and chromosomal abnormalities in ethnic Arabs in Jordan with *de novo* AML. The observed similarities could be explained by the common ethnic, environmental and geographic factors. Further large and crossborder studies are needed to elucidate the cytogenetic pattern of this disease, and to better understand the effects of ethnic and geographical factors that may underlie the biological diversity of AML.

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