Original article

Acute leukemias in Marrakech: epidemiology and cytological profile

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A B S T R A C T

The diagnosis of acute leukemia is based on clinical and biological arguments. The study’s objective is to describe the epidemiology and cytological characteristics of 203 cases of LA collected in the hematologic laboratory of Med VI University Hospital of Marrakech over a period of 2 years between January 1, 2016 and December 31, 2017. Morphological examination of the bone marrow, myeloperoxidase response, and immunophenotyping resulted in the classification of acute leukemias as: myeloblastic AL in 54.47% of cases, lymphoblastic AL in 43.9% of cases and 1.63% of AL were difficult to classify according to the FAB group criteria.

1. Introduction

Acute leukemias (AL): heterogeneous group of clonal hematologic disorders characterized by malignant proliferation in the bone marrow of an abnormal cell clone of hematopoietic tissue and blocked at a specific stage of differentiation with expansion of immature cells (blasts) that may be present in the peripheral blood. Two broad types of AL are defined: lymphoblastic (ALL) and myeloblastic (AML), depending on the origin of the hematopoietic precursor.

The objective of this work is to describe the cytological characteristics of acute leukemia cases collected at the Hematology Laboratory of Med VI University Hospital of Marrakech over a period of 2 years (January 2016 - December 2017).

Materials and methods:

This is a descriptive and analytical retrospective study of 203 cases of patients in whom acute leukemia was diagnosed between January 2016 and December 2017.

In our series, we included all patients of all ages, both sexes, with a acute leukemia confirmed by myelogram.

Blood samples were collected by venipuncture on tubes with EDTA K3 (ethylene diamine tetra potassium tetra acetate).

Puncture of the bone marrow has been performed in adults with sternum and posterior iliac spine in children.

The blood count was determined on the Sysmex XE-5000 i automated system, and the blood and marrow smears were stained with MGG by the conventional manual method.

For each patient, 2 independent readings of blood and marrow smears were assured and validated by 2 cytologists. The diagnosis of AL has been made when there is more than 20% of blasts in the bone marrow. Complement with myeloperoxidase (MPO) staining was done for all specimens.

The use of immunophenotyping was done by flow cytometry mainly for MPO negative marrow infiltration, and uses the BD FACSCanto II flow cytometer.

The data was collected from AL patients' files at the Hematology Laboratory of Med VI University Hospital of Marrakech. Data entry for the study was done on an Excel spreadsheet.

The statistical analysis consisted of a univariate descriptive method with calculation of percentages and averages.

The various stages of our study were carried out respecting the anonymity and confidentiality of clinical and paraclinical data of patients.
Results:
1-Cytological aspect:

Morphological examination of marrow smears and reaction to myeloperoxidase, supplemented in some cases by immunophenotyping, classified leukemias into:

- AML in 54.47% of cases, ALL in 43.9% of cases, and in 1.63% of cases it was impossible to make an accurate diagnosis.

**Figure 1:** Classification of AL according to cytological aspects and MPO staining

2-Age and sex:

- AML: The average age of the patients was 48 years old. Adults (18-80 years) were reached in 81.6% of cases and children (2-18 years) in 18.4% of cases, with an M/F sex ratio of 1.05.

- ALL: The average age of the patients was 16 years old. Adults (18-80 years) were represented in 32.7% of cases and children (2-18 years) in 67.3% of cases (sex ratio M/F: 1.2)

**Figure 2:** Distribution of patients by age

3-The clinic:

In our series, there is obvious variability of clinical manifestations, mainly represented by anemic syndrome (73% of cases), an infectious syndrome (52% of cases), whereas a syndrome of complete spinal cord failure was present in only 25% of cases.

**Figure 3:** Different clinical aspects found in our patients

4-hemogram:

In agreement with the clinical signs; the hemogram’s results show an attack of the 3 hematological lineages with a predominance of a normochromic normocytic regenerative anemia (86% of cases), and major leucocytosis (> 100000 / mm3) in 76% of cases.

**Figure 4:** Distribution of the hemogram’s results in our patients

5-The blood smear:

Examination of the blood smear had established the white blood cell count and contributed to the classification of ALs according to the FAB group. The separation between AL subgroups was based on:
- the assessment of the percentage of blasts in the marrow,
- the type of blasts,
- the absolute count of blood monocytes.

Circulating blasts were present in 86% of children and 72% of adults.

The level of circulating blasts ranged from 4% to 90%.

6-Myelogram:

AML: The study of the different types according to the FAB classification showed a predominance of AML4 and AML2: 38.8% and 25.37% respectively.

**Figure 5:** Classification of AML according to cytological aspects, and MPO staining

ALL: The complementary flow cytometry study of the cytological aspects evoking lymphoblastic leukemias, classify ALLs according to EGIL’s classification; thus type B was predominant: 76% of ALLs.
Figure 6: Classification of the ALL according to the cytological and immunophenotypic aspects

Table I: Comparison by average age in our series and other series of the literature

<table>
<thead>
<tr>
<th></th>
<th>UH Casablanca (Morocco)</th>
<th>Lower Normandy (France)</th>
<th>Brazil</th>
<th>Our series</th>
</tr>
</thead>
<tbody>
<tr>
<td>average age ALL</td>
<td>21 years</td>
<td>25 years</td>
<td>9 years</td>
<td>16 years</td>
</tr>
<tr>
<td>average age AML</td>
<td>38 years</td>
<td>63 years</td>
<td>39 years</td>
<td>48 years</td>
</tr>
</tbody>
</table>

In our series, there is a male predominance with a sex ratio H/F at any age at 1.12.

The distribution of cases by sex was comparable to that of the different series, and confirms the male predominance also found in the literature [4,5].

Table II: Comparison of sex ratio in our series and other series of literature.

<table>
<thead>
<tr>
<th></th>
<th>Madagascar (France)</th>
<th>Tunisia</th>
<th>Brazil</th>
<th>India</th>
<th>Our series</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex ratio</td>
<td>1.38</td>
<td>1.26</td>
<td>1.27</td>
<td>1.48</td>
<td>2.1</td>
</tr>
</tbody>
</table>

In our series, 73% of cases presented an anemic syndrome at diagnosis, the same result found by Sintha et al [71%].

In a study conducted in the Tunisian center between 1998 and 2008 and involving 281 patients, 15% of patients had an hemorrhagic syndrome [6], whereas it was present in 21% of cases in a study conducted by Sintha and al in India [7].

In our patients, the infectious syndrome was present in 52% of the cases. In the series of Rego and al in Brazil [3], 58% of patients had an infectious syndrome at diagnosis, while Sintha and al in India report a higher frequency of around 80%.

The association of all three syndromes was observed in 25% of cases. In the literature, this association is more frequent in ALL than AML, especially in children, in fact, 23% of ALL cases present the triad of medullary insufficiency syndrome at diagnosis [8].

Tumor syndrome is more common in ALL (almost constant) than in AML (50% of cases) [9], and it is the consequence of the leukemic tumor mass [10]. In our series, it was found in 43% of cases.

The majority of our patients had normochromic normocytic aregenerative anemia.

Leukocytosis is a major prognostic factor. The prognosis is more favorable when the leukocytosis is less than 100,000 / mm³ [10,11]. In our series, LAs frequently presented in hyper-leukocyte form (66% of cases) while leukopenia was found in only 31% of cases.

White blood cells were greater than 100,000 / mm³ in 66%, this frequency is higher than those reported in the Sintha and al series in India (8.3%) [7], and in the Tunisian series (14%) [12].

Acute leukaemias can be complicated by disseminated intravascular coagulation (DIC), aggravating thrombocytopenia. Indeed, blast cells are rich in thromboplastinic substances that activate the extrinsic pathway of coagulation, which explains the frequency of DIC in leukemia with a greater procoagulant activity of the myeloblasts notably during promyelocytic acute leukemias [13].

We noted severe thrombocytopenia with a risk of cerebral hemorrhage in 33% of cases. This frequency is comparable to that reported by Jmili and al in Tunisia (35%) [12], while in the Sintha and al series only 11.7% of patients had severe thrombocytopenia [7].

The most important element for diagnosing AL on the blood count is the presence of circulating blast cells. The absence of blast cells does not mean absence of AL, but rather absence of blood invasion by blasts [14].

In our series the level of circulating blasts ranged between 4% and 90%.

In our series, the morphological examination of blood and marrow smears and the reaction to myeloperoxidase allowed to classify ALs in:
- 54.4% of AML;
- 43.9% LAL;
- 1.63% of cases difficult to classify according to the criteria of the FAB group.

The results obtained are consistent with those published in the various series of the literature.

Table III: Comparison of AML and ALL frequencies.

<table>
<thead>
<tr>
<th></th>
<th>UH Casablanca (Morocco)</th>
<th>Tunisia</th>
<th>Madagascar</th>
<th>UR Valence (France)</th>
<th>Our series</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML</td>
<td>64%</td>
<td>51%</td>
<td>56%</td>
<td>82.7%</td>
<td>54.4%</td>
</tr>
<tr>
<td>ALL</td>
<td>30%</td>
<td>40%</td>
<td>41%</td>
<td>15%</td>
<td>43.9%</td>
</tr>
</tbody>
</table>
Acute myeloid leukemias (AML) represent 1% of cancers and 80% of acute leukemias of adults whose incidence is constantly increasing. In children, it represents only 10 to 15% of AL and it is rare before the age of 15 [10]. In our series AML is the most common type accounting for 54.4% of acute leukemias. In Lower Normandy [1], we find higher results, 72% of AL are AML. At the Valencia Hospital Center their frequency is even higher, reaching 82% [15].

Cytologically, the subtypes M1 and M2 are the most frequent representing approximately 30% and 20% respectively. AML6, although relatively rare (3 to 5%), accounts for up to 20% of secondary AL [9].

The cytological characters of AML do not provide information on the prognosis. Studies have shown that the complete remission rate was higher in the M1, M2 and M3 categories than in the M4, M5 and M6 forms, but these findings have not been shared by other authors [16]. At present, cytogenetics and molecular biology, with their considerable contributions, have modified prognostic classifications [17]. We have made a comparison of the frequencies of the different types of AML in our series with other series of the literature.

Table IV: Comparison of the frequencies of the different subtypes of AML.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>UH Casablanca (Morocco)%</th>
<th>Tunisia %</th>
<th>Madagascar %</th>
<th>UH Valence (France)%</th>
<th>Europe %</th>
<th>Mexico %</th>
<th>India %</th>
<th>Our series %</th>
</tr>
</thead>
<tbody>
<tr>
<td>AML0</td>
<td>8</td>
<td>2</td>
<td>99</td>
<td>13</td>
<td>2</td>
<td>4.2</td>
<td>10.65</td>
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</tr>
<tr>
<td>AML1</td>
<td>57</td>
<td>12</td>
<td>25</td>
<td>72</td>
<td>15-20</td>
<td>3.2</td>
<td>9.1</td>
<td>7.46</td>
</tr>
<tr>
<td>AML2</td>
<td>28</td>
<td>17</td>
<td>36</td>
<td>20.9</td>
<td>25-30</td>
<td>20-59</td>
<td>22.37</td>
<td></td>
</tr>
<tr>
<td>AML3</td>
<td>6</td>
<td>5</td>
<td>13</td>
<td>8</td>
<td>5-10</td>
<td>35.5</td>
<td>2.3</td>
<td>1.69</td>
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<tr>
<td>AML4</td>
<td>64</td>
<td>16</td>
<td>13</td>
<td>14.7</td>
<td>20</td>
<td>14.4</td>
<td>18.2</td>
<td>38.8</td>
</tr>
<tr>
<td>AML5</td>
<td>5</td>
<td>35</td>
<td>8</td>
<td>17.5</td>
<td>2-9</td>
<td>10.8</td>
<td>11.3</td>
<td>14.92</td>
</tr>
<tr>
<td>AML6</td>
<td>5</td>
<td>7</td>
<td>6</td>
<td>6</td>
<td>3-5</td>
<td>0.0</td>
<td>1.49</td>
<td></td>
</tr>
<tr>
<td>ALL7</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3-12</td>
<td>0.4</td>
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Table V: Comparison of the frequencies of the different subtypes of ALL.

<table>
<thead>
<tr>
<th>Subtype</th>
<th>UH Casablanca (Morocco)%</th>
<th>Tunisia %</th>
<th>Madagascar %</th>
<th>UH Valence (France)%</th>
<th>Europe %</th>
<th>Mexico %</th>
<th>India %</th>
<th>Our series %</th>
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<tr>
<td>ALL T</td>
<td>9</td>
<td>56.4</td>
<td>11</td>
<td>80</td>
<td>39.5</td>
<td>9</td>
<td></td>
<td></td>
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<tr>
<td>ALL B</td>
<td>75</td>
<td>32.1</td>
<td>79</td>
<td>17</td>
<td>66.5</td>
<td>76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ALL Burkitt</td>
<td>6.5</td>
<td>5.1</td>
<td>11</td>
<td>3</td>
<td>15</td>
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Discussion:

In a study published in 2009 by the regional registrar of malignant hemopathies of Lower Normandy in France over a period of 8 years (1997-2004), the average age for ALL was 25 years against 63 years for AML [1].

In 2011, a retrospective study conducted at the Hematology Laboratory of Ibn Roch University Hospital in Casablanca, Morocco over a period of 4 years (2004-2007) reported an average age of 38 years for AML and 21 years for ALL [2].

In Brazil, the Rego and al study in the state of Piauí, between 1989 and 2000, reported an average of 9 years for LAL versus 34 years for AML [3].

Conclusion:

The diagnosis of ALs is primarily based on cytological and immunophenotypic criteria of bone marrow blasts [24,27]. The contribution of immunophenotyping, then of cytogenetics and finally of molecular biology have made it possible to describe more and more entities [24,27]. Since these specific methods are expensive and not available in hospitals in developing countries, cytology retains its place in the diagnosis of ALs [28].

References:

