Correlation of Cytogenetic Patterns and Clinicobiological Features in Adult Acute Myeloid Leukemia Expressing Lymphoid Markers

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Cytogenetic, biomolecular, and clinicopathologic features were retrospectively studied in 34 adult patients with acute myelogenous leukemia expressing one or more of the following lymphoid-associated markers (LMs): CD7, CD2, CD10, CD19, CD22, TdT. Six patients showed 11q23 rearrangements (group I); three patients had the classic Ph chromosome (group II); 15 patients had aberrations of the myeloid type (group III), including four patients with structural aberrations of 13q or trisomy 13, three patients with 7q and 1q anomalies, and two patients with trisomy 11q. Ten patients had a normal karyotype (group IV). Anomalies exclusively associated with lymphoid malignancies were not seen. Ig H and/or T-cell receptor genes were found to be rearranged in 50% and 88% of patients in cytogenetic groups I and II, respectively, versus 8% in group III and 12% in group IV.

Although lineage fidelity is generally maintained in acute leukemia1 and blast cells reproduce the phenotype of hematopoietic precursors at a particular stage of differentiation, a proportion of cases has been reported in which leukemic cells inappropriately express features normally confined to separate lineages.5,6 Thus, lymphoid markers as well as Ig or T-cell receptor (TCR) gene rearrangements may be detected in otherwise typical acute myelogenous leukemia (AML)4; conversely, myeloid markers may be found in acute lymphoblastic leukemia (ALL).6 Also, dual expression of lymphoid and myeloid markers has been reported in acute undifferentiated leukemia not classifiable by conventional light microscopy analysis.10 Because of variable cytologic and genotypic features, classification of such cases is still controversial; indeed, this spectrum of conditions, often referred to as acute mixed-lineage leukemia (AML/L), encompasses a heterogeneous group of disorders the precise identification of which may prove to be relevant in clinical practice.11,12

Whereas cytogenetic studies of patients in the pediatric age group documented that the t(4;11), t(11;19), and 14q32 rearrangements14,17 may be frequently associated with some subsets of AMLL (especially ALL with myelomonocytic features), chromosome studies in adult patients have only been reported occasionally16,20 in patients with heterogeneous cytologic features. Therefore, we elected to study the cytogenetic features in a series of adult patients with unequivocal diagnoses of AML in which blast cells expressed at least one lymphoid-associated marker (LM).

PATIENTS AND METHODS

Cytogenetic findings, as well as clinical records, cytology, and immunophenotype of 34 patients with AML with LM seen in Leuven, Brussels, and Mont-Godinne, Belgium, and in Ferrara, Italy, were retrospectively studied. Molecular genetic studies had been performed in 27 patients.

Patient Selection

Patients included in the present report are those fulfilling the following three requirements: (1) unequivocal diagnosis of AML (M1 to M7) according to the French-American-British (FAB) criteria12,22 (three patients with undifferentiated leukemia not classifiable by light microscopy analysis23 were also included based on the presence of more than 20% blast cells expressing at least two of the following myeloid-associated markers: CD33, CD13, CD14, CD15); (2) positivity for one or more of the following LMs: CD7, CD2, CD19, CD10, CD22, CD24, terminal deoxynucleotidyl transferase (TdT) in more than 20% of the blast cells; and (3) successful cytogenetic analysis at diagnosis.

Cytogenetic Studies

Bone marrow (BM) and/or peripheral blood (PB) samples were cultured for 24 or 48 hours in RPMI 1640 (GIBCO, Grand Island, NY) with 30% fetal calf serum. Synchronization using methotrexate and bromodeoxyuridine was performed. Metaphases were R-banded with acridine orange. A G-banding method was also used.24 Whenever possible, at least 10 karyotypes were analyzed in each patient. Chromosome aberrations were described according to the International System for Human Cytogenetic Nomenclature (ISCN).25
Cytology

Morphology. Bone marrow (BM) and peripheral blood (PB) smear were reviewed, and the presence of myelodysplastic features of the nonblast-cell population was assessed as previously reported.26 Trilineage myelodysplasia (TMD) was defined by the presence of more than 25% abnormal erythroblasts and by more than 50% dysplastic granulocytes and megakaryocytes.27

Immunologic studies. Cytofluorimetric analysis of the immunophenotype of blast cells was performed by immunofluorescence methods as previously described.26-28 The following panel of monoclonal antibodies was used: HPCA-1 (CD34), My9 (CD33), My7 (CD13), My4 (CD14), Leu-M1 (CD15), anti-Gpl (CD42), anti-GplIIb/IIIa (CD41), Leu-9/OKT16 (CD7), OKT11 (CD2), J5/OKBCalla (CD10), B4 (CD19), Leu-14 (CD22), BA1 (CD24), Isotype-matched myeloma proteins were used as controls. A polyclonal rabbit antiserum (GIBCO BRL, Gaithersburg, MD) was used for TdT assay. Efforts were made to gate on the blast cell population and samples were considered positive if more than 20% of cells showed fluorescence above controls.

Molecular Genetic Studies

The configuration of the Ig and/or TCR gene was analyzed at diagnosis in 27 patients for whom adequate BM and/or PB samples were available. The presence of bcr gene rearrangement (major breakpoint) was assessed in patients with the classic Ph chromosome.

Methods have been detailed elsewhere.31 After DNA extraction by standard techniques, digestion with Bgl II, BamHI, EcoR1, HindIII was performed. DNA fragments were electrophoresed on 0.7% agarose gels and blotted onto Hybond N+ filters. Hybridization to probes 32P-labeled by primer extension was performed. The bcr gene configuration was investigated by the universal genomic probe, a 5-kb Sal I-BamHI fragment (Dr A. Hagemeijer, Department of Biology and Genetics, Rotterdam, The Netherlands). Ig gene rearrangement was assayed using a heavy chain joining (JH) region probe (a 6-kb BamHI-HindIII fragment) and two constant region probes, Ck and Ck4 (2.7- and 0.8-kb EcoR1 fragments; Dr R. Dalla Favera, New York University Medical Center). TCR-b chain gene was studied with a constant region (0.4-kb Bgl II fragment) cDNA probe from the Jurkatt p2 cell line (Dr T.W. Mak, Ontario Cancer Institute, Toronto, Canada). Analysis of the TCR-g chain gene was performed by probing leukemic DNA with the J-g 1.3 probe (0.8-kb EcoR1-HindIII fragment; Dr R. Bolhuis, Dr Daniel den Hoed Cancer Center, Rotterdam, The Netherlands).

RESULTS

Cytogenetics

Clonal chromosome abnormalities were detected at presentation in 24 patients. Six patients showed abnormalities involving band 11q23, and three patients showed a classic t(9;22)(q34;q11) with germline M-bcr. Aberrations involving chromosome 13 were detected in four patients (three translocations or deletions and one trisomy). Deletions or translocations of chromosome 7q were detected in three patients. Structural aberrations of 1q were found in three cases. Trisomy 11q was the primary anomaly in two patients. Other nonrecurring aberrations in this cytogenetic group are reported in Table 1. Four classes of cytogenetic findings could be distinguished: group I, those with 11q23 rearrangements; group II, those with the classical t(9;22)(q34;q11) (M-bcr germline); group III, those with aberrations here referred to as "myeloid" based on the fact that they were previously described in patients with AML, myelodysplastic syndrome (MDS), and myeloproliferative disorders31-33 and that they were not detected as primary aberrations in lymphoproliferative disorders34,35; and group IV, those with normal karyotype. Karyotypes for all patients included in the present study are detailed in Table 1 along with their correlation with immunologic and molecular genetic findings.

Cytology

Morphology. Diagnosis according to the FAB criteria was as follows: MO (two myeloid-associated markers positive), 3 cases; M1, 6 cases; M2, 7 cases; M3, 1 case; M4, 12 cases; M5, 2 cases; M6, 1 case; and M7, 2 cases. Trilineage myelodysplasia was found in 6 of 22 assessable cases and was present only in patients belonging to cytogenetic groups III and IV. Correlation of morphologic features with cytogenetic and clinical findings is reported in Table 2.

Immunophenotype. Percentage of blast cells after separation on Ficoll gradient was higher than 80% in all cases. Positivity for at least two of the granulomonocytic- or platelet-associated antigens tested (CD33, CD13, CD15, CD41) was found in 29 of 34 patients. CD34 was positive in 81% of patients. A minority of blast cells (5% to 20%) expressing platelet glycoproteins (CD41) was detected in six patients (three with AML-M4, two with AML-M2, one with AML-M0).

The most frequently encountered LM was TdT (16 of 31 cases), followed by CD7 (13 of 33 cases), CD19 (6 of 30 cases), CD10 (5 of 31 cases), CD2 (4 of 29 cases), and CD22 (2 of 29 cases). CD24 positivity was not detected. Greater than 15% overlap between percentage of blast cells stained by LM and by myeloid-associated markers was detected in all patients. Percentage positivity for each immunologic marker in the different cytogenetic groups is reported in Table 3.

As reported in Table 1, expression of more than one LM was detected in three patients (50%) in cytogenetic group 1 and in two patients (66%) in group II, versus three patients (20%) and none in cytogenetic groups III and IV, respectively.

Molecular Studies

Overall, clonal rearrangements of the Ig H chain gene were detected in 6 of 27 cases, all of which showed germline configuration of the light chain gene.

The genes coding for the subunit b and g of the TCR were found to be rearranged in 2 of 21 and 1 of 21 cases tested, respectively. As reported in Table 1, Ig H and/or TCR gene rearrangements were detected in 50% of patients with 11q23 rearrangements, in 66% of patients with the Ph chromosome, in 8% of patients with myeloid aberrations, and in 12% of patients with normal karyotype.

No rearrangement of the major-bcr (M-bcr) was detected in the three patients with the classic t(9;22)(q34;q11).

Clinical Findings

All patients were diagnosed as having AML based on clinical, cytologic, and immunologic features.36 Patients
Table 1. Chromosome Aberrations, LMs, and Ig H Chain and TCR Gene Configuration in 34 Patients With AML

<table>
<thead>
<tr>
<th>Patients by FAB Classification (N=34)</th>
<th>Karyotype [no. of cells/total]</th>
<th>LM</th>
<th>Ig H</th>
<th>TCR-β</th>
<th>TCR-γ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M4</td>
<td>46,XY,t(11;19)(q23;p13) [10/10]</td>
<td>TdT+,CD7+</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M1</td>
<td>46,XX,t(11;19)(q23;p13) [10/10]</td>
<td>TdT+,CD19+</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M2</td>
<td>46,XX,t(11;19)(q23;p13) [20/20]</td>
<td>TdT+</td>
<td>R</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M3</td>
<td>50,XX,+6,+8,t(8;11)(p21;q23),+20,+21 [10/10]</td>
<td>CD19+</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M4</td>
<td>47,XY,t(2;7)(q32;7),t(9;11)(p21;q23),+21 [15/15]</td>
<td>CD19++,CD22+,CD7+</td>
<td>R</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M5</td>
<td>46,XY,del(11)(q23q24) [10/10]</td>
<td>CD22+</td>
<td>G</td>
<td>ND</td>
<td>G</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M4</td>
<td>46,XY,t(8;23)(q34;q11) [10/10]</td>
<td>TdT++</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>M1</td>
<td>46,XY,t(11;9)(9;22)(p12;p12q34;q11) [11/11]</td>
<td>TdT++,CD19+,CD10+</td>
<td>R</td>
<td>R</td>
<td>ND</td>
</tr>
<tr>
<td>M2</td>
<td>51,XX,+6,t(8;22)(q34;q11),+10,+19,+der(22) [10/10]</td>
<td>TdT+,CD2++,CD7+</td>
<td>G</td>
<td>ND</td>
<td>G</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>M4</td>
<td>46,XY,t(6;9)(q21;p22),del(7)(q21q32),t(9;14) [p13;q12][11/11]</td>
<td>CD2+</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M1</td>
<td>45,XY,-7 [8/10]/46,XY,-7 [8/2/10]</td>
<td>CD7+++</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M2</td>
<td>46,XY,t(16;7)(q21;p13) [12/12]</td>
<td>CD19++</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M3</td>
<td>47,XY,+11 [8/10]</td>
<td>TdT++</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M4</td>
<td>46,XY,t(6;13)(p21;q13) [4/10]/46,XY, idem,t(1;20)(p12;q12) [1/10]</td>
<td>TdT+</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M5</td>
<td>47,XY,+8 [25/32]</td>
<td>TdT++</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>Group 4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M4</td>
<td>47,XY,+13 [8/8]</td>
<td>TdT++</td>
<td>G</td>
<td>R</td>
<td>G</td>
</tr>
<tr>
<td>M1</td>
<td>46,XY,t(12;13)(p12;q13)[6/10]</td>
<td>CD19++,CD7++,CD10++</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M2</td>
<td>46,XY,del(3) [p21q26],dup(17)(q12q24) [10/10]</td>
<td>TdT+,CD7+</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M3</td>
<td>46,XX,i(1q+)/[11q][16/20]</td>
<td>CD7++</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M4</td>
<td>46,XX,i(6q)[12/14]</td>
<td>CD10+++</td>
<td>G</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M4</td>
<td>47,XX,+del(13)(q13q33)[6/10]</td>
<td>CD10++</td>
<td>G</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M1</td>
<td>46,XY,t(7;7)(q10;7)[2/10]</td>
<td>TdT++,CD7+++</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>M2</td>
<td>47,XY,+8 [10/10]</td>
<td>CD7+</td>
<td>G</td>
<td>G</td>
<td>G</td>
</tr>
<tr>
<td>M3</td>
<td>46,XY,del(5) [q14q23]</td>
<td>CD7+</td>
<td>ND</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

Abbreviations: +, 20% to 40%; ++, 40% to 60%; +++, > 60% positive blasts; idem, same chromosome changes as the previous karyotype plus; G, germ line; R, rearranged; ND, not done.

*Additional nonclonal aberrations.

with Ph chromosome had normal leukocyte alkaline phosphatase score, showed an abrupt disease onset, had only mild spleen enlargement, and exhibited a germline configuration of bcr in the major breakpoint cluster region, thus ruling out a diagnosis of chronic myelogenous leukemia blast crisis.

Patient age ranged between 14 and 77 years (median, 56 years). One patient died before chemotherapy was started, one patient was treated with low-dose cytarabine. The remaining patients were treated according to standard AML protocols, including an anthracycline drug and cytarabine or vindesine, etoposide and cytarabine (VAE regimen). Overall, complete remission (CR) was achieved in 21 of 29 assessable patients, with a median duration of 14 months (range, 4 to 48+ months). Survival ranged between 1 and 48+ months (median, 10.5 months). Age, white blood...
cell (WBC) count at presentation, CR rate, and median survival in patients belonging to different cytogenetic groups are summarized in Table 2.

**DISCUSSION**

**Cytogenetic Profile of AML With LM**

Two operational problems arise in a cytogenetic study of acute leukemia with so-called hybrid phenotype. The first is related to patient selection in view of the remarkable degree of heterogeneity of cytologic presentation of AML. In the present series, we included patients with unequivocal AML according to the FAB criteria and/or immunophenotype to be able to compare the cytogenetic pattern in our patients with that of unselected AML cases. As the cytogenetic features of AML may be different in adults with respect to children, we only included patients aged over 14 years.

The second problem is represented by the choice of the LMs among the large panel of monoclonal antibodies raised against antigens of lymphoid differentiation. In accordance with previous literatures, we considered inappropriate the AML cell expression of some well-characterized molecules of normal lymphoid maturation, almost invariably found on ALL blasts. Of course, as the function of most antigens of lymphoid maturation is poorly understood, the identification of the purely "lymphoid" marker that is inappropriate when found on AML blasts is somewhat arbitrary.

Cases here reported represent a homogeneous cytologic group of adult patients in which the combination of immunologic, cytogenetic and biomolecular studies may help to clarify some of the following questions: What is the cytogenetic profile of AML with LM? Are there aberrations of the lymphoid type in some cases of AML with LM, suggesting that true commitment towards the lymphoid pathway may occur in such cases? Are there recurring abnormalities in AML with LM preferentially associated with extensive lineage infidelity?

Chromosomal findings in our patients seem to indicate that a distinct cytogenetic profile may be associated with AML with LM. Aberrations involving 11q23 and the t(9;22) translocation were detected in 25% and 12.5%, respectively, of patients with abnormal karyotypes in this series and account for over 30% of cases with abnormal karyotypes included in a literature review of previously reported cases of adult AML with LM (Table 4). These figures are strikingly higher than those reported in cytogenetic studies of unselected AML patients, where 11q23 anomalies and the Ph chromosome were found in 3% to 4% and 1% to 2% of cases, respectively. Percentage frequency of 11q23 rearrangements and of the Ph chromosome in all AML cases seen at our institutions during the study period was 4.3% and 1.9%, respectively.

Among aberrations here referred to as myeloid, the two most frequent AML-specific translocations [i.e., t(15;17), t(8;21)], identified at the Fourth International Workshop on Chromosomes in Leukemia in 13% of AML patients, were uncommon in this series. Other recurring aberrations of the myeloid type found in our patients (−7/7q−, abnormalities of 17q) are frequently associated with a spectrum of myeloid stem cell disorders and may be responsible for genetic imbalance conferring proliferative

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**Table 3. Positivity for LMs by Cytogenetic Pattern in 30 AML Patients**

<table>
<thead>
<tr>
<th>Stem Cell Marker CD34</th>
<th>Myeloid Markers CD33</th>
<th>CD13</th>
<th>CD14</th>
<th>CD41*</th>
<th>TdT</th>
<th>CD7</th>
<th>CD2</th>
<th>CD10</th>
<th>CD19</th>
<th>CD22</th>
</tr>
</thead>
<tbody>
<tr>
<td>11q23 rearrangements</td>
<td>4/5</td>
<td>5/6</td>
<td>2/5</td>
<td>1/5</td>
<td>0/6</td>
<td>0/5</td>
<td>0/6</td>
<td>3/6</td>
<td>2/6</td>
<td></td>
</tr>
<tr>
<td>t(9;22)(q34;q11)</td>
<td>3/3</td>
<td>2/3</td>
<td>2/3</td>
<td>3/3</td>
<td>1/3</td>
<td>1/3</td>
<td>1/2</td>
<td>1/3</td>
<td>0/3</td>
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</tr>
<tr>
<td>Myeloid aberrations</td>
<td>11/15</td>
<td>12/15</td>
<td>6/14</td>
<td>1/14</td>
<td>5/14</td>
<td>7/14</td>
<td>2/10</td>
<td>3/14</td>
<td>2/12</td>
<td>0/12</td>
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<tr>
<td>Normal karyotype</td>
<td>9/9</td>
<td>6/10</td>
<td>9/10</td>
<td>4/9</td>
<td>4/7</td>
<td>5/9</td>
<td>3/10</td>
<td>1/10</td>
<td>0/9</td>
<td>0/8</td>
</tr>
</tbody>
</table>

*Including patients with a minor megakaryoblastic component (5% to 20% positive blasts).
advantage to an undifferentiated stem cell, rather than being specifically associated with inappropriate expression of lineage-associated markers. The finding in such patients of myelodysplastic features involving multiple cell-lineages seems to confirm this view.26

In contrast, attention should be drawn to aberrations of chromosome 13 and trisomy 11q, possibly representing primary chromosome changes in four and two patients, respectively. Different types of structural aberrations of 13q were detected; however, the involvement of band q13 appears to be the crucial cytogenetic event. Abnormalities of chromosome 13, as well as trisomy 11q, are rather uncommon in de novo AML, having been described previously in some cases of erythroleukemia, myelofibrosis with myeloid metaplasia, and MDS. Although more cases need to be studied, our findings seem to suggest that aberrations of chromosome 13 and trisomy 11q may be nonrandomly associated with hybrid phenotypes of acute leukemia. Notably, two of our AML patients with 13q aberrations showed more than two LMs (Table 1), thus fulfilling the criteria for the diagnosis of hybrid acute leukemia."27 Trisomy 13 has recently been detected in some patients with minimally differentiated AML expressing LMs.16

Our data seem to indicate a negative answer to the second question. None of the primary aberrations confined to typical ALL or other lymphoproliferative disorders have been observed in our patients (Table 1), a finding confirmed by the literature review summarized in Table 4. Interestingly, recent cytologic studies in some cases of AML with T-cell features showed that cultured blasts may lose LMs and express a full myelomonocytic phenotype, excluding the possibility that commitment toward the lymphoid pathway had occurred in those patients.

Nevertheless, some chromosome changes in our series, such as 11q23 rearrangements and the t(9;22) translocation, have also been reported in a subset of ALL with immature phenotype or with mixed lymphoid and myelomonocytic characteristics, especially in children. These findings introduce the discussion of the third question. Indeed, the single most frequent aberration in this series was the t(11;19)(q23;p13). Although we did not observe the (4;11) translocation, two patients showed a t(9;11)(p21;q23) and one a del(11)(q23q24), suggesting that different chromosome changes having a common involvement of band 11q23 may be detected frequently not only in leukemias with monoblastic differentiation and childhood ALL, but also in adult patients with AML.

### Table 4. Literature Review: Cytogenetic, Cytologic, and Clinical Findings in 54 Adult Patients With AML Expressing LM

<table>
<thead>
<tr>
<th>Reference No.</th>
<th>No. of Cases</th>
<th>Clonal Aberrations</th>
<th>FAB Diagnosis (no. of cases)</th>
<th>LM+ (no. of cases)</th>
<th>Median Age (years)</th>
<th>Median Survival (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>57, 60</td>
<td>2</td>
<td>t(4;11)(q21;q23)</td>
<td>M2, M0</td>
<td>CD22+ TdT (1)</td>
<td>27.5</td>
<td>5</td>
</tr>
<tr>
<td>19</td>
<td>1</td>
<td>-7, 11q-</td>
<td>M4</td>
<td>CD20+CD19 (1)</td>
<td>72</td>
<td>4</td>
</tr>
<tr>
<td>61, 62</td>
<td>2</td>
<td>t(9;11)(p21;q23)</td>
<td>M5*</td>
<td>CD10+CD19 (1)</td>
<td>40</td>
<td>NR</td>
</tr>
<tr>
<td>20, 41, 61, 63, 64</td>
<td>11</td>
<td>t(9;22)(q34;q11)</td>
<td>M1 (5), M2 (2)</td>
<td>CD10+lg R (3)</td>
<td>43</td>
<td>8*</td>
</tr>
<tr>
<td>50, 51, 52</td>
<td>6</td>
<td>+13</td>
<td>M0 (2), M1 (1), M2, M4, M5</td>
<td>TD7+lg R (1)</td>
<td>63</td>
<td>4</td>
</tr>
<tr>
<td>19, 45, 61, 65-67</td>
<td>9</td>
<td>-5/6q- and/or -7/7q-</td>
<td>M0 (3), M1 (3), M2, M4, M5</td>
<td>CD2+CD3 (1)</td>
<td>62</td>
<td>6</td>
</tr>
<tr>
<td>18, 62</td>
<td>8</td>
<td>t(8;21)(q22;q22)</td>
<td>M2 (2)*</td>
<td>TdT +CD19 (2)*</td>
<td>52*</td>
<td>16*</td>
</tr>
<tr>
<td>61, 62</td>
<td>6</td>
<td>t(15;17)(q22;q21)</td>
<td>M3 (6)</td>
<td>CD2+CD4 (1)</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>62</td>
<td>5</td>
<td>inv(16)(p13q22)</td>
<td>M4 (5)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>16</td>
<td>2</td>
<td>t(14;v)(q22;v)</td>
<td>M2, M5</td>
<td>TdT+CD10 (1)</td>
<td>16</td>
<td>8</td>
</tr>
<tr>
<td>68</td>
<td>2</td>
<td>t(6;9)(p21;q34)</td>
<td>M4 (2)</td>
<td>TdT (2)</td>
<td>15</td>
<td>15</td>
</tr>
</tbody>
</table>

Abbreviation: Ig R/TCR R, Ig TCR gene rearranged.

*Data not reported for all patients.
expressing LM. The same holds true for the t(9;22) translocation, a chromosome aberration frequent in ALL with hybrid phenotype and multilineage involvement.\textsuperscript{41,59} Taken together these findings suggest that similar cytogenetic mechanisms may underlie the development of different cytologic entities of acute leukemia both in adults and in children. Therefore, it is reasonable to assume that the involvement of an undifferentiated progenitor cell, capable of limited differentiation towards multilineage pathways, may occur in such cases. Consistent with this view is the observation that our patients in cytogenetic groups I and II showed expression of more than one LM in five of nine cases and exhibited chromosomal rearrangements of the Ig H and/or TCR gene in four of seven cases. According to the stringent criteria offered by Gale and Ben-Bassat,\textsuperscript{11} seven of nine such patients fulfilled the diagnosis of hybrid acute leukemia, while only 5 of 25 patients with aberrations of the myeloid type or with normal karyotype did so. In the literature review, we identified 11 patients having AML with LM and 11q23 rearrangements or the Ph chromosome, 10 of which had more than one LM on their blast cells and/or exhibited chromosomal rearrangements of the Ig H or TCR gene. Hence, 11q23 rearrangements and the t(9;22) translocation stand out as chromosomal aberrations defining a subset of adult AML characterized by extensive lineage infidelity.

Clinicobiologic Correlations

Correlation of cytogenetic patterns with some clinical and biologic features yields the following observations. (1) AML expressing more than one LM, fulfilling stringent criteria for the identification of true hybrid acute leukemia,\textsuperscript{13} are more frequently encountered in cytogenetic groups I and II and in patients with aberrations of chromosome 13. (2) As for patients with ALL, t(9;22) and 11q23 rearrangements are associated in this series with young age and with a high WBC count at presentation, raising the possibility that these cytogenetic abnormalities may identify similar clinical entities presenting with heterogeneous cytologic features. (3) Despite young age, complete remission was only achieved in three of six and one of three cases in patients in groups I and II, respectively. Furthermore, survival in cytogenetic group II was uniformly short, in agreement with previous reports (Table 4).

Although further studies are required for a better definition of the clinicopathologic features of AML with LM, our data suggest that chromosome findings in this form of leukemia may be clinically relevant.

Conclusions

We have studied the cytogenetic pattern at diagnosis in 34 cases of AML expressing lymphoid features in correlation with clinical, morphologic, immunologic, and molecular parameters, and have analyzed similar data from 54 cases in the literature. There is no cytogenetic anomaly specifically associated with these leukemias, and in particular, there is no chromosome change allowing for the identification of true hybrid leukemia. However, this study shows that four chromosomally distinct subgroups emerge: one with 11q23 rearrangements, one with Ph chromosome but without M-bcr rearrangement, one with chromosome changes that as a rule are found in myeloid malignancies, and one with normal karyotype. Anomalies usually or exclusively associated with lymphoid malignancies were not seen.

These data indicate that a Morphologic, Immunologic, and Cytogenetic (MIC) classification of AML with lymphoid features may constitute a working basis for further studies aimed at a better definition of and optimal treatment strategy for these leukemias.

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