Cytogenetic Profile of Minimally Differentiated (FAB M0) Acute Myeloid Leukemia: Correlation with Clinicobiologic Findings

By Antonio Cuneo, Augustin Ferrant, Jean Louis Michaux, Marc Boogaerts, Hilde Demuyynck, Angeline Van Orshoven, Arnold Criel, Michel Stul, Paola Dal Cin, Jesus Hernandez, Bernard Chatelain, Chantal Doyen, Andries Louwagie, Gianluigi Castoldi, Jean-Jacques Cassiman, and Herman Van Den Berghe

Cytogenetic data were studied in 26 patients with de novo acute myeloid leukemia (AML) with minimal myeloid differentiation, corresponding to the M0 subtype of the French-American-British classification, in correlation with cytomorphologic and clinical findings. Clonal abnormalities were detected in 21 cases (80.7%), 12 of which had a complex karyotype. Partial or total monosomy 5q and/or 7q was found, either as the sole aberration or in all abnormal metaphases, in 11 patients; in 8 cases, additional chromosome changes were present, including rearrangements involving 12p12-13 and 2p12-15 seen in 3 cases each. Five patients had trisomy 13 as a possible primary chromosome change; in 5 cases, nonrecurrent chromosome abnormalities were observed. Comparison of these findings with chromosome data from 42 patients with AML-M1 shows that abnormal karyotypes, complex karyotypes, unbalanced chromosome changes (−5/5q− and/or −7/7q− and +13) were observed much more frequently in AML-M0 than in AML-M1. Patients with abnormalities of chromosome 5 and/or 7 frequently showed trilineage myelodysplasia and low white blood cell count. Despite their relatively young age, complete remission was achieved in 4 of 11 patients only. Patients with +13 were elderly males with frequent professional exposure to myelotoxic agents. Unlike patients with clonal abnormalities, most AML-M0 patients with normal karyotype showed 1% to 2% peroxidase-positive blast cells at light microscopy and frequently achieved CR. It is concluded that (1) AML-M0 shows a distinct cytogenetic profile, partially recalling that of therapy-related AML, (2) different cytogenetic groups of AML-M0 can be identified showing characteristic clinicobiologic features, and (3) chromosome rearrangements may partially account for the unfavorable outcome frequently observed in these patients.

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MINIMALLY DIFFERENTIATED acute myeloid leukemia (AML) was recognized as a distinct entity as early as 1987 by Lee et al, who described cytomorphologic, immunologic, and clinical features in 10 patients with morphologically undifferentiated leukemia by light microscopy and positivity for the ultrastructural myeloperoxidase (MPO) as well as for myeloid antigens.

Later on, a number of studies confirmed that a significant fraction of leukemias otherwise classified as “undifferentiated” can be shown to be myeloid in nature, when applying sensitive immunologic and electron microscopy techniques.

However, because diagnostic criteria in these series were not uniform, the French-American-British (FAB) Cooperative group recently proposed guidelines for the recognition of this form of leukemia, now referred to as AML-M0. The 3% upper cutoff for MPO positivity was set for its distinction from AML-M1, and positive (ie, expression of CD33 and/or CD13 myeloid antigens or ultrastructural MPO) as well as negative criteria (ie, negativity for lymphoid antigens) were put forward to avoid confusing this leukemia with leukemia with stem cell phenotype,6 with lymphoblastic leukemias, and with biphenotypic leukemias.7

Little is known about the clinical and biologic significance of this newly identified subset of AML; however, a low complete remission (CR) rate has recently been described in 15 patients classified according to the FAB proposals, suggesting that a poor prognosis may be associated with this leukemia, possibly because of the convergence of unfavorable cytogenetic and immunologic features.8

In view of the well-established importance of cytogenetic findings in acute leukemias,9 we analyzed the cytogenetic profile in 26 cases of de novo AML-M0, in correlation with cytotologic, immunologic, and clinical features.

PATIENTS AND METHODS

Patient population. Major criteria for the diagnosis of AML-M0 adopted in this study are the following: (1) less than 3% blast cells stained by light microscopy MPO and Sudan black-B (SBB); (2) reactivity with CD33 and/or CD13 myeloid antigens; and (3) negativity for lymphoid antigens (the isolated expression of CD7 or terminal deoxynucleotidyl transferase [TdT]) did not preclude the diagnosis of AML-M0. Two patients without expression of myeloid and lymphoid antigens were classified as AML-M0 based on the presence of 1% to 2% positive blast cells with MPO and SBB.10

Forty-one patients with a presumptive diagnosis of de novo AML-M0 were selected among approximately 700 newly diagnosed AMLs, seen at the University Institutes of Hematology in Brussels, Leuven, Mont-Godinne, Brugge, and in Ferrara since 1984. Fifteen patients were excluded from this analysis for the following reasons: (1) a diagnosis of AML-M1, of AML-M5, and of biphenotypic leukemia was thought to be more appropriate at review of cytology and immunophenotype (7, 1, and 2 cases, respectively); and (2) karyotype not available (5 cases).

To compare cytogenetic findings in this cohort of patients and in a cytologically similar subset of AML, 42 patients with an AML-M1 FAB diagnosis, seen at our institutions during the study period, were selected for karyotype review. Differences in the distribution
of clonal abnormalities among different groups were compared using the $X^2$ test.

**Morphologic studies.** Review of bone marrow (BM) and peripheral blood smears stained by May-Grunwald-Giemsa and by cytochemical reactions including MPO, SBB, and alpha-naphthyl acetate esterase with and without fluoride inhibition, period-acid Schiff (PAS), and acid phosphatase (ACP) was performed, and the patients were classified according to the FAB criteria. Attention was devoted to the presence of dysplastic features of BM cells. When all three lineages were affected, AML with trilineage myelodysplasia (MDS) was diagnosed as previously reported.

**Immunologic studies.** Cytofluorimetric analysis of the phenotype of BM and/or peripheral blood cells was performed as previously described, gating primarily on the blast cell population. To minimize nonspecific Fc-receptor binding, all samples were preincubated with 2.5% human AB serum. Nonspecific isotypic mouse monoclonal antibodies (MoAbs) served as negative control for the primary agent.

The expression of following antigens was tested using commercially available reagents (Ortho Diagnostics, Raritan, NJ; Becton Dickinson, Mountain View, CA) (1) myeloid, erythroid, and platelet antigens: CD33, CD13, CD15, CD11b, CD14, glycoporphine, CD41, and/or CD61; and (2) lymphoid antigens: CD7, CD2, CD3, CD5, CD22, CD10, and CD19. The expression of the CD34 stem cell marker was also tested; reactivity for the 17F11 MoAb, recognizing an epitope of the c-kit protein product (CD117), was assayed since 1993. A polyclonal antiserum was used for TdT assay (Gibco BRL, Gaithersburg, MD).

A sample was considered positive when 20% of blast cells showed fluorescence above control. However, in accord with previous reports, the 10% cutoff was thought to be more appropriate for the MoAb detecting the c-kit protein product.

**Cytogenetic and molecular genetic studies.** Cytogenetic analysis was performed at diagnosis in all patients by a synchronization technique with methotrexate and bromodeoxyuridine or thymidine. Metaphases were either R-banded or G-banded. Chromosome aberrations were described according to the International System for Human Cytogenetic Nomenclature. Complex karyotypes were defined by the presence of three or more events of translocation and nondisjunction in the same clone or by the presence of multiple unrelated clones. The configuration of the Ig and T-cell receptor (TCR) genes were analyzed at diagnosis in 15 patients for whom representative frozen samples were available.

Methods have been detailed elsewhere. After DNA extraction by standard techniques, digestion with Bgl II, BamHI, EcoRI, HindIII, and Kpn I, respectively, was performed. DNA fragments were size-fractionated on 0.7% agarose gels and blotted onto Hybond N+ filters. Hybridization to probes labeled by primer extension was performed. Ig gene rearrangement was assayed using a heavy chain joining (JH) region probe (a 3.8-kb BamHI-HindIII fragment) and two constant region probes, Ck and Ck (2.7- and 0.8-kb EcoRI fragments; from Dr R. Dalla Favera, New York University Medical Center, New York, NY). TCR genes were analyzed for the presence of less than 5% BM blast cells with more than 1.5 x 10^9/L neutrophils and more than 100 x 10^9/L platelets and hemoglobin greater than 10 g/dL.

**RESULTS**

**Morphology and cytochemistry.** All patients classified as AML-M0 showed little or no maturation along the granulocytic lineage. The overall morphologic picture was that of undifferentiated leukemia, with small- to medium-sized cells, round nuclei, and open chromatin. One or more nucleoli were evident, and scanty, moderately basophilic cytoplasm was observed in the majority of cases, whereas heterogeneity of cell size was observed in some cases.

In 9 cases, 1% to 2% positive cells for the MPO and SBB stain were detected, whereas only occasional MPO+ cells were observed in the remaining 17 cases. Weak diffuse positivity for the nonspecific esterase stain that was not inhibited by sodium fluoride was observed in 15 cases; PAS block-positivity or strong, localized positivity for the ACP was not observed in any patient, whereas small granular positivity for the PAS stain was detected in 10 cases. A moderate increase (2% to 5% of total cellularity) of morphologically normal eosinophils in late stage of differentiation was noted in 4 cases (no. 13, 15, 16, and 26).

Because of overwhelming blast cell infiltrate of the BM, morphologic features of the residual nonblast cell population could not be assessed in 10 patients. Dysplastic features of the nonblast cell population fulfilling criteria for the definition of trilineage MDS were present in 7 cases (no. 1, 4, 8, 10, 11, 14, and 21), whereas dysplastic features were confined to 1 or 2 cell lineages in 2 and 3 patients, respectively.

**Immunophenotype.** The immunologic profile of our patients is shown in Table 1. Positivity for two or more myeloid-associated antigens was detected in 22 cases, in the absence of coordinate expression of lymphoid-associated antigens; whereas, in 2 cases, only one myeloid marker (either CD13 or CD33) was found to be positive in more than 20% of blast cells (cases no. 11 and 15). Two patients with SBB and MPO positivity in 1% to 2% blast cells had a stem cell phenotype with CD34 and HLA-DR positivity with negative myeloid and lymphoid markers (patients no. 13 and 25). No patient expressed the CD14, glycoporphine, and CD41 antigens normally detected in leukemias with monocytic, erythroid, or megakaryoblastic differentiation, respectively.

**Cytogenetic and molecular genetic findings.** Results of chromosome investigations are detailed in Table 2. Clonal abnormalities were detected at diagnosis in 21 patients.

**Table 1. Immunologic Findings in 26 Patients With AML-M0**

<table>
<thead>
<tr>
<th>Immunologic Marker</th>
<th>No. Positive/No. Tested</th>
<th>% Positive Cells Median Value (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD117</td>
<td>3/6</td>
<td>22 (12-51)</td>
</tr>
<tr>
<td>CD34</td>
<td>22/22</td>
<td>70 (21-83)</td>
</tr>
<tr>
<td>CD33</td>
<td>21/26</td>
<td>62 (25-80)</td>
</tr>
<tr>
<td>CD13</td>
<td>22/25</td>
<td>60 (20-87)</td>
</tr>
<tr>
<td>CD15</td>
<td>8/16</td>
<td>36 (20-52)</td>
</tr>
<tr>
<td>CD11b</td>
<td>11/18</td>
<td>54 (22-72)</td>
</tr>
<tr>
<td>CD7</td>
<td>14/26</td>
<td>61 (25-84)</td>
</tr>
<tr>
<td>TdT</td>
<td>7/26</td>
<td>43 (25-75)</td>
</tr>
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</table>
complex karyotypes, including 2p and 12p rearrangements carrying -5/15q- and/or -7/17q- were detected in 13 patients; in 8 cases, these abnormalities were associated with 5q- and/or -7/17q- were consistently present in all abnormalities were analyzed in 26 cases of AML-M0. The observed frequency of recurrent primary chromosome rearrangements in AML-M0 with respect to AML-M1 is shown in Table 3. Molecular genetic studies showed clonal rearrangement of the IgH chain gene and of the TCR genes in 4 of 15 cases and 3 of 15 cases, respectively (see Table 2). In 2 cases (no. 9 and 18), both the IgH and the TCR genes were in a rearranged configuration. There was no rearrangement of the TCR-β gene in all cases examined.

Clinical features. Hematologic findings at presentation and correlation of chromosome findings and clinicobiologic features in patients with AML-M0 are summarized in Tables 4 and 5. The profession was known for 20 patients, 7 of whom (no. 1, 2, 6, 7, 13, 14, and 15; 2 truck drivers, 2 factory painters, and 3 farmers) were considered exposed to petroleum products, organic solvents, or pesticides. Myeloablative chemotherapy was administered to 24 patients: whereas 1 patient was treated by low-dose cytarabine, and 1 patient died before treatment was started. CR was achieved in 13 of 24 assessable patients, of whom 4 underwent BM transplantation (3 allogeneic, 1 autologous) in first CR. Median duration of CR in the remaining patients was 6 months. One patient (no. 16) was successfully transplanted in second CR. Overt relapse was preceded by an MDS phase with pancytopenia and 5% to 10% BM blasts in 2 patients (no. 3 and 7). Cytologic and immunologic data in 26 cases of AML-M0 are summarized in Table 2.
lymphoid features (ie, negativity for the AcP stain, for the patients, given the absence of coordinate expression of T- that should be attributed to lineage-associated antigens,' we felt that a diagnosis of AML-MO was appropriate in these CYTOGENETICS

arranged pattern for the TCR gene. Those patients, such as case no. 9, showing a clonally re-

This problem may be particularly important, especially for differentiation, such as CD19 and CD10," the differential

expression of myeloid antigens.

The diagnosis of AML-M0 in our patients fulfilled the diagnostic criteria and was supported by immunophenotyping and by cytochemical features of the blast cell population. Interestingly, SBB appeared to be more sensitive than MPO in this study, and 7 patients who would have otherwise been classified as AML-M0 because of the presence of less than 3% positivity for MPO were included among AML-M1 at cytologic review, showing 3% to 12% SBB-positive cells.

While a pro-B–lymphoid nature of leukemic cells could be ruled out by negativity for early markers of B-lymphoid differentiation, such as CD19 and CD10, the differential diagnosis with early T-cell acute lymphoblastic leukemia was not unequivocal for those patients with blast cell immaturity and TdT positivity, the incidence of such genetic events in our series is not dissimilar as compared with previous studies of unselected AML cases.

Clinical and cytotologic follow-up in this series yields the following observations confirming the "nonlymphoid nature" of these leukemias: (1) the presence of trilineage MDS in 7 of 16 evaluable cases; (2) an MDS phase preceding overt relapse in 2 cases achieving CR; and (3) a more differentiated myeloid phenotype at relapse in 5 of 10 cases, in the absence of lineage switch. These features would be unusual in lymphoblastic leukemias because trilineage MDS has been described in approximately 15% of de novo AML and, more frequently, in erythroleukemia and megakaryoblastic leukemias.

Immunologic findings in AML-M0 document the consistent expression of the CD34 stem cell marker in association with CD13 and/or CD33 and with other myeloid associated antigens, such as CD11b and CD15. However, no patient was found with isolated expression of CD15 or CD11b, thus confirming the notion that CD13 and CD33 are to be considered the most sensitive and reliable markers for the immunologic diagnosis of AML with minimal myeloid differentiation.

Finally, attention should be drawn to the fact that the anti-CD117 MoAb 17F11, recognizing an epitope of c-kit protein product, functioning as a receptor for the stem cell factor (c-kit ligand), was found to be reactive with more than 10% leukemic cells in 50% of our cases (3 of 6). The distribution of the CD117 antigen in different FAB subtypes of AML is still controversial, some investigators having found 100% positive cases in AML-M0 and AML-M1 and others having reported on a 14.9% positivity in children AML-M1. Obviously, more cases need to be studied to clarify the clinico-biologic significance of CD117 positivity in AML.

Cytogenetic profile of AML-M0: Comparison with unselected AML cases and with AML-M1. A preliminary methodological problem in the definition of the cytogenetic profile of AML-M0 was represented by the selection of an appropriate control group serving as reference for comparative analysis. Data for comparison of AML-M0 with unse-

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>AML-M0 (No. of Cases/Total)</th>
<th>AML-M1 (No. of Cases/Total)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>−5/5q− and/or −7/7q−</td>
<td>11/26</td>
<td>4/42</td>
<td>.0001</td>
</tr>
<tr>
<td>+13 (+/− additional)</td>
<td>5/26</td>
<td>1/42</td>
<td>&lt;.0003</td>
</tr>
<tr>
<td>Others</td>
<td>5/26</td>
<td>14/42</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>5/26</td>
<td>23/42</td>
<td></td>
</tr>
<tr>
<td>Complex</td>
<td>12/26</td>
<td>3/42</td>
<td></td>
</tr>
<tr>
<td>1-2 abnormalities</td>
<td>9/26</td>
<td>16/42</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Normal</td>
<td>5/26</td>
<td>23/42</td>
<td></td>
</tr>
<tr>
<td>Unbalanced chromosome changes</td>
<td>20/21</td>
<td>12/42</td>
<td></td>
</tr>
<tr>
<td>Balanced chromosome changes</td>
<td>1/26</td>
<td>7/42</td>
<td>.001</td>
</tr>
<tr>
<td>Normal</td>
<td>5/26</td>
<td>23/42</td>
<td></td>
</tr>
</tbody>
</table>

relapse were consistent with a diagnosis of AML-M0 in 5 cases; whereas, the features of AML-M1 were observed in 4 cases, and those of AML-M2, in 1 case. Three transplanted patients (no. 16, 22, and 24) are alive and free of leukemia at 15, 40, and 96 months; whereas the remaining patients died at less than 1 to 37 months, with a median overall survival of 8 months.

DISCUSSION

Diagnosis of AML-M0. Although the formulation of a generally accepted system of classification of acute leukemias by the FAB group (5,12) has provided a framework of reference for the identification of various subtypes of AML, the unequivocal recognition of AML-M0 may still pose some problems, with particular reference to the possibility of confusing early lymphoblastic leukemia with inappropriate expression of myeloid antigens.

The diagnosis of AML-M0 in our patients fulfilled the FAB criteria and was supported by immunophenotyping and by cytochemical features of the blast cell population. Interestingly, SBB appeared to be more sensitive than MPO in this study, and 7 patients who would have otherwise been classified as AML-M0 because of the presence of less than 3% positivity for MPO were included among AML-M1 at cytologic review, showing 3% to 12% SBB-positive cells.

While a pro-B–lymphoid nature of leukemic cells could be ruled out by negativity for early markers of B-lymphoid differentiation, such as CD19 and CD10, the differential diagnosis with early T-cell acute lymphoblastic leukemia was not unequivocal for those patients with CD7 positivity. This problem may be particularly important, especially for those patients, such as case no. 9, showing a clonally rearranged pattern for the TCR gene.

In the absence of consensus on the diagnostic importance that should be attributed to lineage-associated antigens, we felt that a diagnosis of AML-M0 was appropriate in these patients, given the absence of coordinate expression of T-lymphoid features (ie, negativity for the AcP stain, for the TdT as well as for the CD5, CD2, and CD3 molecules). It is noteworthy that, although the finding of inappropriate rearrangement of the IgH chain and TCRα or γ gene is not surprising in AML, especially in those patients with blast cell immaturity and TdT positivity, the incidence of such genetic events in our series is not dissimilar as compared with previous studies of unselected AML cases.

Clinical and cytotologic follow-up in this series yields the following observations confirming the "nonlymphoid nature" of these leukemias: (1) the presence of trilineage MDS in 7 of 16 evaluable cases; (2) an MDS phase preceding overt relapse in 2 cases achieving CR; and (3) a more differentiated myeloid phenotype at relapse in 5 of 10 cases, in the absence of lineage switch. These features would be unusual in lymphoblastic leukemias because trilineage MDS has been described in approximately 15% of de novo AML and, more frequently, in erythroleukemia and megakaryoblastic leukemias.

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Cytogenetic profile of AML-M0: Comparison with unselected AML cases and with AML-M1. A preliminary methodological problem in the definition of the cytogenetic profile of AML-M0 was represented by the selection of an appropriate control group serving as reference for comparative analysis. Data for comparison of AML-M0 with unse-

Table 4. Clinical Findings in 26 Patients With AML-M0

| Age in years | 60 (15-79) |
| WBC (×10^9/L) | 4.9 (1.2-64) |
| Plts (×10^9/L) | 57 (24-550) |
| Hb (g/dL) | 8.7 (4.1-12.1) |
| %BM blasts | 91 (49-99) |
| %CR | 54 |
| Duration of CR (mo)* | 6 (2-25) |
| Survival (mo) | 8 (1-96) |

Values shown are given as the median with range in parentheses, and * indicates that the patient is alive.

Abbreviations: WBC, white blood cell count; Plts, platelets; Hb, hemoglobin.

* Excluding patients transplanted in CR.
selected AML cases were derived from the report of the Sixth
International Workshop on Chromosomes in Leukemia
(SIWCL). In addition, we elected to include into this study
original cytogenetic data from a cohort of patients affected
with de novo AML without maturation, corresponding to the
M1 type of the FAB classification, to be able to compare
chromosome findings in these cytologically similar forms of
leukemia, the distinction of which may not be immediate on
cytologic grounds and may appear somewhat artificial from
a biologic point of view.

According to our data, de novo AML-M0 stands out as a
disease entity with a higher percentage of abnormal karyo-
types (80.7%) as compared with unselected cases of AML
reported at the SIWCL, where up to 46% cytogenetically
normal cases were found. In addition, the type of chromo-
some changes in AML-M0 differs significantly with respect
to the general cytogenetic profile of AML, a conclusion rein-
förmed by a literature review of previously reported cases
with AML-M0 diagnosed according to the FAB proposals
(see Table 6).

None of the chromosome translocations associated with
well-defined cytologic subsets of AML was encountered in
this series, nor was any previously unrecognized transloca-
tion found as a recurrent chromosome change in our patients
with AML-M0. Notably, 11q23 rearrangements, possibly
associated with stem cell involvement in acute leukemia, were
not observed in this series. Chromosome changes, such
as 5q and 7q abnormalities, normally found in many FAB
subtypes of AML were detected in 13 of 21 (61.9%) AML-
M0 cases with abnormal karyotype, a figure significantly
higher than the 21% derived from 357 de novo AML cases
with abnormal karyotype reported at the SIWCL.

Interestingly, a 66% and 72.4% frequency of 5q and/or
7q aberrations was found in two studies of 39 and 58 therapy-
related AML (t-AML) cases with abnormal karyotype. These
findings show that some cytogenetic features in our patients
with AML-M0 recall those typically found in a subset of
t-AML and may suggest that similar leukemogenic mechanism
may frequently be operative in these forms of leukemia.

The cytogenetic profile of AML-M0 shows similar differ-
ences even when compared with the cytologically closest
form of leukemia, namely AML-M1. In addition, analysis of
our data shows that trisomy 13 and aberrations of 2p are
more frequently observed in AML-M0, that 3q21/q26
rearrangements may be confined to AML-M1, and that the
observed frequency of primary chromosome changes in
AML-M0 differs significantly with respect to AML-M1. Be-
sides abnormalities of 5q and 7q, complex karyotypes and
unbalanced chromosome changes leading to gain or loss of
chromosome material, normally regarded as characteristic chro-
mosome changes in t-AML, appeared more frequently in
AML-M0 than in AML-M1. In this respect, it is interesting
to note that a view is emerging that balanced reciprocal
translocations and unbalanced chromosome abnormalities
may contribute differently to malignant transformation, the
former type possibly resulting from exposure to agents tar-
getting DNA topoisomerase I1 and the latter type being char-
acteristically associated with genetic damage following "in vivo"
and "in vitro" exposure to mutagens, such as alkylating
agents. Finally, it is noteworthy that aberrations of
5q and 7q and deletions or translocations of 12p are also
very common in erythroleukemia, which is usually re-
garded as a stem cell disorder with multiple cell-lineage
involvement. In the absence of reliable markers of early erythroid
derdifferentiation, the theoretical possibility should be
considered that some leukemias fulfilling the FAB criteria
for AML-M0 may in fact represent proliferations of immat-
ure erythroid precursors.

Correlation of chromosome findings with clinicobiologic
features. Further insights into the significance of chromo-
some findings in AML-M0 may be derived from the observation
that, in this study, 11 cases had -5q- and/or -7q- as
a possible primary chromosome change, 5 cases had +13,
5 patients had different nonrecurring primary chromosome
aberrations, and 5 patients had a normal karyotype.

As shown in Table 5, analysis of clinicobiologic findings
in these cytogenetic groups of AML-M0, yields important

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Table 5. Correlation of Cytogenetic Findings, Cytologic Features, and Clinical Outcome in 26 Patients With AML-M0

<table>
<thead>
<tr>
<th>Primary Clonal Abnormality</th>
<th>No. of Cases</th>
<th>Age (yr)</th>
<th>WBC Count (×10^9/L)</th>
<th>% BM Blast*</th>
<th>1%–2% SBB/MPO +/Total</th>
<th>TMDS/Total</th>
<th>CR (Yes/Total)</th>
<th>CD7 or TdT/Total</th>
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<tbody>
<tr>
<td>-5q- and/or -7q-</td>
<td>11</td>
<td>44 (33-73)</td>
<td>3.6 (1.2-29)</td>
<td>79 (49-93)</td>
<td>3/11</td>
<td>5/7</td>
<td>4/11</td>
<td>8/11</td>
</tr>
<tr>
<td>+13</td>
<td>5</td>
<td>72 (55-73)</td>
<td>11.8 (5.7-64)</td>
<td>95 (74-97)</td>
<td>1/5</td>
<td>1/2</td>
<td>2/5</td>
<td>5/6</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>5</td>
<td>66 (59-66)</td>
<td>4.6 (1.4-91)</td>
<td>96 (63-97)</td>
<td>1/6</td>
<td>1/3</td>
<td>3/4</td>
<td>4/5</td>
</tr>
<tr>
<td>Normal</td>
<td>5</td>
<td>49 (26-79)</td>
<td>1.6 (1.5-16)</td>
<td>92 (68-99)</td>
<td>4/5</td>
<td>0/4</td>
<td>4/4</td>
<td>4/5</td>
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</table>

Abbreviation: TMDS, trilineage MDS; * Data not available for all cases.

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Table 6. Cytogenetic and Clinical Findings in AML-M0

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>No. of Cases</th>
<th>Median Age (Range)</th>
<th>Cr (Yes/Total)</th>
<th>Reference</th>
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<tbody>
<tr>
<td>Normal</td>
<td>12</td>
<td>60 (32-59)</td>
<td>4/7</td>
<td></td>
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<tr>
<td>-5q- and/or -7q-</td>
<td>10</td>
<td>62 (29-70)</td>
<td>0/6</td>
<td>1, 4, 8, 44, 46</td>
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<td>+8</td>
<td>7</td>
<td>62 (54-68)</td>
<td>2/3</td>
<td>1, 5, 8, 46</td>
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<tr>
<td>+19</td>
<td>4</td>
<td>45 (66)</td>
<td>1/1</td>
<td>5, 8, 43, 45</td>
</tr>
<tr>
<td>+13</td>
<td>3</td>
<td>62 (61-67)</td>
<td>2/3</td>
<td>8, 39, 40, 43</td>
</tr>
<tr>
<td>del(3)</td>
<td>2</td>
<td>61-70</td>
<td>0/2</td>
<td>8</td>
</tr>
<tr>
<td>t(12;13)(p13;q14)</td>
<td>2</td>
<td>61-70</td>
<td>NR</td>
<td>47</td>
</tr>
</tbody>
</table>

Only those cases with clonal aberrations observed in at least 2 patients are shown. del(3p) was associated in both cases with -5 or -7; +19 was associated with +13 in 1 case.

Abbreviation: NR, not reported.

* Data not available for all cases.
These findings indicate that the identification of AML-M0 as a distinct entity may be justified on cytogenetic and clinicobiologic grounds and indicate that chromosome changes may partially account for the unfavorable outcome usually associated with this leukemia.

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Cytogenetic profile of minimally differentiated (FAB M0) acute myeloid leukemia: correlation with clinicobiologic findings [see comments]

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