Biological Profile of 23 Cases of Minimally Differentiated Acute Myeloid Leukemia (AML-M0) and Its Clinical Implications

To the Editor:

In a recent issue of Blood, Cuneo et al described the cytogenetic and immunophenotypic features of 26 cases of minimally differentiated acute myeloid leukemia (AML-M0). On cytogenetic ground they found a more frequent appearance of abnormal/complex karyotypes and unbalanced chromosome changes (80.7%) in AML-M0 as compared to its closest French-American-British (FAB) group AML-M1. The authors concluded that AML-M0 has a peculiar cytogenetic profile often resembling that of secondary AMLs, which may partially explain the poor prognosis of these leukemias. Based on the recurrent presence of 5q and 7q deletions or translocation 12p, which are common findings in erythroleukemia, the authors also hypothesized the possibility that some cases of AML-M0 may be in fact part of immature erythroid proliferation. On immunologic ground they observed the prevalent expression of the CD34 stem cell marker along with CD13 and/or CD33 and with other myeloid markers such as CD11b and CD15. However, no isolated expression of CD11b or CD15 was detected. The authors stated that these findings confirm the notion that “CD13 and CD33 are to be considered the most sensitive and reliable markers for the immunologic diagnosis of AML with minimal differentiation.” We would like to contribute with our experience in 23 cases of AML-M0 that were diagnosed among 256 consecutive AMLs seen at our Institution between January 1987 and June 1995. Leukemic cells were morphologically marked by agranular basophilic cytoplasm, finely dispersed chromatin, and prominent nucleoli. In 2 cases, heavily vacuolated and monocytoid-shaped blasts were also observed. Cytochemistry (MPO, SBB, αANAЕ, αNBE, NASDCAE, AP, PAS) was inconclusive in all cases but five that showed a very faint cytoplasmic positivity for αNBE (not exceeding 30% of the blasts) and αANAЕ (not exceeding 41% and sodium fluoride resistant). In these cases no myelomonocytic markers (eg, CD14) were detected and a diagnosis of M4/M5 was excluded. The expression of immaturity markers was a frequent event; 23 cases (96%) were CD34+ whereas terminal deoxynucleotidyltransferase (TdT) was positive in 56% and the remaining cases showed positivity for at least one of the following markers: CD34+ (43%), CD33+ (26%), CD11b+ (13%), CD15+ (9%), bcr/abl (7%).

Table 1. Incidence of Observed Chromosome Abnormalities Among AML-M0 and AML-M1

<table>
<thead>
<tr>
<th>Karyotype</th>
<th>AML-M0 (No. of cases/total)</th>
<th>AML-M1 (No. of cases/total)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>–5/5q and/or –7/7q</td>
<td>5/19</td>
<td>1/28</td>
<td></td>
</tr>
<tr>
<td>(+/- additional)</td>
<td>1/19</td>
<td>1/28</td>
<td>NS</td>
</tr>
<tr>
<td>+13 (+/- additional)</td>
<td>2/19</td>
<td>0/28</td>
<td>NS</td>
</tr>
<tr>
<td>+8 (+/- additional)</td>
<td>6/19</td>
<td>9/28</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>4/19</td>
<td>7/28</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>8/19</td>
<td>4/28</td>
<td></td>
</tr>
<tr>
<td>1-2 abnormalities</td>
<td>7/19</td>
<td>17/28</td>
<td>NS</td>
</tr>
<tr>
<td>Normal</td>
<td>4/19</td>
<td>7/28</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NS, not significant.
dyl transferase (Tdt) was expressed in 15 cases (65%), Hla-DR in 21 cases (91%), and CD7 in 7 cases (30%). By immunocytochemistry assay, myeloperoxidase (anti-MPO) tested positive in all cases, a cut-off level of 10% being regarded as a major diagnostic criterion. CD13 and CD33 were expressed in 16 (70%) and 15 (65%) cases, respectively; in 12 samples (50%) they were combined whereas in 3 (13%) were both negative. One of these patients carried CD15 as the only membrane myeloid marker, the remainders showed no surface myeloid antigens. CD2, CD10, and CD19 were detected in 3 (13%), 2 (9%), and 1 (4%) of the cases, respectively. The concurrent expression of lymphoid markers was observed in 5 cases (1 Tdt+CD19, 1 CD7+CD2, 1 CD7+CD10, 1 CD7+CD2+Tdt, and 1 CD2+CD10+Tdt). Despite lymphoid markers expression we believed these cases to be qualified as AML-M0 with minimal phenotypic deviation rather than biphenotypic leukemia, based on the cCD3/cCD22 negativity and the low score for biphenotypic leukemia as proposed by Buccheri et al. MDR protein and c-kit tested positive in 5 of 15 (40%) and 6 of 10 (60%) samples examined, respectively. Nineteen cases were subjected to cytogenetic evaluation and 15 cases (79%) were found abnormal. Lesions were generally complex, trisomy 8 and 4 and anomalies of chromosome Y, 2, 3, 5, 6, 7, 9, 11, 13, 19, and 21 being the most common findings. Following the model proposed by Cuneo et al we selected from our file AML-M1 cases (n = 50) for comparative analysis. The groups were homogeneous as regard to age and white blood cell count; AML-M0 and M1 were found to share several phenotypic and karyotypic aspects. In fact they expressed Hla-DR, CD7, CD13, CD33, p170, c-kit, and lymphoid markers in a similar fashion. The only statistically significant difference was relative to the expression of Tdt more frequently detected in AML-M0 (65% vs 30% P = .009). Even karyo-
typic evaluation confirmed the similarities between the two groups. The incidence of chromosome abnormalities was 75% among AML-M1 (79% among AML-M0) and again we observed complex karyotypes, although less frequently as compared to AML-M0, trisomy 8 and frequent involvement of chromosome 2, 3, 5, 6, 7, 9, 11, and 17 (Table I). Despite the biological links between AML-M0 and M1, clinical management yielded different results as showed in Fig 1 and 2; AML-M1 did considerably better than AML-M0 (CR 50% v 22% P = .02). We conclude that (1) anti-MPO is an extremely sensitive reagent to recognize AML-M0; it is probably more useful than CD13/CD33 that were both negative in 3 cases, whereas anti-MPO was always expressed; (2) the expression of lymphoid markers is not necessarily against a diagnosis of AML-M0. Based on the anti-MPO, CD13, CD33 positivity, cCD3/cCD22 negativity, and the insufficient score for biphenotypic leukemia, a diagnosis of AML-M0 was assigned to our cases bearing lymphoid markers; (3) under certain conditions AML-M0 might be part of monoblastic/monocytic proliferation. In fact 3 of our cases eventually relapsed as M4/M5 forms thus suggesting that M0 leukemic cells might have been immature monoblasts that expressed dimly differentiation antigens and faintly nonspecific esterase or did not at all. The occurrence in 1 case of the t(6;11)(q15;q23) that is strongly associated with monoblastic/monocytic leukemia supports this view; (4) although no substantial phenotypic, karyotypic, and clinical differences were identified between AML-M1 and M0, the latter clearly showed a more aggressive outcome often leading to treatment failure. This observation prompts the question of what causes leukemias sharing mutual characteristics to behave so differently in terms of prognosis. It probably relies on intrinsic features to M0 blast cells and implementation of molecular studies should answer this question.

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REFERENCES

Biological profile of 23 cases of minimally differentiated acute myeloid leukemia (AML-M0) and its clinical implications [letter; comment] [see comments]

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