Clinical Importance of CD7 Expression in Acute Myelocytic Leukemia

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Forty patients (9 females and 31 males; mean age 41.9 years) with CD7+ acute myelocytic leukemia (AML) were investigated; they were classified into the following subgroups according to French-American-British classification: 15 M1, 18 M2, 3 M4, and 4 M5. Leukemic cells from all the patients were negative for T-cell-specific antigens, surface CD3, and T-cell-receptor molecules. The cation: 15 MI, 18 M2, 3 M4, and 4 M5. Leukemic cells system involvement were also frequent in the CD7+ AML patients.

EMATOLOGIC investigations in the past decade show that, to make precise diagnoses of acute myelocytic leukemia (AML), it is necessary to consider information from the various fields. Patients with several kinds of karyotypic abnormalities, such as t(8;21) and t(15;17), are well known to manifest unique cytologic and clinical features. Immunophenotyping has made it possible to recognize AML cells according to appropriate stages of myeloid differentiation, and, further, has enabled the identification of peroxidase (POX)-negative AML. However, approaches involving myeloid antigen expression, as compared with the cytogenetical approach, have not always succeeded in aiding in the diagnosis of AML, because no distinct myeloid phenotype related to the clinical features of this disease has yet been identified except that of acute promyelocytic leukemia.

It has been shown that considerable numbers of AML patients had both myeloid and lymphoid antigens. A pan T-cell antigen, CD7, is one of the lymphoid antigens often expressed on AML cells. Several investigators have drawn attention to the immaturity of CD7+ AML cells manifested by, for instance, their frequent expression of terminal deoxynucleotidyl transferase (TdT). With regard to acute lymphoblastic leukemia (ALL), Kurtzberg et al. proposed CD7+CD4−CD8− ALL as "lymphohematopoietic stem cell leukemia" because of its multipotentiality for myeloid and lymphoid differentiation. CD7 expression in AML leads us to the issue of whether or not these two types of acute leukemia can be recognized as part of a continuous disease spectrum, disregarding the division of AML and ALL. Clinically, the expression of myeloid antigen in ALL is recognized as one of the prognostic risk factors. CD7 expression in AML is also speculated to have some clinical importance, but little is known about it.

In the present study, a large number of AML patients were investigated to clarify the relationship between the cellular characteristics and clinical features. Our results show that CD7 expression on AML cells is indicative not only of phenotypic, but also of functional immaturity and can be regarded as a prognostic risk factor in AML.

H MATERIALS AND METHODS

Patients. Two hundred ten Japanese adult patients (older than 15 years) with AML were enrolled in this study between January 1987 and June 1991. All patients gave their informed consent for the procedures involved. Bone marrow (BM) and peripheral blood (PB) smears were prepared for May-Giemsa, POX, naphthol AS-D chloroacetate esterase, and naphthyl butyrate esterase staining. Leukemic cells from all patients fulfilled French-American-British (FAB) criteria for AML, and the patients were classified as follows: 40 patients as M1, 72 as M2, 40 as M3, 32 as M4, and 26 as M5. In this study, we excluded M6 and M7 patients because it is usually difficult to determine the phenotype of their leukemic cells. We also excluded acute leukemia after myelodysplastic syndrome.

Immunophenotyping. Mononuclear cells (MNC) were separated from heparinized PB and BM by Ficoll-Hypaque centrifugation (Pharmacia LKB Biotechnology AB, Uppsala, Sweden). Stocked samples, which had been isolated and frozen at −196°C in RPMI 1640 medium with 20% heat-inactivated fetal calf serum (FCS) and 10% dimethyl-sulfoxide, were also used as needed.

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Before immunostaining, MNC were treated with 5% heat-aggregated human AB serum for blocking of binding due to receptors for IgG Fc portion (FcR). CD11b (recognized by OKM1), CD13 (by M-CSF), CD15 (by LeuM1), CD33 (by My9), and CD34 (by My10) were tested as myeloid cell markers: CD2 (by T1), CD5 (by Leu1), CD7 (by TP40), CD3 (by Leu4), CD4 (by Leu3a), CD8 (by Leu2), CD1 (by OKT6), T-cell receptor (TCR) α and β chain complex (by WT31), and TCR γ chain (TCRG: by TCRGI) as T-cell markers; and CD19 (by Leu12 and/or B4), CD20 (by Leu16), and CD22 (by Leu14) as B-cell markers. CD10 and HLA-DR were examined with J5 and OK6a, respectively. Goat antimouse Ig fluorescein-conjugates (GAM-FITC) was used as the second reagent.

Cytoplasmic CD3 (cCD3) was stained by labeled avidin-biotin-alkaline phosphatase technique on acetone-fixed cytosin smears. TdT was tested by indirect immunofluorescence with rabbit anti-TdT antibody or anti-TdT monoclonal antibody (MoAb) on methanol-fixed cytosin smears.

Samples were evaluated by flow cytometry (Cytoron; Ortho Diagnostic Systems, Tokyo, Japan), light microscopy (Olympus, Tokyo, Japan), or immunofluorescence microscopy (Olympus). At least 5,000 cells were examined for surface marker study, and 200 cells were examined for the cCD3 and TdT studies. Samples were considered as positive for an MoAb if more than 15% of cells showed specific labeling above that of controls.

The MoAb TP40 and MCS2 were kindly provided by Drs R. Ueda (Aichi Cancer Center, Nagoya, Japan), and E. Tatsurni (Kobe University, Kobe, Japan), respectively. The Leu series, My10, and WT31 MoAb were purchased from Becton Dickinson (Mountain View, CA); My4, My9, B4, J5, anti-TdT MoAb, and GAM-FITC were from Coulter Inc (Hialeah, FL); the OK series were from Ortho; TCRγ1 MoAb was from T-Cell Science Inc (Cambridge, MA); and rabbit anti-TdT antibody was from Bethesda Research Labs. (Gaithersburg, MD). Whole mouse Igs, IgG1, and IgG2 used as the controls were purchased from Chemicon Int Inc (Temecula, CA).

**Southern blot study and DNA probes.** Extraction of high molecular weight DNA from MNC, and Southern blot DNA analysis were performed as described previously. DNA probes for determining the gene structures of Ig heavy chain (IgH), TCRα, TCRγ, and TCRδ were as follows: JH for IgH joining (J) region genes, Cβ1 for TCRβ constant (C) region genes, Jγ1 for TCRγ Jγ1 region genes, Jό1 for TCRό Jό1 region genes, and Cό1 for TCRό C region genes. DNA probes, except for TCRδ genes, were kindly provided by Dr T. Honjo (Kyoto University, Kyoto, Japan). Probes for TCRδ genes were kindly provided by Dr Y. Takihara (Osaka University, Osaka, Japan).

**Cell cultures.** The T-cell- and adherent cell-eliminated MNC fraction was used as the leukemic cell-eliminated fraction. Response of leukemic cells to various growth factors was tested by [3H]TdR incorporation method in short-term liquid culture as described previously.

**Karyotype analysis** Karyotype analysis was performed on aspirated BM cells, as described previously.

**Statistical analysis.** Differences in cellular and clinical characteristics between CD7+ and CD7− patients were evaluated by chi-squared statistics or Student's t-test. The survival of CD7+ and CD7− AML patients was calculated by the Kaplan-Meyer method, and the difference was evaluated by generalized Wilcoxon's test. Cox's proportional hazard model for estimating prognostic significance for these AML patients was tested, and selection of the best-fit model in the multivariate analysis was based on Akaike's information criterion.

**RESULTS**

**Clinical manifestations of CD7+ AML patients.** CD7 expression was found in 15 M1, 18 M2, 3 M4, and 4 M5 patients (Table 1). The clinical manifestations in these CD7+ AML patients are shown in Table 2. CD7+ AML occurred in younger males than CD7− AML (P < .01). There were no differences of age and sex distribution among the FAB subtypes of CD7+ AML. The incidence of hepatomegaly and percentage of blasts in PB were higher in CD7+ AML than in CD7− AML. Central nervous system (CNS) involvement at initial diagnosis and relapse was also frequent in CD7+ AML.

**Cellular characteristics of CD7+ AML cells.** AML cells show morphologic heterogeneity in common, and they are widely spread on the cytogram in the flow cytometric study. In principle, to clarify the phenotypes of the leukemic stem cells, we focused on the blastic fraction of the cytogram, as reported previously. Nonspecific binding caused by FcRγ was avoided by sufficient pretreatment with human AB serum.

The lymphoid antigens, CD7, CD2, and CD19, were detected on AML cells of 40, 26, and 38 patients, respectively. No other T-cell and B-cell lineage-restricted antigens, surface CD3 (sCD3), TCR molecules, or CD20 were expressed on AML cells in any of the patients. Positivities of CD7, CD2, and/or CD19 on AML cells were judged to the population overlapping of percentage of cells expressing each antigen (data not shown). CD7+, CD2+ and CD19+ positivity between CD7+ and CD7− AML (Table 2).

**Table 1. Incidence of CD7+ Patients in Each AML FAB Classification Category**

<table>
<thead>
<tr>
<th>FAB Category</th>
<th>No. of Patients Examined</th>
<th>No. of CD7+ Patients</th>
<th>Incidence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M1</td>
<td>40</td>
<td>15</td>
<td>37.5</td>
</tr>
<tr>
<td>M2</td>
<td>72</td>
<td>18</td>
<td>25.0</td>
</tr>
<tr>
<td>M3</td>
<td>40</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>M4</td>
<td>32</td>
<td>3</td>
<td>9.4</td>
</tr>
<tr>
<td>M5</td>
<td>26</td>
<td>4</td>
<td>15.4</td>
</tr>
<tr>
<td>Total</td>
<td>210</td>
<td>40</td>
<td>19.0</td>
</tr>
</tbody>
</table>
Two CD7+ patients had sole rearrangement of TCRβ or TCRγ genes, respectively. IgH gene rearrangement was not found in any CD7+ samples examined. The incidence of rearranged immunogenotype in CD7+ AML did not differ from that in CD7- AML (Table 2).

Effects of exogenous hematopoietic growth factors on CD7+ AML cells. The effects of exogenous growth factors on leukemic cells were evaluated by determining [3H]TdR incorporation in 23 CD7+ and 53 CD7- AML samples. The response of leukemic cells to any factor was considered to be positive when the difference between [3H]TdR uptake counts in the cells cultured with the factor and the control was more than 2,000 cpm and over twice the standard deviation (SD) of the control value.

Leukemic cells from 15 CD7+ and 37 CD7- AML patients were stimulated by one or more of the growth factors. Prominent spontaneous growth or no response was recorded from the remaining 7 CD7+ and 9 CD7- samples. IL-3 was the most powerful stimulator of DNA synthesis in leukemic cells from 15 of the CD7+ responders, while IL-3 exerted such effects on only 8 of the CD7- responders. The differences between CD7+ and CD7- AML samples in responsiveness to IL-3 were significant (P < .01; Table 4). The responsive behavior of CD7+ M2 samples to IL-3 was not different from that of CD7+ M1 samples.

Karyotypes of CD7+ AML patients. A normal karyotype was found in 20 of 31 CD7+ AML patients examined. Abnormal karyotypes were found in 11 patients as follows: +8
The incidence of CD2 expression in t(15;17) and CD19 expression in t(8;21) was significantly higher than that in patients; the remaining 16 patients were excluded because of 

bicin [DNR], 6-mercaptopurine [6-MP], and prednisolone 

in 1, +13 in 1, +21 in 2, Yq+, Yq+ in 1, -7 in 1, -X, -11, -12, -13 in 1, -15, -18, +del(15)(15:?) in 1, t(11;17) in 1, t(8;21) in 1, and -13, -14, t(5;16), t(6;11), +del(14)(14:?), +mir in 1 patient. Thus, no common form of karyotypic abnormality was identified in CD7+ AML. On the other hand, 10 of 14 CD7-CD2+ AML patients had t(15;17), and 20 of 26 CD19- AML patients had t(8;21). The incidence of CD2 expression in t(15;17) and CD19 expression in t(8;21) was significantly higher than that in patients with normal karyotype or other karyotypic abnormalities. 

Therapeutic outcome of CD7+ AML patients. In this study, 180 patients were treated with BHAC-DMP chemotherapy (adenosylcobalamin [BHAC], daunorubicin [DNR], 6-mercaptopurine [6-MP], and prednisolone [PDN], which is a standard regimen for AML in Japan. Chemotherapeutic effects could be evaluated in 164 of those patients; the remaining 16 patients were excluded because of early death, ie, within 2 weeks (14 patients) and nonpathologic death (2 patients). The survival of these patients was evaluated on December 31, 1991. Two CD7+ and 6 CD7- AML patients died (2 patients). The survival of these patients was evaluated in 164 cases at the time of BMT. Scheduled intensification chemotherapy, which consisted of three to six drugs selected from DNR (or acracinomycin or mitoxantron), BHAC (or cytosine arabinoside), 6-MP, etoposide, vincristine (or vin- 

Table 4. Response Pattern of CD7+ and CD7- AML Cells to Hematopoietic Growth Factors

<table>
<thead>
<tr>
<th>IL-3</th>
<th>G-CSF</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-3 &gt; GM-CSF/ICF</td>
<td>16</td>
<td>15</td>
</tr>
<tr>
<td>Others*</td>
<td>44</td>
<td>8</td>
</tr>
<tr>
<td>IL-3 Nonresponder</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: N, evaluable case number.

* Case showing the greatest response to IL-3.
† Case showing the greatest response to GM-CSF and/or G-CSF.

In 1, +13 in 1, +21 in 2, Yq+, Yq+ in 1, -7 in 1, -X, -11, -12, -13 in 1, -15, -18, +del(15)(15:?) in 1, t(11;17) in 1, t(8;21) in 1, and -13, -14, t(5;16), t(6;11), +del(14)(14:?), +mir in 1 patient. Thus, no common form of karyotypic abnormality was identified in CD7+ AML. On the other hand, 10 of 14 CD7-CD2+ AML patients had t(15;17), and 20 of 26 CD19- AML patients had t(8;21). The incidence of CD2 expression in t(15;17) and CD19 expression in t(8;21) was significantly higher than that in patients with normal karyotype or other karyotypic abnormalities. 

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Table 5. Favorable Effects of Secondary Therapeutic Regimens for CD7+ AML Patients After Failure of Remission Induction With BHAC-DMP

<table>
<thead>
<tr>
<th>Patients</th>
<th>FAB</th>
<th>2nd Tx.</th>
<th>Effect</th>
<th>CR</th>
<th>Duration</th>
<th>POX</th>
<th>CD13</th>
<th>CD34</th>
<th>CD2</th>
<th>CD6</th>
<th>cCD3</th>
<th>TdT</th>
</tr>
</thead>
<tbody>
<tr>
<td>H.S.</td>
<td>M1</td>
<td>AdVP-L</td>
<td>CR</td>
<td>8 M</td>
<td>15</td>
<td>54</td>
<td>82</td>
<td>96</td>
<td>0</td>
<td>39</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>N.A.</td>
<td>M1</td>
<td>AdVP-L</td>
<td>CR</td>
<td>14 M</td>
<td>82</td>
<td>7</td>
<td>73</td>
<td>80</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>T.M.</td>
<td>M2</td>
<td>AdVP-L</td>
<td>CR</td>
<td>&gt;29 M</td>
<td>42</td>
<td>70</td>
<td>50</td>
<td>82</td>
<td>30*</td>
<td>2</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>I.M.</td>
<td>M1</td>
<td>AcrMVP</td>
<td>CR</td>
<td>13 M</td>
<td>7</td>
<td>96</td>
<td>90</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>89</td>
<td></td>
</tr>
<tr>
<td>K.H.</td>
<td>M2</td>
<td>MAP</td>
<td>CR</td>
<td></td>
<td>80</td>
<td>36</td>
<td>46</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Tx, therapy; POX, peroxidase; CR, complete remission; NT, not tested; AdVP-L, adriamycin, vincristine, prednisolone, and 1-asparaginase; AcrMVP, acracinomycin, mitoxantron, etoposide, and vincristine; MAP, mitoxantron, cytosine arabinoside, and prednisolone. 

* CD5 was expressed on leukemic cells.

DISCUSSION

In this study, we describe the clinical importance of CD7 positivity in AML fulfilling the FAB criteria. Patients with CD7+ AML were younger males who had a higher incidence of hepatomegaly and CNS involvement than CD7- AML patients. They responded poorly to standard chemotherapy for AML, and had an unfavorable outcome. Thus, the CD7+ AML patients showed unique and characteristic clinical manifestations.

CD7+ AML cells showed a common form of phenotypic and proliferative properties. The incidence of positivity for the myeloid progenitor-associated antigens, CD34 and HLA-DR, and TdT was significantly higher in CD7+ AML than in CD7- AML. Recombinant hematopoietic growth factors have been used in hematologic investigations, and this has made it possible to examine the proliferative and differentiation behaviors of AML cells along the developmental stages of hematopoietic differentiation. However, the prolifer-

Table 6. Neither CD2 nor TdT positivity in AML patients fulfilling the FAB criteria. Patients with both CD2+ and TdT+ AML had a lower CR rate than CD7+ patients.

The survival rate of the CD7+ AML patients calculated by the Kaplan-Meyer method and generalized Wilcoxon's test was lower than that of the CD7- patients (P < .01; Fig 1A), but there was no difference in disease-free survival between these two groups. Multivariate life-table analysis was performed on 156 patients with AML on whom 10 variables including age, sex, hepatomegaly, CD7, CD2, CD19, HLA-DR, CD13, CD33, and CD34 were all available, and all of the possible combinations were estimated. The best model included age, CD7, and CD33 as predictors, and next model included age and CD7. Because CD33+ patients were less than 10%, the model of age and CD7 was considered to be suitable for estimated relative hazard model; P value for global null hypothesis was .004655 (X2 = 10.74, degree of freedom: 2), P value for CD7 was .003354, and P value for age was .023088.
Table 6. Differences Among Subgroups in Therapeutic Effects of AML Therapy

<table>
<thead>
<tr>
<th>Phenotype</th>
<th>N</th>
<th>CR</th>
<th>PR/NR</th>
<th>CR Ratio (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD2+</td>
<td>21</td>
<td>15</td>
<td>6</td>
<td>71.4</td>
</tr>
<tr>
<td>CD2-</td>
<td>143</td>
<td>114</td>
<td>29</td>
<td>79.7</td>
</tr>
<tr>
<td>CD2+CD7+</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>20.0</td>
</tr>
<tr>
<td>CD2+CD7-</td>
<td>15</td>
<td>14</td>
<td>1</td>
<td>93.3</td>
</tr>
<tr>
<td>CD2+CD7+</td>
<td>6</td>
<td>1</td>
<td>5</td>
<td>20.0</td>
</tr>
<tr>
<td>CD2-CD7</td>
<td>29</td>
<td>16</td>
<td>13</td>
<td>55.2</td>
</tr>
<tr>
<td>CD2+CD7+</td>
<td>29</td>
<td>16</td>
<td>13</td>
<td>55.2</td>
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<td>CD2-CD7+</td>
<td>29</td>
<td>16</td>
<td>13</td>
<td>55.2</td>
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<tr>
<td>CD2+CD7-</td>
<td>114</td>
<td>97</td>
<td>17</td>
<td>85.1</td>
</tr>
<tr>
<td>TdT+</td>
<td>29</td>
<td>13</td>
<td>7</td>
<td>65.0</td>
</tr>
<tr>
<td>TdT-</td>
<td>77</td>
<td>64</td>
<td>13</td>
<td>83.1</td>
</tr>
<tr>
<td>TdT+CD7+</td>
<td>10</td>
<td>4</td>
<td>6</td>
<td>40.0</td>
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<td>TdT+CD7-</td>
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<td>9</td>
<td>1</td>
<td>90.0</td>
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<tr>
<td>TdT-CD7</td>
<td>13</td>
<td>6</td>
<td>7</td>
<td>46.2</td>
</tr>
<tr>
<td>TdT-CD7+</td>
<td>13</td>
<td>6</td>
<td>7</td>
<td>46.2</td>
</tr>
<tr>
<td>TdT-CD7-</td>
<td>64</td>
<td>58</td>
<td>6</td>
<td>90.6</td>
</tr>
</tbody>
</table>

Abbreviations: N, number of patients evaluated; CR, complete remission; PR, partial remission; NR, no response.

The outcome behavior of CD7+ AML cells is still uncertain. In this study, we found that IL-3, which acts on pluripotent stem cells,22 promoted the greatest increase in DNA synthesis in leukemic cells in CD7+ AML, including M2 and M4. This finding supports the phenotypic immaturity of the CD7+ AML cells.

The incidence of TCR gene rearrangements in CD7- AML remains controversial.27,29 In this study, TCR genes were found in germline configurations in most of the cases examined, as Cuneo et al.29 reported previously. In T-cell ontogeny, CD7 is expressed on most immature T cells, and TCR gene rearrangements are considered to occur during intrathymic development.30-32 Therefore, the presence of TCR gene rearrangements is not regarded as a decisive indicator of CD7+ AML cell immaturity. Thus, CD7+ AML cells are more apt to preserve nature of myeloid progenitor cells or more immature hematopoietic stem cells.

It is well known that several kinds of karyotypic abnormalities are related to the cellular and clinical manifestations of AML,45 and Koefler3 has proposed each of such variations in AML to be a syndrome. However, it remains unclear whether distinct clinical categories of AML are represented by AML with normal karyotype or sporadic karyotypic abnormalities. As shown in our results, no common karyotypic abnormality including any of ALL-associated karyotypes33 was identified in CD7+ AML, whereas the cellular and clinical characteristics of CD7+ AML were sufficiently consistent to allow us to recognize this type of AML as a distinct clinical category.

The clinical outcome finding indicates that CD7 positivity can be considered to be a phenotypical risk factor for AML. Several investigators have documented phenotypical prognostic factors for AML.11,13,19,34,35 Cross et al.11 reported that CD2+ childhood AML had a poor prognosis. We should note that all of the CD2+ childhood AML in that study were positive for CD7. The CD7+CD2+ patients in this study had a poorer response to the AML therapy, as did the childhood AML patients. Nevertheless, when we evaluated all AML populations, we found no significant difference of prognosis between CD2+ and CD2- patients. Patients with CD2+ AML in this study were frequently M3 which was negative for CD7.

Fig 1. Survival probability of CD7+ AML patients. The survival curve was calculated by the Kaplan-Meyer method. (A) Difference between CD7+ and CD7- groups was statistically significant by generalized Wilcoxon's test (P < .01). (B) Differences of survivals among subgroups defined by two significant prognostic factors, CD7 (P = .003354) and age (P = .023888), because of multivariate analysis are presented. The relative hazard of CD7- Young, CD7- Old, CD7+ Young, and CD7+ Old were 0.6424, 1.1465, 1.4284, and 2.6470, respectively. This result was obtained from 156 AML patients who were tested for CD34. Young, < 50 years old; Old, >50 years old.
M3 has a favorable outcome, if the patient escapes early death due to disseminating intravascular coagulation. Indeed, Ball et al. described CD2 expression as a favorable prognostic factor for AML, although in that study the details of the CD2+ AML cells were not always clear. Besides, in our study there was no difference in clinical outcome between TdT+ and TdT- patients. Thus, the diagnostic value of CD7 positivity for overall AML patients was superior to either CD2 or TdT positivity.

Patients with CD7+ AML showed heterogeneous responses to chemotherapy in relation to morphology and phenotype of the leukemic cells. Patients with morphologically immature blasts (M1 and M5a) had a poorer response to the BHAC-DMP therapy than others. In particular, CD7+CD2- M1 and M5a patients did not achieve CR with any of the therapeutic regimens used. It is worth noting that CD7+CD2+ AML patients who failed to respond to the BHAC-DMP therapy achieved CR with ALL therapy. Therefore, since, at present, an effective regimen for CD7+ AML has not been established, we should choose an appropriate therapeutic regimen for these patients according to the morphology and phenotype of their leukemic cells.

Therapeutic response of CD7+ AML in our study was different from that in Schwarzinger et al.35 report. Different anti-CD7 antibody isotypes and immunodetection methods between theirs (WT1, mouse IgG2a, and fluorescence microscopy) and ours (TP40, mouse IgG1, and flow cytometry) might cause different patient populations: mouse IgG2a binds with high affinity to FcγR,36 and intensity of lymphoid antigen expression on AML cells varies among samples.3 Also, we could not rule out a possibility according to different therapeutic regimens.

Recently, CD13/CD33+POX− acute leukemia, which is unrelated to CD7 positivity, has been proposed as a new category, “M0,” by the FAB cooperative group.37 However, the morphologic, biologic, and clinical features of “M0” are not always clearly defined, as mentioned in the report. Kurtzberg et al.38 proposed CD7+CD4−CD8− ALL as a syndrome “lymphohematopoietic stem cell leukemia.” This type of ALL cell frequently expresses myeloid antigens37,38 and shows responsiveness to several growth factors with myeloid differentiation. The clinical manifestation of this type of ALL were similar to those in CD7+ AML; high incidence in males, frequent CNS involvement, and poor response to conventional therapies for acute leukemias. These similarities suggest a fascinating idea: CD7+ AML can be recognized as part of a continuous disease spectrum that includes CD7+CD4−CD8− ALL, at least with germline TCR genes and myeloid antigens, and CD7+ “M0.” This may require us to develop a new diagnostic formulation that would be applicable to both AML and ALL.

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