Acute Myeloid Leukemia With T-Lymphoid Features: A Distinct Biologic and Clinical Entity

By Anne H. Cross, Rakesh M. Goorha, Rachelle Nuss, Frederick G. Behm, Sharon B. Murphy, David K. Kalwinsky, Susana Raimondi, Geoffrey R. Kitchingman, and Joseph Mirro, Jr

We studied the clinical and biologic features of 10 cases of acute leukemia that met standard French-American-British (FAB) criteria for acute myeloid leukemia (AML) but in which the blast cells also expressed the T-cell–associated CD2 surface antigen. All cases had >3% myeloperoxidase and Sudan black B-positive leukemic blasts, and blasts from seven cases contained Auer rods. Reactivity of the cells with a panel of monoclonal antibodies (MAbs) indicated that leukemic cells in all cases expressed myeloid-associated (CD11b, CD13) surface antigens, further supporting the diagnosis of AML. However, blasts from every patient coexpressed the T-cell–associated surface CD2 and CD7 as well as cytoplasmic CD3 antigens. Blasts from five patients expressed surface CD25, whereas blasts from only one expressed surface CD3. Five patients had rearranged T-cell receptor β-chain genes, whereas only three had rearranged T-cell receptor γ-chain genes. This pattern of lineage-related gene expression appears to define a distinct subtype of AML with T-lymphoid features (CD2+ AML) and could reflect either aberrant gene expression in leukemic blasts or transformation of a pluripotent stem cell having a flexible pattern of gene expression. Clinically, these 10 patients presented at an older age with a higher leukocyte count and a higher frequency of lymphadenopathy than did children whose blast cells were characteristic of myeloid leukemia. Patients with CD2+ AML also had poorer responses to remission induction therapy (50% v 80% entered complete remission, P = .05). However, each of the five children who failed induction chemotherapy on AML protocols had a striking response to drug combinations usually reserved for lymphoid leukemias. We conclude that this leukemia with mixed lymphoid and myeloid characteristics is a distinct biologic and clinical entity.

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Most current models of hematopoietic differentiation are based on evidence that normal pluripotent precursors commit to a single lineage, such as myelocytes or T lymphocytes, as a discrete developmental step. The acute leukemias are believed to arise from a clonal expansion of cells after their transformation and arrest at a normal stage of differentiation. Support for this concept comes from studies in which leukemic blast cells adhere morphologically and immunologically to a single lineage. Analysis of gene rearrangements involving the T-cell receptor (TCR) or immunoglobulin (Ig) genes, has confirmed monoclonality and, in most cases, commitment to a single lineage.

Instances in which individual leukemic cells simultaneously express characteristics of both lymphoid and myeloid lineage have been reported. This suggests that acute leukemia may arise from malignant transformation of a progenitor cell capable of differentiating into, or expressing characteristics of, more than one lineage ("lineage promiscuity"). Alternatively, these cases may result from aberrant gene regulation not representative of normal hematopoiesis ("lineage infidelity"). Because selection of leukemia therapy is based largely on whether a case is classified as myeloid or lymphoid, the presence of markers of both lineages could have important implications for treatment.

Since February 1983, we identified 10 patients whose blast cells met standard FAB criteria for AML (myeloperoxidase and Sudan black B positive) but also expressed the T-cell–associated CD2 surface antigen, which is usually associated with sheep erythrocyte binding by T cells. This article reports the clinical, immunophenotypic, and molecular genetic findings that distinguish these cases from typical AML. Evidence indicates that AML patients with blasts that express surface CD2, CD7, and cytoplasmic CD3 antigens have a poor response to therapy and might benefit from alternative therapy.

Materials and Methods

Patients. All patients with the diagnosis of AML evaluated at this institution since February 1983 were tested for expression of the CD2 antigen. Nine patients with CD2+ blast cells were prospectively identified among 94 consecutive AML patients seen at this center from February 1983 to March 1987. Another child was selected retrospectively on the basis of studies using cryopreserved blasts. By morphologic and cytochemical findings, all patients had AML according to conventions of the French-American-British (FAB) Cooperative Group. All blast cells studied were from diagnostic bone marrow samples. Informed consent was obtained for all studies and chemotherapy after approval by the institution's Clinical Trials Committee.

Treatment. The patients were treated according to either of two protocols for AML that included intensive multiagent chemotherapy during all phases. The first protocol (AML-80) included daunorubicin and cytarabine (ara-C) for remission induction, followed by etoposide (VP-16) and 5-azacytidine (5-AZ) for consolidation. Continuation therapy included rotating drug pairs: doxorubicin/ara-C, VP-16/5-AZ, and 6-thioguanine/ara-C. The second protocol (AML-83) consisted of sequential VP-16/ara-C, daunorubicin/6-thioguanine/ara-C, and VP-16/5-AZ for induction, with maintenance therapy including doxorubicin, ara-C, 6-thioguanine, m-AMSA, vincristine, and cyclophosphamide. The induction rate and
event-free survival at 2 years was the same in both protocols. To induce remissions in the five children who failed induction chemotherapy for AML, we relied on vincristine (1.5 mg/m²/week × 4), prednisone (40 mg/m²/day × 28) and L-asparaginase (10,000 U/m³ 3 times/week × 4).

**Immunophenotyping.** The expression of cell-surface antigens by leukemic cells was detected by a standard indirect immunofluorescence assay. Staining of >30% of the cells was arbitrarily considered a positive result, but the percentage of positive staining cells is reported in all experiments. Monoclonal antibodies (MAbs) from cluster of differentiation (CD) groups defined by the International Workshops on Leukocyte Differentiation Antigens were used for phenotype determinations (Table 1). The CD2 antigen was analyzed with at least three different MAbs (T11, MT26, and D66). After being stained, the leukemic cells were analyzed with an EPICS C flow cytometer equipped with a 5-W coherent laser (Coulter, Hialeah, FL). Isotypically matched myeloma immunoglobulins (Igs) at the same protein concentration were used as negative controls in all experiments. Terminal deoxynucleotidyl transferase (TdT), detected by an immunofluorescence assay (Super Techs, Bethesda, MD), was considered positive if >20% of cells demonstrated nuclear fluorescence.

Leukemic cells were also examined for cytoplasmic expression of the CD22 (Leu-14, Becton Dickinson, Mountain View, CA) and CD3 (Leu-4, Becton Dickinson) antigens by an immunoperoxidase assay. Isotypic myeloma Igs at the same protein concentrations were used as negative controls. Cells were examined, without counterstaining, under a light microscope.

**Simultaneous analysis of two cell surface antigens.** Two-color immunofluorescence measurements were carried out on the EPICS C flow cytometer using the dual-immunofluorescence (FITC-PE) protocol. Human lymphocytes dual-labeled with CD4 conjugated to phycoerythrin (RD) and CD8 conjugated to fluorescein (FITC) (Simultest, Becton Dickinson) were used to correct for fluorescent spectrum overlap. In all experiments, negative controls included mouse immunoglobulin directly conjugated to FITC or RD. In experiments with Mo1, mouse immunoglobulin conjugated to biotin followed by avidin-RD were included as negative controls.

CD2 antibody conjugated to FITC (T11-FITC), CD13 antibody conjugated to RD (MY7-RD) (Coulter Immunology), and CD7 antibody conjugated to FITC (Leu9-FITC, Becton Dickinson) were from commercial sources. Mo1 antibody conjugated to biotin (Coulter Immunology) and avidin conjugated to RD (avidin-RD, Vector Laboratory, Burlingame, CA) were used to detect CD11b expression. Cells (5 x 10⁶) were incubated with heat-inactivated human AB serum and then with an excess of the directly conjugated MAbs in a total volume of 150 μL for 40 minutes at 0°C. After being washed with phosphate-buffered saline (PBS) >10,000 cells were analyzed immediately by flow cytometry.

**Cytogenetic analysis.** Cytogenetic analysis was performed by the method of Williams and colleagues that includes treatment with trypsin and Wright’s staining to obtain G banding. The chromosomal abnormalities are described as recommended by the International System for Cytogenetic Nomenclature.

**Molecular genetic analysis.** High-mol-wt DNA was extracted from marrow blasts obtained at the time of diagnosis by the method of Wigler and co-workers. DNA was quantified with a fluorometer (Hoefer Scientific Instruments, San Francisco). DNA was then digested with BamHI (Boehringer Mannheim, Indianapolis), EcoR1 (Bethesda Research Laboratories (BRL), Gaithersburg, MD), or HindIII (BRL) restriction endonucleases (3 to 10 U/μg DNA) and was electrophoresed through 1% agarose gels (SeaKem, FMC BioProducts, Rockland, ME); it was then transferred to nitrocellulose (Schleicher and Schuell, Keene, NH). Blots were probed with oligolabeled DNA probes for genes encoding the β and γ chains of the TCR or the heavy-chain Ig gene (Cμ). The probe for the β chain of the TCR was pB400, which contains ~0.4 kb from the Cβ1 region and hybridizes equally well to Cβ1 and Cβ2. The γ-chain probe, pγ1, contains 0.7 kb from the joining region of the γ-TCR gene. The Cμ probe used was Jμ, a 3.3-kb EcoR1/HindIII fragment representing 2.2 kb of the Jμ region and 1.1 kb of the 3' flanking sequences of the Cμ gene. After hybridization, the filters were washed (52°C) in 0.1 x SSC/0.1% sodium dodecyl sulfate (SDS) and exposed to Kodak XAR film (Kodak, Rochester, NY).

**Statistical analysis.** Differences in median values were analyzed with the Kruskal-Wallis test; frequencies were compared with Fisher's exact test. All P values are two-tailed.

**RESULTS**

**Morphological and cytochemical characteristics.** Wright-stained bone marrow smears from each of the ten patients consisted of a mixture of blast cells, with variable morphology ranging from myeloid-like to lymphoid-like. Figure 1A shows the variation in cellular morphology. The cells ranged in size from small with high nuclear/cytoplasmic ratios, inconspicuous or absent nucleoli, and regular nuclear shape through large with distinct nucleoli and a larger amount of cytoplasm. In seven cases (cases 1, 2, 4 through 7, and 9), rare Auer rods could be identified in the

**Table 1. MAbs Used in Immunophenotyping Studies**

<table>
<thead>
<tr>
<th>Prototype MAb</th>
<th>Cluster of Differentiation</th>
<th>Predominant Reactivity</th>
<th>Mol Wt of Antigen (kD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T11, MT26, D66</td>
<td>CD2</td>
<td>T cells, rare cases of AML</td>
<td>50</td>
</tr>
<tr>
<td>T3</td>
<td>CD3</td>
<td>Mature T cells</td>
<td>19-29 (heterotrimer)</td>
</tr>
<tr>
<td>T101</td>
<td>CD5</td>
<td>T cells, CML</td>
<td>67</td>
</tr>
<tr>
<td>Leu-9, T30</td>
<td>CD7</td>
<td>T-ALL, rare cases of AML</td>
<td>41</td>
</tr>
<tr>
<td>Anti-Tac</td>
<td>CD25</td>
<td>IL-2 receptor</td>
<td>55</td>
</tr>
<tr>
<td>Mo1</td>
<td>CD11b</td>
<td>Granulocytes, monocytes, peripheral blood mononuclear cells</td>
<td>155, 94 (heterodimer)</td>
</tr>
<tr>
<td>MY7, SJD1</td>
<td>CD13</td>
<td>Granulocytes, monocytes, macrophages</td>
<td>150</td>
</tr>
<tr>
<td>B4</td>
<td>CD19</td>
<td>B cells</td>
<td>95</td>
</tr>
<tr>
<td>B1</td>
<td>CD20</td>
<td>B cells</td>
<td>37, 32</td>
</tr>
<tr>
<td>B2</td>
<td>CD21</td>
<td>B cells</td>
<td>140</td>
</tr>
<tr>
<td>Leu-14</td>
<td>CD22</td>
<td>B cells</td>
<td>140, 130</td>
</tr>
</tbody>
</table>

PHA, phytohemagglutinin.
larger blasts. Cells containing Auer rods, however, were very rare, occurring only as often as 1 in 200 cells. In all cases, \( \geq 3\% \) (median 7\%, range 3\% to 14\%) of the leukemic cells reacted with myeloperoxidase when examined by standard light microscopy. All cases also had \( \geq 3\% \) Sudan black B-positive blasts (median 10\%; range 4\% to 34\%). Therefore, all cases fulfilled the FAB criteria for AML. Electron microscopic studies demonstrated myeloid characteristics and a higher percentage of peroxidase-positive blasts (Fig 1B). The morphological characteristics of these cases is unusual for AML, but there was no apparent correlation between individual blast cell morphology and immunophenotype.

**Immunophenotype.** Table 2 shows the results of single-color immunophenotyping. Cells from all ten patients expressed myeloid-associated antigens identified by MAbs in the CD13 or CD11b groups. The CD13 (MY7, SJD1) antigen was detected most often (9 of 10 patients), whereas blasts from only five patients expressed CD11b antigens.

More than 75\% of the cells from every patient reacted with T11 and MT26, which are believed to recognize the same epitope of the T-cell–associated CD2 antigen (Table 2).

Evidence for the expression of an additional CD2 epitope was provided by the reactivity of MAb D66 with cells from patients 8 and 10. Additional T-cell–associated antigens were expressed by leukemic blasts. The pan T-cell–associated CD7 antigen identified by MAbs Leu-9 and T30 was uniformly expressed on the cell surface. The CD3 antigen identified by Leu-4 was uniformly expressed in the cytoplasm. Blasts from five patients expressed the interleukin-2 (IL-2) receptor (CD25) seen on mature, activated T cells. The surface CD3 antigen, which usually is associated with mature T cells, was detected on cells from a single patient. Blasts from eight of the nine patients tested were TdT positive.

Evidence for B-cell differentiation was limited to expression of surface CD21 (B2) antigen on blast cells from patient 4. No patient had blasts that expressed surface CD19, CD20, or cytoplasmic CD22.

In all cases, the sum of blasts expressing myeloid antigens and lymphoid antigens was \( \geq 100\% \), suggesting that some blasts coexpressed antigens of both lineages (Table 2). Five patients were examined by dual-color immunofluorescence...
studies for coexpression of T-cell–associated antigens (CD2, CD7) and myeloid-associated antigens (CD13, CD11b). In all cases, individual blasts coexpressing T-cell–associated and myeloid-associated antigens were identified (Fig 2). CD2 (T11) and CD13 (MY7) were the antigens most commonly coexpressed in this group of patients. Blasts coexpressing CD2 and CD11b (Mo1) as well as blasts coexpressing CD7 (Leu-9) and CD13 were also easily identified (Table 3).

Molecular genetic findings. We also examined high-mol-wt DNA, extracted from the blast cells of all ten patients, for rearrangement of TCR and Ig genes (Table 2). When examined with the probe for the TCR \( \beta \) chain (pB400), the DNA from five patients (patients 2, 3, 6, 7, and 8) showed rearranged \( \beta \)-chain genes (Table 2). Patients 6 through 8 showed rearrangements after EcoRI digestion (Fig 3A), and patients 2 and 3 showed rearrangements after BamHI digestion (Fig 3B). Analysis with the \( \gamma \)-TCR gene probe (pJyl) disclosed \( \gamma \)-chain gene rearrangement only in patients 1, 2, and 4 (Table 2 and Fig. 3c). Patients 4 and 6 also showed rearranged Ig heavy-chain genes (data not shown).

Karyotype. Cytogenetic analysis was performed on all patients at diagnosis. In general, the karyotypes were normal or showed complex abnormalities. No consistent abnormalities were evident, and no specific AML- or ALL-associated translocations were identified. Three patients (patients 3, 8, and 9) had translocations involving 14q32, the location of the immunoglobulin heavy-chain genes; however, none of these three patients had immunoglobulin gene rearrangement. Patient 3 also had a translocation involving 7q35, the region containing the genes for the \( \beta \) chain of the TCR. This patient did have \( \beta \)-TCR rearrangements when analyzed by the Southern gel method.

Clinical features and response to therapy. The presenting clinical features of the 10 patients are shown in Table 4. As compared with 84 children who had typical FAB-defined AML, the CD2+ AML subgroup was characterized by older age (median 15.8 v 6.9 years, \( P = .001 \)) and a higher frequency of lymphadenopathy (90% of patients v 50%, \( P = .02 \)). The severity of adenopathy, although difficult to assess, appeared to be greater in the CD2+ AML group. Whereas 5 of the 10 CD2+ AML patients initially sought medical attention because of adenopathy, only 2 of the 84 patients in the typical AML group had a chief presenting complaint of enlarged lymph nodes. Patient 2 had a documented mediastinal mass, but the other nine patients had normal chest radiographs at the time of diagnosis. Although not statistically significant, leukocyte counts were higher in the CD2+ subgroup (median 46 x 10^9/L v 22 x 10^9/L, \( P = .24 \)) and the percentage of myeloperoxidase-positive cells was lower (median 7% v 50%, \( P = .07 \)).

Table 5 summarizes responses to induction chemotherapy. With anthracycline- and cytarabine-based treatment, complete remissions were achieved in 50% of patients with CD2+ AML and in 80% of patients with typical AML (\( P = .05 \)). Only one of the five patients (patient 5) who achieved a complete remission with AML-directed therapy remains in remission after undergoing allogeneic bone marrow transplant. Patients 4, 6, 9, and 1 relapsed after achieving 1, 8, 10,
Fig 2. Log-log dot-contours of the staining of blast cells from patient 4. (A) Quadrants were set using the negative controls to exclude nonspecific binding. (B) CD2 binding (FITC, green fluorescence) is plotted on the abscissa; CD13 binding (PE, red fluorescence) is plotted on the ordinate. Reactivities as graphed are CD2, CD13 = 70%; CD2, CD13 - 10%; CD2, CD13 = 15%.

Table 3. Dual Expression of Cell Surface Antigens

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Lymphoid</th>
<th>Myeloid</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>CD2+</td>
<td>CD13+</td>
</tr>
<tr>
<td>5</td>
<td>CD2+</td>
<td>CD13+</td>
</tr>
<tr>
<td>6</td>
<td>CD2+</td>
<td>CD13+</td>
</tr>
<tr>
<td>7</td>
<td>CD2+</td>
<td>CD13+</td>
</tr>
<tr>
<td>8</td>
<td>CD11b+</td>
<td>CD13+</td>
</tr>
<tr>
<td>9</td>
<td>CD3+</td>
<td>CD13+</td>
</tr>
</tbody>
</table>

Results given as percentage of dual-labeled blasts.

and 16 months of relapse-free survival, respectively. The pattern of relapse in patient 4 (testicular followed by ocular and then hematologic) was unusual for myeloid leukemia; however, this patient did not respond to vincristine, prednisone, and l-asparaginase induction therapy (Table 5). Patient 9 relapsed after 10 months of maintenance therapy and achieved a second complete remission with vincristine, prednisone, and l-asparaginase therapy (Table 5).

After initial AML-directed therapy failed in five patients, a switch to therapy with a 4-week course of vincristine, prednisone, and l-asparaginase resulted in complete remission in four patients (patients 2, 7, 8, and 10). Patient 3 had an antileukemic response but died of sepsis during marrow aplasia.

Only patients 8 and 10 remain free of leukemia, for 28+ and 2+ months, respectively. Both patients received pulses of vincristine and prednisone during maintenance therapy. Patient 2 relapsed after a 6-month remission. Patient 7 underwent an allogeneic bone marrow transplantation but died in complete remission of graft-versus-host disease (GVHD) 1.7 years after transplantation. In this small series, we were unable to identify factors other than the CD2+ phenotype that might have influenced responses to therapy.

At relapse, all patients studied had >3% myeloperoxidase-positive blasts and most had a higher percentage of myeloperoxidase positive blasts than were present at diagnosis. Blasts from all five patients studied at relapse still expressed the CD2 surface antigen.

DISCUSSION

Use of MAbs and molecular probes show that a substantial percentage of leukemic cells possess characteristics of more than one hematopoietic lineage. Our results indicate that ~10% (9 of 94 consecutive cases) of children with AML by FAB criteria may have blasts that express T-cell features. Myeloid differentiation was evident from the presence of Auer rods, myeloperoxidase-positive, and Sudan black B-positive blasts. Additional evidence of myeloid differentiation was the high percentage of cells expressing the myeloid-associated surface antigens CD13 and CD11b. However, leukemic blasts from these patients coexpress the T-cell-associated CD2, CD7, and cytoplasmic CD3 antigens, indicating an early stage of T-cell differentiation. However, blasts from five patients also displayed the CD25 antigen (IL-2 receptor), and blasts from another patient had surface CD3, features that are usually restricted to mature T cells. Furthermore, in all patients, these T-cell-associated antigens were coexpressed with myeloid-associated antigens (CD13 and CD11b). This pattern of membrane antigen expression does not follow normal T-cell differentiation and may be unique to CD2+ AML.

Molecular genetic findings support the contention of abnormal differentiation based on surface antigen expression. In normal T-cell development, rearranged \( \gamma \) and \( \beta \) chain TCR genes are present in cells, and all cases of T-cell leukemia expressing CD2+ have undergone \( \gamma \) and \( \beta \)-chain rearrangements. Therefore, if these were cases of T-cell leukemia or followed normal T-cell differentiation, all ten would be expected to have rearranged \( \gamma \)- and \( \beta \)-chain genes. However, only 5 of the 10 CD2+ AML
patients in our series had rearranged TCR β-chain genes and only 3 had rearranged γ-chain genes. Furthermore, in leukemia, the TCR γ-chain gene rearranges before the TCR β-chain gene.39,43,45 In contrast to this usual hierarchy, two of our patients had germline configuration γ-chain genes but rearranged β-chain genes.

The presence of myeloid gene expression and the "disordered" pattern of T-cell developmental gene expression in these cases of acute leukemia suggest aberrant gene regulation in transformed blast cells and is consistent with the concept of "lineage infidelity."16 However, transformation of a multipotential progenitor that normally expresses characteristics of myeloid and lymphoid lineages (lineage promiscuity) may explain our findings.13 Until further studies provide information on the molecular control of differentiation in leukemia, the exact explanation for our findings will remain unknown.

Most patients in the CD2+ AML subgroup were adolescents with lymphadenopathy. However, by other clinical measures, they were similar to the other 84 AML patients lacking the CD2 antigen in this prospective study (Table 4). Because all patients had AML based on the FAB criteria, they were initially treated on AML protocols. A significantly lower percentage of CD2+ AML patients entered complete remission as compared with the more typical AML patients. Attempts to identify prognostically relevant subgroups of AML have been difficult.46 Our data, however, suggest that the CD2+ phenotype in AML patients may predict a poor response to induction therapy.

Four of the five patients who were initially resistant to

Fig 3. Autoradiographs of Southern blots showing rearrangements of the T-cell receptor β- and γ-chain genes. Arrows indicate germline fragments. (A) EcoRI digests hybridized with the β-chain constant region probe. The lane numbers correspond with each patient’s number. DNA from patients 5, 7, and 8 shows rearrangements. Lanes C+ and C− contain control DNA showing the rearranged and germline configuration, respectively. (B) BamHI digests hybridized with the β-chain constant region probe. Lane 1 contains control DNA in the germline configuration. Lanes 2 and 3 contain DNA from patients 2 and 3, respectively, and show rearrangements. (C) EcoRI digests hybridized with the γ-chain joining region probe. Lanes are numbered corresponding with each patients' number. DNA from patients 1, 2, and 4 show γ-chain TCR rearrangements. Lanes C+ and C− contain DNA showing the rearranged and germline configuration, respectively.
Table 4. Comparison of Presenting Features of CD2+ and CD2− AML Subgroups

<table>
<thead>
<tr>
<th>Feature</th>
<th>CD2+ AML (n = 10)</th>
<th>Median Value (Range)</th>
<th>CD2− AML (n = 84)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (yr)</td>
<td>15.8 (11.7-19)</td>
<td>7.0 (9.1-20)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>M:F ratio</td>
<td>1.5</td>
<td>1.5</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Leukocytes (x 10⁹/L)</td>
<td>46 (6-171)</td>
<td>22 (0.3-751)</td>
<td>0.24</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>9.1 (6.3-14)</td>
<td>8.7 (3.5-15)</td>
<td>0.41</td>
<td></td>
</tr>
<tr>
<td>Platelets (x 10⁹/L)</td>
<td>104 (23-296)</td>
<td>56 (4-510)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Myeloperoxidase (%)</td>
<td>7 (3-14)</td>
<td>50 (0-100)</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Adenopathy</td>
<td>9 (90%)</td>
<td>41 (50%)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Adenopathy as presenting complaint</td>
<td>5 (50%)</td>
<td>2 (2%)</td>
<td>0.0001</td>
<td></td>
</tr>
<tr>
<td>Blasts in cerebrospinal fluid*</td>
<td>2 (20%)</td>
<td>26 (31%)</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>Auer rods</td>
<td>7 (70%)</td>
<td>34 (41%)</td>
<td>0.10</td>
<td></td>
</tr>
</tbody>
</table>

*Presence of any leukemic cells in cytospin preparations of cerebrospinal fluid that lacked RBC contamination.

Table 5. Results of Induction Chemotherapy in CD2+ AML Subgroup

<table>
<thead>
<tr>
<th>Response According to Patient No.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>To therapy for AML</td>
<td>CR</td>
<td>RD</td>
<td>RD</td>
<td>CR</td>
<td>CR</td>
<td>CR</td>
<td>RD</td>
<td>RD</td>
<td>CR</td>
<td>RD</td>
</tr>
<tr>
<td>To therapy for ALL</td>
<td>ND</td>
<td>CR</td>
<td>— *</td>
<td>RD</td>
<td>ND</td>
<td>ND</td>
<td>CR</td>
<td>CR</td>
<td>CR</td>
<td>CR†</td>
</tr>
</tbody>
</table>

Abbreviation: CR, complete remission; RD, residual disease; ND, not done; ALL, acute lymphoblastic leukemia.

*Patient died of sepsis during period of bone marrow aplasia (described in text).

†Achieved a second complete remission with ALL-directed therapy (described in text).

therapy on AML protocols promptly achieved complete remissions when switched to drugs for lymphoid leukemia: prednisone, vincristine, and L-asparaginase. The fifth child had clearing of his leukemic blasts but died of sepsis. The clinical response of CD2+ AML patients is consistent with our findings that these leukemic cells also have lymphoid characteristics. CD2+ AML patients who fail to achieve a complete remission with conventional AML therapy may benefit from agents effective against acute lymphoid leukemia (Table 5). Our studies demonstrate that these are not cases of ALL because all cases had myeloid characteristics (Auer rods, myeloperoxidase, CD13, and CD11b antigens) and some had germline TCR genes. Unfortunately, our studies do not indicate which CD2+ AML patients will respond to therapy for myeloid leukemia and which will respond to therapy for lymphoid leukemia.

In conclusion, the presence of the T-cell-associated antigens CD2, CD7, and cytoplasmic CD3 on AML blast cells with obvious myeloid features identifies a clinically and biologically distinct form of acute leukemia. Additional studies and more patients are needed before firm conclusions about alternative methods for treatment CD2+ AML patients can be made.

ACKNOWLEDGMENT

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Acute myeloid leukemia with T-lymphoid features: a distinct biologic and clinical entity

AH Cross, RM Goorha, R Nuss, FG Behm, SB Murphy, DK Kalwinsky, S Raimondi, GR Kitchingman and J Jr Mirro