CONCISE REPORT

Occurrence of the Common Acute Lymphoblastic Leukemia Antigen on Blast Cells of a Patient with Chronic Myelomonocytic Leukemia in Non-Lymphoid Blastic Phase

By Volker Gressler, Manfred Garbrecht, and Dieter K. Hossfeld

Leukemias showing a conspicuous lymphoid phenotype, i.e., those that are HLA-DR positive, common acute lymphoblastic antigen (cALLA) positive, terminal deoxynucleotidyl transferase (TdT) negative, as well as myeloperoxidase positive (MPO), could be considered so-called mixed leukemias. Leukemias with biphenotypic blasts have to be distinguished from cases comprising two separate subpopulations that express different lineage-associated characteristics. By use of a simple new method (Immunogold Staining) we examined a case of chronic myelomonocytic leukemia in blastic phase and demonstrated simultaneous staining for MPO/alpha-naphthyl-esterase and expression of the HLA-DR-positive, cALLA-positive, and TdT-negative phenotype. The cALL antigen was detected only on mono- and myeloid-monoblasts; its expression was inversely related to the MPO positivity, and it disappeared together with these types of blasts after chemotherapy. On the basis of our findings it remains obscure whether the cALL antigen at the initial presentation was due to the immature monocyctic features of the leukemic cells or disclosed an additional lymphoid differentiation pattern of the blasts.

THE REACTION of antisera with the cALL antigen of leukemic cells was first reported by Greaves et al. Further investigations revealed that the cALL antigen is not specific for "non-T-non-B" lymphoblastic leukemias; cALLA was shown in some high-grade lymphomas, especially Burkitt's lymphoma, normal "lymphoid" cells in regenerating bone marrow, and blasts of patients with chronic myeloid leukemia in lymphoid transformation. The latter authors, surprisingly, found the cALL antigen in four out of 86 cases of acute myeloid leukemia (AML). The observation of HLA-DR-positive, TdT-negative, yet MPO-positive leukemias raises the question of whether these characteristics are displayed simultaneously by individual blasts or by two different populations of leukemic cells. This is a report of a patient with chronic myelomonocytic leukemia (CMML) who developed a non-lymphoid blastic phase. Using a new dual staining method these blasts were found to be cALLA positive and to exhibit myelomonocytic features.

MATERIALS AND METHODS

Patient. The 73-year-old man was first noted to have an abnormal peripheral blood picture in July 1983. At this time he presented with anemia (hemoglobin 8.8 g/dL) and leukocytosis (WBC 15.0 × 10^9/L). Peripheral blood differential and bone marrow aspirate were compatible with the diagnosis of CMML. The index of leukocyte alkaline phosphatase (LAP) was normal. Chromosome analysis of the bone marrow cells revealed a normal karyotype. Apart from blood transfusions no therapy was given. The patient was referred to us in October 1984. On physical examination he had petechiae and livid skin changes of the lower extremities that were referred to us in October 1984. Apart from blood transfusions no therapy was given. The patient was referred to us in October 1984.

Further investigations revealed that the cALL antigen is not specific for "non-T-non-B" lymphoblastic leukemias. cALLA was shown in some high-grade lymphomas, especially Burkitt’s lymphoma, normal "lymphoid" cells in regenerating bone marrow, and blasts of patients with chronic myeloid leukemia in lymphoid transformation. The latter authors, surprisingly, found the cALL antigen in four out of 86 cases of acute myeloid leukemia (AML). The observation of HLA-DR-positive, TdT-negative, yet MPO-positive leukemias raises the question of whether these characteristics are displayed simultaneously by individual blasts or by two different populations of leukemic cells. This is a report of a patient with chronic myelomonocytic leukemia (CMML) who developed a non-lymphoid blastic phase. Using a new dual staining method these blasts were found to be cALLA positive and to exhibit myelomonocytic features.
 marker analysis shows the majority of cells belonging to the granulocytic and myelomonocytic lineage (MA 66%, Ia 26%). During relapse, the percentage of blasts in the differential blood count is 35; immunofluorescence and immunogold staining for cALLA is now completely negative.

**DISCUSSION**

There are some reports suggesting the occurrence of distinct populations of blasts with lymphoid and myeloid phenotypes in acute leukemia. Additionally, leukemic cells show lymphoid and myeloid characteristics simultaneously. These findings are based on the assumption that MPO positivity signals myeloid and TdT positivity signals lymphoid differentiation pathways. Yet recent studies revealed that the presence of TdT activity has to be interpreted as an early state of maturation rather than a special differentiation lineage. Pui et al. reported three children with acute leukemia, at least one of whom showed a wide overlap in the percentage of blasts expressing an unusual lymphoid (Ia+, cCALLA+, TdT-) and myeloid (MPO+) phenotype providing some evidence of a so-called mixed leukemia.

To our knowledge, the case described here seems to be the first one that demonstrates MPO and cALLA antigen on the same cell. The simultaneous cytologic, cytochemical, and immunologic characterization of leukemic cells by the immunogold staining method excludes the existence of separate subpopulations with different lineage associated features. On the other hand, the degree of cALLA positivity of blasts could be shown to be inversely related to MPO staining of these cells. Strongly cALLA-positive blasts appeared cytologically as monoblasts, reacted with moAbs to monocytic antigens (M 5, MY 4) and did not stain for MPO. This type of cell disappeared after chemotherapy and a population of more mature, cALLA-negative cells emerged.

Our findings suggest two possible explanations. First, the blast cells show an aberrant expression of monocytic and myelogenous features; the cALLA has to be regarded as an antigen associated with an early stage of monocytic differentiation. A second possibility is that the leukemic cells of our patient are pluripotent stem cells showing a varying accentuation of lymphoid, myeloid, and monocytic differentiation characteristics. The latter explanation would be supported by the detection of MPO+, cCALLA+, TdT−, monocytic antigens bearing cells in normal bone marrow. For that purpose, further studies on a larger number of normal bone marrow cells have to be carried out.

**Table 2. Immunologic Findings**

<table>
<thead>
<tr>
<th>Disease State</th>
<th>Surface Marker Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ia</td>
</tr>
<tr>
<td>Blastic phase of CMML</td>
<td>56+</td>
</tr>
<tr>
<td>Partial remission</td>
<td>26+</td>
</tr>
<tr>
<td>Relapse</td>
<td>40+</td>
</tr>
</tbody>
</table>

Bone marrow cells; numbers indicate percentage of positive mononuclear cells. To quantitate results obtained by immunofluorescence analysis an intensity scale ranging from weakly positive (+) to strongly positive (+++) was used.

(*) Not done.
REFERENCES


Occurrence of the common acute lymphoblastic leukemia antigen on blast cells of a patient with chronic myelomonocytic leukemia in non-lymphoid blastic phase

V Gressler, M Garbrecht and DK Hossfeld