HLA-Dr Negative Acute Non-lymphocytic Leukemia*

JOHN LAZARCHICK, M.D.
and MELANIE HOPKINS, M.D.

Department of Pathology and Laboratory Medicine,
Medical University of South Carolina,
Charleston, SC 29425

ABSTRACT

Absent or diminished HLA-Dr antigen representation on the cell surface of both normal and leukemic promyelocytes is a hallmark of this stage of myeloid maturation. In order to document the specificity of this finding for acute promyelocytic leukemia, flow cytometric analysis of leukemic blasts was utilized on 36 cases of acute non-lymphocytic leukemia. All 15 of the promyelocytic leukemias (FAB-M3) studied showed absent or markedly decreased HLA-Dr antigen on their cell surface. However, the majority of cases (21) in which this finding was noted were other than promyelocytic leukemias and included all FAB subtypes, most particularly FAB-M2, i.e., myeloblastic leukemia with maturation. It is concluded that absent to decreased HLA-Dr antigen representation on leukemic blasts lacks specificity and can be seen in all acute myeloid/monocytic leukemic subtypes.

Introduction

The French-American-British (FAB) classification system for acute myeloid leukemias was instituted in an attempt to establish guidelines for distinguishing acute leukemia subtypes. The basis was inclusive of morphologic criteria and histochemical staining with myeloperoxidase and dual esterase. Accordingly, subgroups were recognized and designated as FAB Mo through My depending on the extent of morphologic differentiation and histochemical staining. The subtype M3 (acute promyelocytic leukemia) is distinguished by the presence of cytoplasmic granules which are intensely myeloperoxidase positive. A variant form of M3 is recognized in which granules are either markedly reduced or not apparent on Wright staining but the cells are still myeloperoxidase positive. A characteristic feature of M3 leukemias compared to the other subtypes is either the absence of markedly diminished expression of the HLA-Dr antigen on the membrane of these cells as detected using flow cytometry. In normal cell (maturation), this antigen is present on hematopoietic progenitors and granulocyte/monocyte, erythrocyte and megakaryocytic precursors but absent at the promyelocytic stage of myeloid cell maturation.

All of our non-lymphoid cases of acute leukemia for the past three years were reviewed to determine the incidence of decreased or absent HLA-Dr expression and to correlate finding this with the FAB classification in these cases.
Materials and Methods

Morphologic and flow cytometric data obtained from bone marrow specimens submitted to the Hematopathology and Immunology Services from 1993 through 1996 were retrospectively analyzed to determine the degree of HLA-Dr antigen representation on the leukemic cell population on patients diagnosed as having acute non-lymphocytic leukemia (ANNL). Any patients diagnosed as having acute lymphocytic leukemia (ALL) or biphenotypic leukemia, i.e., ALL with associated myeloid antigen expression or AML with lymphoid antigen coexpression were excluded from the study. The group analyzed consisted of 36 patients, 21 males and 15 females, ranging in age from four months to 72 years.

Morphologic analyses were performed on Wright-Giemsa stained bone marrow aspirates. Additional histochemical staining was performed using myeloperoxidase and dual esterase staining. Cell surface antigen marking for CD designations was done on a Coulter Epics XL-MCL using standard leukemia panels of monoclonal antibodies for CD-3, 5, 7, 10, 13, 14, 19, 20, 33, 34, 38 and HLA-Dr. The percent of leukemic blasts expressing HLA-Dr antigen was read directly from the instrument. If less than 20 percent of the blast population showed reactivity for the HLA-Dr antigen, the leukemia was designated as HLA-Dr negative. All specimens considered by morphologic and histochemical analyses to be consistent with acute promyelocytic leukemia (M3 or M3v) were verified by demonstrating a 15:17 translocation on cytogenetic analysis and/or PML/RARα product on molecular analysis using RT-PCR.5,6

Results and Discussion

The percent HLA-Dr reactivity and FAB classification for the patient study group are illustrated in table I. Fifteen of the 36 patients analyzed met criteria for acute promyelocytic leukemia and included three patients who had the microgranular variant form. The HLA reactivity ranged from 1 to 20 percent for the group, with six of the cases having reactivity greater than 10 percent. All three microgranular variant cases demonstrated HLA-Dr reactivity of less than 10 percent.

Although decreased to absent HLA-Dr antigen representation is a hallmark of both normal and leukemic promyelocytes, this finding is not specific for promyelocytic leukemias (FAB-M3). In fact, the majority (58 percent) of the cases in our series with this finding were non-M3 FAB subtypes, and, somewhat surprisingly, it was noted in all other FAB myeloid leukemic subtypes. The largest non-M3 group (10 cases) was seen in the M2 subtype, i.e., acute myeloblastic leukemia with maturation.
Since the M2 subtype is the most frequent acute myeloid leukemia (12), this seemingly high incidence of decreased to absent HLA-Dr representation is misleading in that it was noted in less than 10 percent of the total FAB-M2 leukemias seen over the time period of this study. This relative infrequency of this finding in leukemic subtypes other than FAB-M3 is reinforced by the observation that there were only two cases with this finding in the FAB-M4 subtype, i.e., acute myelomonocytic leukemia, even though this is the second most common leukemic subtype.

In conclusion, our results reaffirm the decreased to absent HLA-Dr representation on all cases of both M3 and M3v leukemias but demonstrate that this finding is not restricted to this acute myeloid leukemic subtype since it could be shown in all myeloid subtypes, especially FAB-M2.

References