Acute Lymphoblastic Leukemia in Childhood with an Unusual Immunophenotype (CD7+/CD56+/CD33+)

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Abstract. We have identified and characterized an unusual and unrecognized type of acute leukemia with features of T-lymphoid, myeloid and natural killer cell (NK) associated markers in a five year old girl with morphologically and cytochemically undifferentiated acute leukemic blast cells.

The bone marrow and peripheral blood smears showed ALL FAB-L1/2 morphology with immunological features of CD7+, CD33+, CD56+ myeloid/natural killer cell precursor type. The marker analysis exhibited the coexpression pattern of cyCD3, CD34, CD38, CD45, CD54, CD71 and HLA-DR antigens just as the neutrophil marker CD11b. In 50% of the blast cells cytoplasmic CD3 was detectable but on the other hand this leukemic entity failed to express other NK associated antigens (e.g. CD16/CD57) additionally no other expressions of T- and B-cell lineage associated markers could be observed. The blasts expressing the stem cell marker CD34 failed to express AC133 and CD117.

This unusual phenotype seems to be very similar to the recently by Scott et al. [24] and by Suzuki et al. [20] proposed »myeloid/NK cell precursor acute leukemia« entity in adults. In comparison to our case the Scott’s type was characterized by mature myeloid morphology with MPO reactivity but without information about the expression of CD7. Their cases were described to be exclusively negative for HLA-DR. The phenotype of our case seems to be more identical to the recently reported entity by Suzuki et al. (1997), with exception of MPO expression and missing cyCD3 positivity in their cases of adults. CD7 is a T-cell marker which is expressed in immature NK cell progenitors and was a feature of the myeloid/NK cell precursor acute leukemia in our and Suzuki’s cases.

Introduction

Acute leukemias are traditionally classified according to their morphological and cytochemical features. However, some acute leukemia cases lack characteristic that are currently important to be diagnostic parameters for ALL or AML within the morphological French-American-British (FAB)-classification system [1-4]. Diagnostic importance has increased with the development and usage of immunological techniques. Since the recent availability of highly specific monoclonal antibodies (MoAbs) recognizing differentiation antigens (CD cluster code) the diagnostic precision for leukemic cells and various tumor cell types has increased. The application of morphology, cytochemistry and immunological methods in combination with selective antibodies makes it possible to subclassify of leukemic blast cells.

Flow cytometry has become the preferred technique for the lineage assignment (T- and B-lineage ALL) and maturational analysis of malignant cells in acute leukemias and lymphomas. Furthermore, the multiparametric immunophenotyping allows the detection of aberrant antigen coexpressions (i.e. ALL coexpression of myeloid antigens: My+ -ALL, or AML with coexpression of lymphoid markers: Ly+ -AL) [5-8].
Despite these advances, the lineage of the leukemic blasts may still remain uncertain in a minority of acute leukemia (AL) cases. This is due to the lack membraneous expression of some lymphoid and myeloid antigens or to the expression of an atypically marker constellation on the same cells.

In the last few years, it has become apparent that at least a proportion of the unclassifiable AL (AUL) cases can be meticulously classified by analysing cytoplasmic expressions of early T, B and myeloid antigens such as CD3, CD22, CD13, MPO as well as nuclear TdT [6,9-13].

The »European Group for the Immunological Characterization of Leukemias« (EGIL) recognised a rare subtyp of acute leukemias in which the leukemic blast cells do not express lineage specific markers [14]. At the present time, the nature of this rare entity can not be clarified by immunophenotyping.

Here we report a child case of acute leukemia fitting into neither of standardized categories. We describe the immunological findings in an acute lymphoblastic leukemia with the immunophenotype of a putative precursor cell common to the T-/NK and myeloid cell.

Case report

A 5 1/2 year old girl was admitted to our clinic of pediatrics-III in november 1997, in order to clarify the diagnosis hematological malignancy.

Examination of peripheral blood (PB) displayed 4.70 g/dl hemoglobin, a platelet count of 59 x 10^3/µl and leukocyte count about 11.100/µl. PB-white blood cells could be subdevided to neutrophils (21%), lymphocytes (34%), monocytes (1%) and pathological blast cells (42%). Bone marrow (BM) smears disclosed leukemic blast cell population of nearly 100%. The blasts consisted of two different morphological features fulfilling criteria of FAB-ALL-L1/L2.

The major population reflects mainly lymphoblastic morphology (66%), while the remaining 34% showed rather undifferentiated myeloblastic signs but lacking of azurophilic granules.

Cytochemical staining of leukemic blasts in bone marrow did usually not reveal POX or PAS reactivity, consistent with an acute undifferentiated leukemia. All of the pathological blast cells were negative for tested Esterase, too. Acid phosphatase was demonstrated to be negative as well in most cells; only a few blasts were diffuse positive, some seemed to be positive in a polar manner. Immunological profile is reported below. DNA-index of blast cell population was shown to be diploid.

To the child a chemotherapeutic regimen according to the ALL-protocol (ALL-BFM-95) was administered. On day 8 following starting with therapy, PB demonstrated remaining 25% pathological blast cells. No peripheral blast cells were detectable on day 15. At this time bone marrow aspirates showed participation of still 83% blast cells. Remission was achieved on day 28. Till now the reported child is shown to be in complete remission.

Materials and Methods

Bone marrow (BM) aspirates were obtained from a five year old girl with de novo acute leukemia. BM smears were stained with panoptical May-Gruenwald-Giema dyes according to Pappenheim, cytochemistry stainings (i.e. Peroxidase, alpha-naphthyl butyrate esterase, and periodic acid Schiff’s reagents, acid phosphatase) respectively to standard procedures.

Morphological diagnosis was made according to the FAB classification system [1-4]. Immunological characterization of leukemic blast cells in terms to their lineage commitment and differentiation stage was done by multiparametric flow cytometry [8,12].

Flow Cytometry (FACS)

FACS analysis was carried out in a standard manner applying whole lysed blood procedure [8,12]. A large panel of monoclonal antibodies as listed in Table 1 was used. Detailed information is given in Table 1 as well.

The expression of antigens on blast cells was assessed by direct immunofluorescence using appropriate double and triple staining combinations with the following flurochromes; fluorescein isothiocyanate (FITC), phy-