short report
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INCREASED CD10/TdT POSITIVE CELLS IN THE BONE MARROW OF AN INFANT WITH IMMUNE THROMBOCYTOPENIA

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ABSTRACT

We describe the case of an infant with immune thrombocytopenia whose bone marrow showed an increased percentage of CD10/TdT-positive lymphoid cells that resembled the onset of an acute lymphoproliferative disorder. Genotypic analysis of bone marrow, however, failed to reveal the malignant origin of these B cell precursors. After 8 months of follow-up, the child is alive and well, and shows a chronic form of ITP. Although a relation between this B cell proliferation and the onset of ITP cannot be excluded, it is important to consider this atypical pattern as a benign hematologic condition.

Key words: CD10/TdT positive lymphocytes, bone marrow, immune thrombocytopenia

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An elevated percentage of CD10 (Calla)-positive lymphoid cells may occur in the regenerating bone marrow of children cured of acute lymphoblastic leukemia (ALL), even several months after the cessation of therapy.[1] More recently, an increase in immature B cell precursors (CD10, CD19, HLA-DR positive) has been described in the bone marrow of children with non malignant hematologic disorders[2,3] such as immune thrombocytopenia (ITP), agranulocytosis or transient erythroblastopenia. It may be difficult to distinguish these cells from leukemic blasts immunologically:[4] however, careful morphological examination of bone marrow specimens suggests no evidence of leukemia or lymphoma in these patients, in whom genotypic analysis also fails to detect a monoclonal expansion of lymphoid cells. Furthermore, peanut agglutinin (PNA) binding, which occurs in regenerating lymphoid cells, could be helpful in these cases.

In the present paper we describe an infant affected by ITP at nine months of age whose bone marrow showed an elevated percentage of CD10, CD19, HLA-DR and TdT positive lymphoid cells, that mimicked a common ALL. However, no monoclonal rearrangements of the immunoglobulin (Ig) heavy and light chain genes were detected. After eight months of follow-up, the child is alive and well, thus confirming the benign nature of his bone marrow pattern.

Case report

The patient was a female infant who developed an ITP at nine months of age. The platelet count at diagnosis was 10×10^9/L and white blood cell count 15×10^9/L, with 40% neutrophils, 52% lymphocytes, 7% monocytes and 1% eosinophils; hemoglobin was 11.6 g/dL. Platelet bound antibodies (IgG class) were detected in the peripheral blood.

A bone marrow (BM) aspiration showed nor-

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mal cellularity with an increased number of megakaryocytes and an elevated percentage (50%) of lymphocytes. Flow cytometic analysis (Fascan, Becton-Dickinson) revealed an abnormal lymphocyte pattern, with a predominant population of CD10 (68%), CD20 (54%), HLA-DR (83%)-positive cells. TdT, detected by either indirect immunofluorescence or immunoperoxidase techniques, stained about 70% of the cells examined. In order to evaluate the clonal origin of lymphocytes, a genotypic analysis with Southern blot (Oncor-B and T Blue kit) was performed, but no monoclonal rearrangements in either the heavy chain or kappa chain Ig genes were detected.

The child was treated with high-dose intravenous immunoglobulins (400 mg/kg) on each of five consecutive days, which produced a rapid increase of the platelet count to 365×10^9/L. Three weeks later the platelets fell back to 35×10^9/L.

The infant received a new course of iv Ig that bought transient relief from thrombocytopenia. Two more bone marrow examinations at intervals of 4 weeks revealed a progressive decrease in immature B cell precursors (Table 1).

Eight months after diagnosis, the child is alive without evidence of malignant lymphoproliferative disease, but with a chronic form of ITP.

Table 1. Bone marrow immunophenotype and genotype at diagnosis and at +4 and +8 weeks.

	% of lymphoid cells positive and genotype at diagnosis	*+4 weeks*	*+8 weeks**
CD2	6	10	ND
CD5	10	10	ND
CD7	ND	9	ND
CD20	54	30	ND
CD19	ND	68	41
CD10	68	64	33
OKDR	83	61	35
K	0.6	ND	ND
λ	0.7	ND	ND
IgHC	6	6	6
IgLC	6	6	6
TdT	70	35	ND
Cyt u	ND	7	ND

IgHC-IgLC: immunoglobulin heavy and light chain; G: germline; ND: not detected. *BM performed by Department of Pediatrics, University of Bologna

Discussion

An increased percentage of CD10, CD19, HLA-DR and TdT-positive cells has been described in the bone marrow of children with non malignant hematologic disorders,[2,3] as well in regenerating bone marrow treated for ALL,[1] or even in acute myeloid leukemia or after autologous or allogeneic bone marrow transplantation.[5,6]

This atypical immunological pattern must be carefully evaluated in order to rule out the presence of a lymphoproliferative disease, such as in the case of the infant described in this paper, who presented with very high values of lymphoid cells positive for these antigens.

The CD10 antigen, which is present on the majority of lymphoid cells in fetal bone marrow, represents up to 30% of B cell precursors in normal children < 5 years old;[7] its frequency decreases with age (< 1% in adult), but myeloablative chemotherapy of bone marrow transplantation for leukemia or lymphoma could once again expand this compartment. In these cases PNA binding, which occurrs in regenerating lymphoid but not in blast cells, could clarify the reactive nature of this population.

In the bone marrow of children with ITP, transient erythroblastopenia or agranulocytosis,[2,3] CD10 may be expressed on up to 70% of the lymphoid infiltrate. Morphologically, these cells correspond to the so called *hematogones* (marrow stem cells), often difficult to distinguish from immature lymphocytes but generally larger, with a homogeneous nucleus without nucleoli and scant cytoplasm.[8] They also express CD19, HLA-DR and TdT[9] and their presence, if pronounced, may mimick the onset of leukemia in previously healthy subjects or might be interpreted as a persistence or recurrence of disease in children treated for ALL.

A genotypic analysis that excludes the monoclonal origin of these cells, and an accurate morphological evaluation of bone marrow permit recognition of the benign nature of this

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infiltrate, which is always confirmed by the long-term clinical outcome of the children.[10] Finally, a linkage between the expansion of B cell precursors and the onset of ITP should be considered.

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