A case of juvenile myelomonocytic leukemia presenting with a B-lymphoblastic immunophenotype

Juvenile myelomonocytic leukemia (JMML) represents no more than 2% of leukemias in children. To facilitate the diagnosis of this pathology, centralized diagnostic facilities have been established in our country. The validity of such facilities was confirmed in a case of monocytosis associated with an immunophenotype suggestive of B-lymphoblastic leukemia.

The classification of myelodysplastic syndromes (MDS) in childhood has been the subject of controversy during the last decade. Although some investigators have argued that childhood MDS can be classified into the same subgroups as the French-American-British (FAB) nomenclature for adult cases, others have pointed out that this is rarely used in practice.[1] Children with MDS are subdivided into two groups, i.e. those with a more adult-type MDS and those suffering from a disorder with myeloproliferative features primarily observed in infancy and early childhood. The latter pathology is characterized by prominent hepatosplenomegaly, frequent skin involvement, leukocytosis, monocytosis, and the presence of immature precursors in peripheral blood and has traditionally been described as chronic myelomonocytic leukemia (CMML)[2,3] or juvenile chronic myelogenous leukemia (JCML).[4] The new term JMML has recently been proposed to avoid further confusion.[5]

A 15-month old child with panniculitis of the right leg was referred to our Pediatric department. Peripheral blood analysis showed: Hb 9.5 g/dL, platelets 231×10^9/L, WBC 20.8×10^9/L, and the presence of monocytosis (25.4%; 5.2×10^9/L) with dysmorphologic features. Blood chemistry values were within normal ranges and viral serology was negative. The patient also had axillary lymphoadenopathy and hepatosplenomegaly. Flow cytometric analysis showed the presence of an abnormally high percentage of B-lymphocytes (40% $CD19^+$) in the peripheral blood, 18% of which were positive for co-expression with CD10 antigen, frequently observed in common lymphoblastic acute leukemia. Fever ranging from 37°C to 38°C was also present and was resolved by antibiotics. The suspicion of an oncohematologic disease indicated the need for a close follow-up and the a bone marrow examination done after a month showed the presence of a high percentage of B-lymphocytes $CD10^+/CD19^+$, poor representation of hematopoietic series with slight dysmyelopoiesis and 2% of blasts. Splenomegaly, leukocytosis (WBC 17.8×10^9/L) with monocytosis (24.1%) and circulating myeloid precursors were still present. Although other hematologic criteria of JMML were missing (bone marrow hypercellularity with less than 20% myeloid blasts and >10% of HbF),[6,7] the probability of this diagnosis began to emerge. As the *International and Italian Registry for Juvenile Myelogenous Leukemia* indicates that clonogenic assay of bone marrow and peripheral blood mononuclear cells (MNC) is needed to confirm the diagnosis,[8] *in vitro* cultures in semisolid medium were carried out using the centralized facilities of the Registry. In basal culture conditions the growth of myeloid bone marrow progenitors was clearly greater than that of progenitors from normal healthy donors (Table 1). Moreover, as frequently observed in JMML patients,[9] the number of granulo-macrophage colony-forming units (GM-CFU) was high despite the absence of colony-stimulating factors (CSFs); the conditioned medium from 5637 tumor cell line was used as the source of CSFs at a final concentration of 10% in Iscove's modified Dulbecco's medium (IMDM). This trend was confirmed when clonogenic assays were performed on peripheral blood MNC: in the absence of exogenous CSFs, the number of erythroid-colony forming units (BFU-E) was found to be particularly high, as previously described in JMML.[10] Fluorescent *in situ* hybridization (FISH) assay for monosomy 7 and trisomy 8 and 21, often reported to be present in children with myelodysplastic syndrome, did not reveal any chromosomal abnormalities.

Table 1. Clonogenic assay of bone marrow and peripheral blood mononuclear cells.

	CFU-GM		*BFU-E*	
	with CSFs	*without CSFs*	*with CSFs*	*without CSFs*
Patient BM MNC	175	130	49	31
Normal BM MNC	35-190	0	30-95	0
Patient PB MNC	192	178	78	116
Normal PB MNC	18-178	0	20-77	0

BM MNC: bone marrow mononuclear cells; PB MNC: peripheral blood mononuclear cells; CFU-GM: granulo-macrophage colony-forming unit; BFU-E: burst-forming unit-erythroid; CSF: exogenous colony stimulating factors in conditioned medium from the 5637 tumor cell line; the number of patient's colonies is expressed as 5×10^4 MNC/mL for bone marrow cultures and as 2×10^5 MNC/mL for peripheral blood cultures; as control, normal donor cells are cultured at a final concentration of 1×10^5 MNC/mL and 5×10^5 MNC/mL, respectively, for bone marrow and peripheral blood.

The benefit of centralized diagnostic facilities, such as those provided by the Italian National Registry, was demonstrated in this case of JMML presenting with an immunophenotype suggestive B-lymphoblastic leukemia.

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