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# A Case with Micromegakaryocytes

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## ABSTRACT

A boy with no previous history of bleeding presented with ecchymoses and splenomegaly. He was followed up for thrombocytopenia and micromegakaryocytes for 20 months till clinically malignancy was diagnosed.

Micromegakaryocytes must always be treated with suspicion, as they may provide an important clue for dyshematopoiesis.

Key Words: Micromegakaryocytes, Leukemia, Dismegakaryopoiesis.

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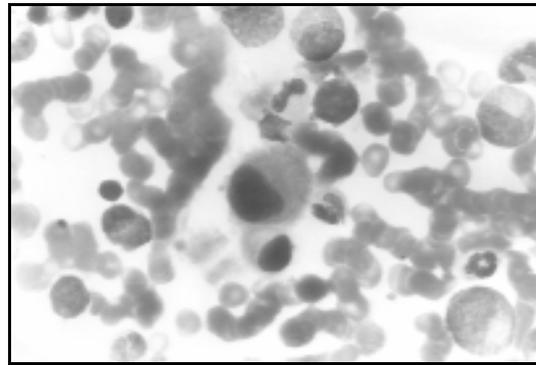
## INTRODUCTION

The most common cause of thrombocytopenia in children is immune thrombocytopenic purpura. Other etiologic factors include viral infections, aplastic anemia, megakaryocytic syndromes or pre-leukemic phases<sup>[1]</sup>. Bone marrow aspirates are essential for the evaluation of the differential diagnosis. Under normal circumstances, bone marrow aspirates are known to contain normal to increased numbers of small and large immature megakaryocytes and there are no standard methods for quantitating megakaryocytes<sup>[2]</sup>; the count is usually visual impression of the observing physician. Normal marrow cells > 20 µm in diameter were always megakaryocytes<sup>[3]</sup>. Cells 14-20 µm were be-

ing larger than general marrow population should be examined for micromegakaryocytes<sup>[3]</sup>. Size is a useful criterion for identification of megakaryocytes. There is a relationship between megakaryocyte size, ploidy and maturation<sup>[3,4]</sup>. The size of megakaryocytes increases with maturation stage<sup>[1-3]</sup>. Micromegakaryocytes have been reported in thrombocytopenia-absent radius syndrome (TAR), preleukemia, chronic myelogenous leukemia, myelodysplastic syndromes, pseudo-Pelger-Huet abnormality and in some familial thrombocytopenias<sup>[1-10]</sup>. Here we present a boy with thrombocytopenia and micromegakaryocytes.

## CASE REPORT

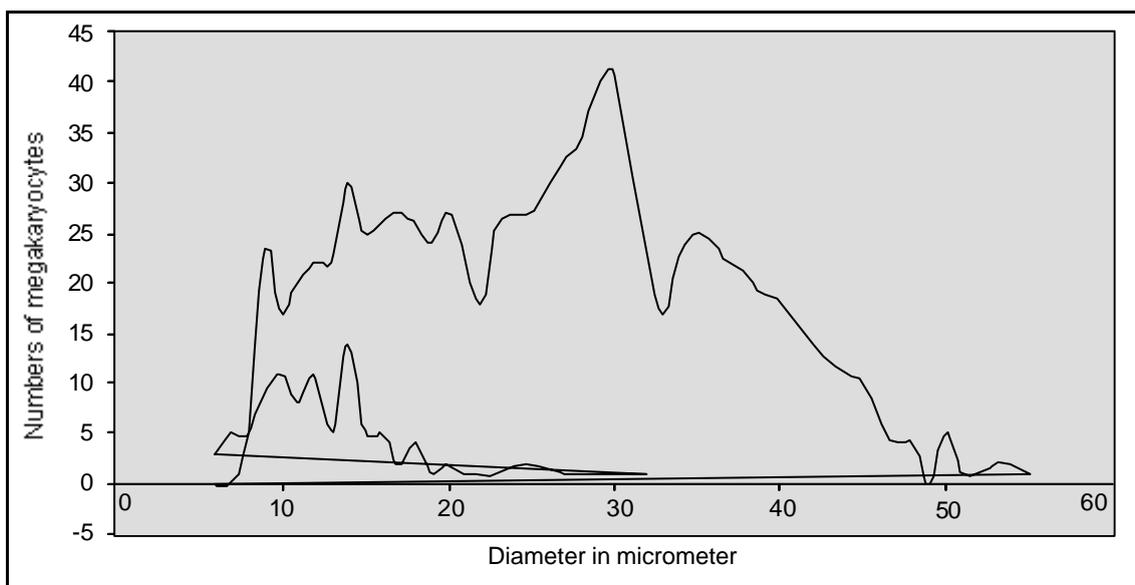
An 11.5-year-old boy was first evaluated for easy bruising from a period of 1 year. There was no history of prior bleeding, recent viral infection and drug ingestion. On physical examination, he was a well-appearing boy. The only positive physical findings were small ecchymoses on the extremities and 2 cm splenomegaly. A complete blood count showed a white blood cell count (WBC) of 8300/mm<sup>3</sup>, Hb 12.5 g/dL, Hct 36.9% and platelet count 32000/mm<sup>3</sup>. The differential count was 64% neutrophils, 28% lymphocytes, 6% monocytes and 2% eosinophils. The platelets appeared to be normal in size and color. Bleeding time was found to be 1.5 minute with Ivy method. Viral serology was positive for EBV and CMV IgG only (negative for IgM and antigen). The bone marrow aspirate showed normal to increased numbers of megakaryocytes with many small mononuclear forms (micromegakaryocytes) (Figure 1). One hundred megakaryocytes from the patient and an adolescent (at the same age with the patient and diagnosed JRA) were sized in microns. The smallest megakaryocyte of this boy was measured to be 6 µm in diameter and the biggest one 32 µm (Figure 2). The megakaryocytes were also investigated with electron microscope. In the early phase disturbed megakaryocyte ploidization and maturation with demarcations, granular phase with no nuclear mi-



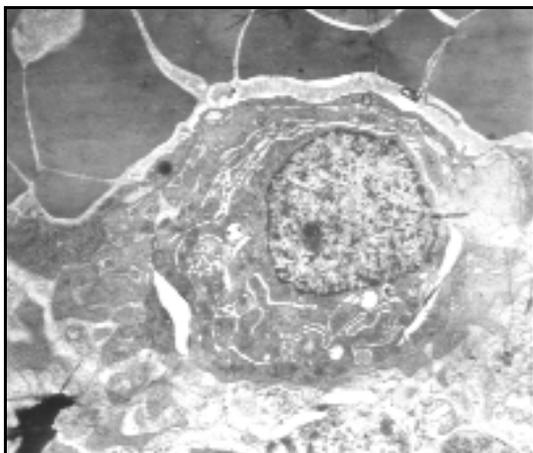
**Figure 1.** Photomicrograph of Wright-Giemsa -stained micromegakaryocytes.

tosis and no ploidy, no trombocytes around the cytoplasm were found (Figure 3). Platelet antibodies and rheumatological parameters were normal range. Chromosomal evaluation showed no abnormality.

The patient was followed for 20 months without any symptoms or change in laboratory values. During this period bone marrow aspirations were repeated every 6 months in which hypogranular myeloid precursors and atypical mononuclear cells 3-4% were interpreted. After this silent period, he was interned to the hospital because of fever, vomiting with a WBC of 6500/mm<sup>3</sup>; Hb 10.8



**Figure 2.** Size distribution of marrow megakaryocytes of the patient and normal case.



**Figure 3.** Electron microscopic evaluation (early phase according to ploidy but demarcations were detected. There were no platelets and granule).

g/dL, Hct 31.1% and platelet count 29000/mm<sup>3</sup>. As no focus was found for identification of the fever bone marrow aspiration was planned for two purposes: marrow culture and any different diagnosis for micromegakaryocytes. Bone marrow material was insufficient because of dry taps. Although no blasts were detected in the peripheral blood smears, the biopsy material revealed the diagnosis of ALL as diffuse CD3 positivity was shown immunohistochemically. He was treated with BFM 95 protocol for 2 months till clinical progression and peripheral blasts were detected. Immunphenotyping of the blasts taken from the peripheral blood revealed CD 34: 90%, HLA-DR: 80%, CD 13: 50% and CD 3: 20% This time he was diagnosed as AML M0. He was able to finish BFM 95 AML protocol. Generally the remission that we achieve does not last too long, and blasts are usually detected before a new block of therapy, and as we presumed, he relapsed in the 1-month period after the cessation of the therapy and extirpated 9 months after his admission for clinical complainments and fever.

### DISCUSSION

Myelodysplastic syndrome (MDS) in childhood is difficult to diagnose, follow and treat<sup>[5,6]</sup>. Dyspoesis in some cases are subtle and more than one bone marrow aspirations are necessary for the diagnose<sup>[6,7]</sup>.

The megakaryocyte are the largest cell in films of normal aspirates, ranging from 30 to 100 µm in diameter<sup>[4]</sup>. The nuclei undergo endomitosis, as well as marked lobulation without division of the cytoplasm. This results in a polyploid nucleus, which may be 4, 8, 16, 32, 64 or even 128n<sup>[1-6]</sup>. The size of the cells correlates with their ploidy, with cells of low ploidy being smaller than those of high ploidy. Thrombocytopenia is usually associated with large megakaryocytes in all ploidy classes. In our case electron microscopic evaluation revealed that in early phase although demarcations were detected there was no platelets and in late granular phase nuclear mitosis and ploidy could not be demonstrated. There was an asynchrony between the nucleus and cytoplasm. Besides this dispoetic features almost all megakaryocytes were smaller than 20 µm while in normal case most of the cells were about 50 µm (Figure 2).

Micromegakaryocytes are one of the most important clues of dyspoetic bone marrow. The presence of more than 10% micromegakaryocytes in the megakaryocyte population suggest a preleukemic condition or non lymphatic leukemia<sup>[3]</sup>. But there are also some familial thrombopenic syndromes with micromegakaryocytes<sup>[10]</sup>.

As no chromosomal pathology was found and there were no more displastic signs in the bone marrow of this boy at the beginning and parents were cousins, we suspected one of familial thrombocytopenias. Olson, et al. defined a family who suffered from thrombocytopenia with micro and bilobed shaped megakaryocytes just like ours<sup>[10]</sup>. The family that Olson, et al. defined has size and ploitation affected megakaryocytes more than maturation. They suggested these megakaryocytes might lack an appropriate growth factor on receptors. But the familial evaluation of our case was normal except him and splenomegaly that we detected at the beginning which made us to be alert for MDS or malignancy. During follow-up period first myelodysplastic signs in the bone marrow began and than he was diagnosed first ALL than AML and extirpated 3 years after first complainments. We have been suspicious about the diagnosis ALL as in vast majority of cases the trans-

formation of MDS is AML, just as the end result of our case. De novo AML cases have better prognosis than MDS related AML. Although clinical remission was achieved we had never been able to achieve bone marrow remission.

As a conclusion micromegakaryocytes in the bone marrow must be followed carefully as it could be the only sign of myelodysplasia and malignancy.

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