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Title: Megakaryocyte in peripheral blood smear

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Dear editor

Megakaryocytes (MK) are large polypoidal cells found within Bone Marrow (BM), comprising 0.01% of all nucleated cells [1]. Circulating MK have been described in literature but normal MK in Peripheral Blood Smears (PBS) have rarely been reported[2]. We report here 4 cases where we found MK in PBS.

1st case: A 10-year-old boy presented with weakness and decreased appetite. PBS showed Microcytic Hypochromic anemia (MHA), leucocytosis and reactive thrombocytosis. 2nd case: A 30-year-old female presented with fever and skin rash with positive dengue serology. PBS showed MHA with thrombocytopenia. 3rd case: A 15-year-old female presented with fever with chills and rigor. PBS showed macrocytic anemia, thrombocytopenia and trophozoites of Plasmodium vivax. 4th case: A 14-year-old male admitted for grafting for burn on his hand. PBS showed MHA with reactive thrombocytosis. A MK, round-elongated in shape, with moderate-abundant amount of granulated cytoplasm, compact lobulated nucleus, was seen in each of these cases at the tail end of PBS (Fig 1a-d). None of these patients had hepatosplenomegaly or evidence of any haematological disorder. Table 1 shows the hematological parameters.

MK develop from hematopoietic stem cells that reside in BM. Finding of MK in Peripheral Blood (PB) is usually indicative of serious disorder of BM such as myelodysplasia, granulocytic leukemia or other myeloproliferative disorders [3]. The PBS in such cases may show leucoerythroblastic reaction, large cytoplasmic fragments of MK and dwarf

micromegakaryocytes [3]. Though normal MK has been reported in PBS in a case of post essential thrombocythemia – myelofibrosis but the PBS in addition showed presence of leukoerythroblastic reaction and blasts[2]. Our patients neither had a history of myeloproliferative disorder nor such additional findings in PBS.

In 1965 Kaufman et al demonstrated that 20-25% of mature MK leave BM with sufficient cytoplasm to enter PB and migrate to lungs and 7-17% of body's platelets are released in pulmonary capillaries [4]. Hence implicating that MK normally circulate in PB and are normal constituents of PB [4]. But the identification of normal MK in PBS of normal patients has never been reported.

In response to anemia, there is stimulation of Erythropoietin (EPO) receptors by EPO, present on erythroid precursors as well as on MK in BM [5]. There is also an increase in TPO levels in response to thrombocytopenia, with resultant increase in MK differentiation. This might be a cause of increase in number of circulating MK with consequent detection in PBS.

To conclude, detection of MK in PB is usually indicative of a serious BM disturbance. But one should keep in mind that mature MK normally circulate in PB and can also be seen in PBS in cases having increased MK differentiation. Though clinical significance of this finding is unclear, but as large cells like blasts, large atypical lymphocytes, organisms, or in this case megakaryocytes can be found at the edge of PBS, hence a routine examination of the feathered edge of PBS is advised as it has diagnostic importance.

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Figure 1 (b,c) 100×: A large megakaryocyte is seen at the tail end of the PBS in case 2 and 3. (a-d) High power view of Giemsa stained PBS of case 1-4 respectively showing megakaryocyte, round - elongated in shape, with moderate-abundant amount of granulated cytoplasm, compact lobulated nucleus, at the tail end of the PBS.

Table 1: Hematological parameters with diagnosis

S NO.	CASE 1	CASE 2	CASE 3	CASE 4
Hb (g/L)	58	87	87	63
RBC (/μL)	3.66×10^6	3.46×10^6	2.36×10^6	2.55×10^6
HCT (proportion of 1)	0.21	0.24	0.26	0.20
MCV (fL)	57.9	70	113	81
MCH (pg)	15.8	24.8	36	24.6
TLC (/L)	14.4×10^9	6.4×10^9	5.4×10^9	6.4×10^9
PLT (/L)	922×10^9	0.58×10^9	0.90×10^9	7.27×10^9
DIAGNOSIS	MHA	MHA, thrombocytopenia, with dengue	Macrocytic anemia, thrombocytopenia with malaria (P. vivax)	MHA

Hb: Hemoglobin, Hct: Hematocrit, RBC Red blood cell, MCV: Mean corpuscular volume, MCH: Mean corpuscular Hemoglobin, MHA: Microcytic hypochromic anemia, TLC: Total leucocyte count, PLT: Platelet count

