Micromegakaryocytes in peripheral blood in a case of AML, t(6;11)(q27;23)

Garima Jain , Chandan Kumar, Anita Chopra

Laboratory Oncology, All India Institute of Medical Sciences, New Delhi, Delhi, India

Correspondence to
Dr Anita Chopra;
chopraanita2005@gmail.com

GJ and CK are joint first authors.

Accepted 28 April 2021

DESCRIPTION

Micromegakaryocytes (MMGKs), a common finding in bone marrow, have been rarely described in peripheral blood (PB). MMGKs are known to occur commonly in PB of patients diagnosed with Chronic Myeloid Leukemia (CML).¹ A characteristic of chronic phase of CML, they are considered to be dysplastic, although they produce morphologically normal platelets. Circulating MMGKs (ie, MMGK in PB) have also been reported in more aggressive types of myelodysplasia (such as refractory anaemia with excess blasts (RAEBs) and refractory anaemia with excess blasts in transformation (RAEB-t) and have been known to correspond to a poor prognosis.² Circulating MMGKs are also known to occur in cases of hypoplastic myelodysplasia (MDS).³ We highlight a case of acute myeloid leukaemia (AML) demonstrating many MMGKs in PB.

A 25-year-old man presented with chief complaints of left mandibular region swelling for 1 month and gum bleeding with fever for 2 weeks. On examination, the patient had gum hypertrophy, 2 cm palpable liver and cervical lymphadenopathy. His laboratory tests at presentation showed haemoglobin (Hb) level of 61 g/L, a Total leucocyte count (TLC) of $10.47 \times 10^3/\text{L}$ and a platelet count of $19 \times 10^9/\text{L}$. Other laboratory parameters were within normal limits. PB examination showed 86% blasts with many circulating MMGKs (figure 1A). Flow cytometric immunophenotyping (FCMI) of PB showed 62% CD45 dim+blasts which were cMPO+, CD13+, CD34+, CD117+, CD38+ and negative for CD79a, CD7, cCD3, sCD3, CD16, CD123, CD11b, CD36, CD56, CD64, CD4, CD14, CD22 and CD20. Flow cytometry immunophenotyping (FCMI) also identified a cCD41 and cCD61 bright positive population representing MMGK (figure 1B). Bone marrow aspirate showed near total replacement by blasts and occasional megakaryocyte showed dysplastic changes.

BCR-ABL 1 was negative while cytogenetics showed translocation t(6;11)(q27;23). The translocation breakpoint involves the *MLL* gene, which is the human homologue of the *Drosophila trithorax* gene, at 11q23 and the *AF6* gene at 6q27. The patient was diagnosed as Acute Myeloid Leukemia (AML) M1 (according to French-American-British classification) and AML not otherwise specified according to the WHO classification. Our patient has been given 3+7 induction of cytarabine and is on follow-up.

Thorough search of literature revealed that the first case of circulating MMGK associated with a

Figure 1 Peripheral blood (PB) examination showed 86% blasts with many circulating micromegakaryocytes (MMGKs) (A–C). Flow cytometric immunophenotyping of PB showed 62% CD45 dim+blasts which were cMPO+, CD13+, CD34+, CD117+, CD38+. Flow cytometry immunophenotyping also identified a cCD41 and cCD61 bright positive population representing MMGK (D, E). Electron microscopy of PB showed these MMGKs with the presence of target bodies and granules in the cytoplasm (F, G).

leukaemia was reported in 1984 in a 26-year-old man diagnosed with erythroleukaemia.⁴ Megakaryocytic features were defined by morphological and cytochemical studies using light and electron microscopy with platelet-megakaryocyte peroxidase staining. In another study to gain perspective on platelet production in the fetus and the newborn, large numbers of megakaryocytes, mostly mature, were found in umbilical arteries and veins, more than previously observed circulating in adult blood.⁵

Circulating MMGKs may be often missed by a naïve screener as they are not only rare but also often lack specific morphological features and may resemble small lymphocytes. These may be missed on routine Romanowsky stains and some studies³ detected these immunocytochemically with monoclonal antibodies to platelet glycoprotein IIa. As many as 34 % of MDS cases demonstrated

© BMJ Publishing Group Limited 2021. No commercial re-use. See rights and permissions. Published by BMJ.

To cite: Jain G, Kumar C, Chopra A. *BMJ Case Rep* 2021;**14**:e235176. doi:10.1136/bcr-2020-235176

Learning points

- ▶ This is an interesting and first case of circulating micromegakaryocytes associated with AML.
- ▶ It highlights the importance of morphological evaluation of peripheral blood.
- ▶ Its association with impact on prognosis or treatment outcome, if any, needs to be evaluated by observing such cells in other smears of AML.

MMGK in peripheral blood.² Elghetany *et al*'s study sharply contrasted with observations of FAB group⁶ which stated that 'rarely micromegakaryocytes can be seen in peripheral blood'. MMGKs were also found to be more common in RAEB-1 and RAEB-2 which are known to possess dysmegakaryocytic features in bone marrow. The study also postulated that the presence of these circulating MMGKs may predict their evolution into acute leukaemia and hence a routine evaluation of PB films for these cells could be warranted in the future as a part of clinical workup. In some cases of acute myeloid leukaemia, Immuno-alkaline phosphatase staining (APAAP) staining of blood smears revealed circulating pro-megakaryoblasts and MMGKs.⁷

Contributors CK, GJ and AC screened the morphology slides and reported the flow cytometry. CK and GJ wrote the manuscript and AC approved the same with suggestions and guidance.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Disclaimer Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD

Garima Jain <http://orcid.org/0000-0001-8625-0868>

REFERENCES

- 1 Anand M, Hazarika B, Kumar L, *et al*. High abundance of circulating megakaryocytic cells in chronic myeloid leukemia in Indian patients. revisiting George Minot to re-interpret megakaryocytic maturation. *Blood Cells Mol Dis* 2016;60:28–32.
- 2 Erber WN, Jacobs A, Oscier DG, *et al*. Circulating micromegakaryocytes in myelodysplasia. *J Clin Pathol* 1987;40:1349–52.
- 3 Elghetany MT, Hudnall SD, Gardner FH. Peripheral blood picture in primary hypocellular refractory anemia and idiopathic acquired aplastic anemia: an additional tool for differential diagnosis. *Haematologica* 1997;82:21–4.
- 4 Yamauchi K, Miyauchi J, Nagao T. Identification of circulating micromegakaryocytes in a case of erythroleukemia. *Cancer* 1984;53:2668–73.
- 5 Levine RF, Olson TA, Shoff PK, *et al*. Mature micromegakaryocytes: an unusual developmental pattern in term infants. *Br J Haematol* 1996;94:391–9.
- 6 Bennett JM, Catovsky D, Daniel MT, *et al*. Proposals for the classification of the myelodysplastic syndromes. *Br J Haematol* 1982;51:189–99.
- 7 Erber WN, Breton-Gorius J, Villeval JL, *et al*. Detection of cells of megakaryocyte lineage in haematological malignancies by immuno-alkaline phosphatase labelling cell smears with a panel of monoclonal antibodies. *Br J Haematol* 1987;65:87–94.

Copyright 2021 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <https://www.bmj.com/company/products-services/rights-and-licensing/permissions/>
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

Customer Service

If you have any further queries about your subscription, please contact our customer services team on +44 (0) 207111 1105 or via email at support@bmj.com.

Visit casereports.bmj.com for more articles like this and to become a Fellow