Megakaryocyte emperipolesis in a child with chronic neutropenia: an unusual coexistence

Deniz Aslan, Sevgi Yetgin

Hematology Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey

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The term emperipolesis defines the temporary presence of one cell within another's cytoplasm. In clinical use, megakaryocyte emperipolesis is the penetration of hematopoietic cells into the cytoplasm of megakaryocytes. The pathophysiological significance of megakaryocyte emperipolesis is uncertain. It has been described in association with neoplastic disorders, and in a few instances in idiopathic thrombocytopenic purpura, iron deficiency anemia, bleeding, and during the administration of recombinant human granulocyte colony-stimulating factor. However, megakaryocyte emperipolesis in a patient with chronic neutropenia has not been reported. In the current report, emperipolesis of hematopoietic cells within megakaryocytes in a boy with chronic neutropenia is described and the possible mechanisms are discussed.

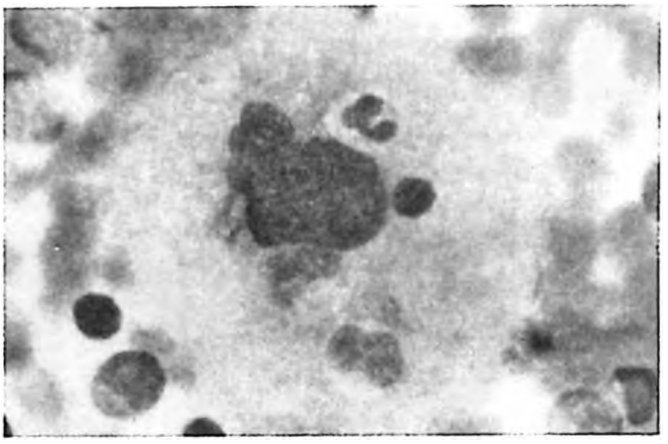
Key words: megakaryocyte emperipolesis, chronic neutropenia.

Marrow cells may enter megakaryocytes by a phenomenon that is referred to as emperipolesis[1]. Although the morphological appearance of this process is quite striking, the pathophysiological significance of mekaryocyte emperipolesis is uncertain. It has been described in association with neoplastic disorders[2,3], and in a few instances in idiopathic thrombocytopenic purpura (ITP), iron deficiency anemia[4], bleeding[1], and during the administration of recombinant human granulocyte colony-stimulating factor (rhG-CSF)[5], in order of decreasing frequency. However, megakaryocyte emperipolesis in a patient with chronic neutropenia (CN) has not been reported. In this article, emperipolesis of hematopoietic cells within megakaryocytes in a boy with CN is described.

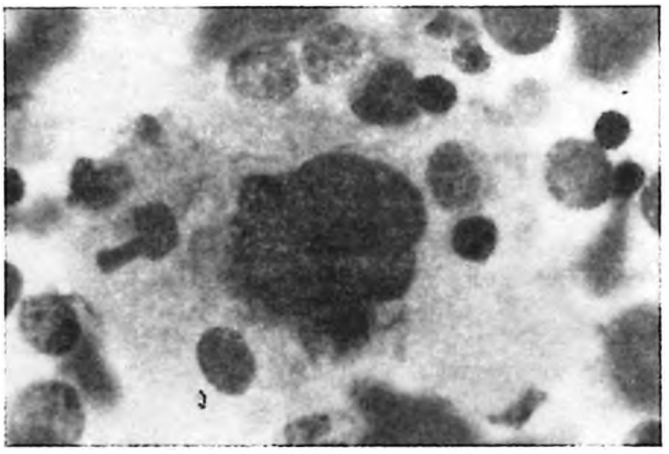
Case Report

A four-year-old boy was admitted with the complaint of bilateral earache. Physical examination revealed bilateral redness and swelling of the tympanic membranes consistent with otitis media. His hemoglobin level was 10.9 g/dl, white blood cell (WBC) count 3.0×10^9/L with 10% neutrophils, 68% lymphocytes, 16% monocytes, and 6% eosinophils, and platelet 316×10^9/L. His past history revealed recurrent infections (2 episodes of otitis media, 2 of sinusitis, and 1 of acute gastroenteritis) between the age of one and four years. Neutropenia was found to be constant during a follow-up period of two months (WBC mean 2.7 ± 0.2, range $2.4\text{-}3.1 \times 10^9$/L; absolute neutrophil count mean 322 ± 121, range 156-540). Immunoglobulin levels were within normal range and viral markers such as cytomegalovirus, herpes simplex virus, hepatitis B virus, and hepatitis C virus were negative. In his past history there was neither a chronic use of any drug nor an exposure to chemicals. There was no evidence of any systemic illness. The complete blood counts and the total neutrophil counts of the peripheral blood of the parents were within normal limits.

In bone marrow aspiration smear emperipolesis of hematopoietic cells (cells of myelocytic origin, lymphocytes, and normoblasts) by megakaryocytes was observed (Figs. 1a, 1b). Cells of myelocytic origin were the most comon marrow cell engulfed by megakaryocytes. The patient was treated with antibiotics for otitis media. Megakaryocyte emperipolesis in bone marrow smear and neutropenia were noted to be persistent six weeks after the first marrow.



(a)



(b)

Figs. 1a and b. The phenomenon of emperipolesis with megakaryocytes containing cells of myelocytic origin, lymphocytes, and erythroid precursors.

Discussion

Emperipolesis is a phenomenon characterized by the temporary presence of one cell within another's cytoplasm, but it differs from phagocytosis in that the engulfed cell remains viable and can ultimately exit from the engulfing cell. Electron microscope findings by Larsen[6] demonstrated that neutrophils engulfed by megakaryocytes had intact membranes. Although all types of marrow cells (myelocytic, erythroid, and lymphoid) have been involved in emperipolesis by megakaryocytes, mature neutrophils are the most common. It is widely accepted that megakaryocytic emperipolesis is possibly mediated by some adhesion molecules[7] and by IgG bound to the surface membrane of hematopoietic cells[5].

Megakaryocyte emperipolesis has been most often reported in association with neoplastic disorders (e.g. lymphoma, Hodgkin's disease, lymphocytic leukemia, myelodysplastic syndrome, myeloma, carcinoma, neuroblastoma), and in a few instances in ITP, iron deficiency anemia, bleeding, and during the administration of rhG-CSF. However, to our knowledge, megakaryocyte emperipolesis in association with CN has not been reported previously. In the present case a diagnosis of CN was made based on recurrent infections starting from the first year of age and persistent neutropenia.

Several possibilities could be considered for the association of megakaryocyte emperipolesis and CN. 1) Megakaryocyte emperipolesis is most often described in association with malignancy, and since CN is regarded as a premalignant condition, emperipolesis should be an expected feature of CN. 2) In our patient neutropenia might be a secondary phenomenon due to the engulfment of myelocytic cells by megakaryocytes. 3) Some serological or cell membrane changes due to frequent bacterial infections associated with chronic neutropenia might be the cause of this phenomenon.

Therefore, we suggest that evaluation of patients with CN is required for a definite conclusion about the relationship between CN and megakaryocyte emperipolesis.

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