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► To cite this version:

J.-F. Lesesve, B. Thomas, J. Broséus, B.J. Bain. Macropolycytes: Severe stress time for neutrophils. *Morphologie*, 2020, 104, pp.214 - 216. <10.1016/j.morpho.2020.04.001>. <hal-03492144>

HAL Id: hal-03492144

<https://hal.science/hal-03492144v1>

Submitted on 21 Sep 2022

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Rubrique proposée : cas clinique

5 pages dactylographiées, **895** mots (avec références), 9 références, 1 illustration (.tif, 300dpi)

Titre en français: Macropolycytes

Titre an anglais: Severe stress time for neutrophils

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Abstract

Macropolycytes are giant neutrophils found in a variety of benign and neoplastic conditions. Since megaloblastic anaemia is one of the recognised causes of macropolycytes, other blood film features of megaloblastic anaemia should be sought when they harbor hypersegmented nuclei. When they are hypolobulated and hypogranular, the occurrence of a myelodysplastic syndrome must be investigated. Finding macropolycytes in the context of a nonspecific reactive granulopoiesis is more questionable but is often associated with stressed myelopoiesis and/or granulocyte colony-stimulating factor therapy.

Résumé

Les macropolycytes sont des polynucléaires géants observés dans des circonstances bénignes ou malignes variées. Il faut rechercher une carence vitamique (B9, B12) si leurs noyaux sont hypersegmentés **et que d'autres signes morphologiques de carence sont présents**, ou un syndrome myélodysplasique si des noyaux **hypolobulés** ainsi qu'une hypogranulation sont observés. **La présence de macropolycytes dans un contexte de granulopoïèse réactionnelle non spécifique peut** également témoigner d'un état d'« hématopoïèse de stress », avec ou sans utilisation concomitante de facteurs de croissance.

Key words

Macropolycytes, giant neutrophils, megaloblastic anemia, myelodysplastic syndrome, stressed hematopoïesis

Mots Clés

Macropolycytes, polyucléaires neutrophils géants, anémie mégaloblastique, syndrome myélodysplasique, hématopoïèse de stress

Introduction

Macropolycytes are giant neutrophils being occasionally seen in the peripheral blood (PB) film from patients with various conditions [1]. Here we discuss the significance of the finding of macropolycytes as an isolated cytologic anomaly in a patient presenting with a non-Hodgkin lymphoma treated with multiple courses of chemotherapy and ending in the context of a fatal sepsis.

Case report

A 78-year-old man had been diagnosed with germinal center type diffuse large B-cell lymphoma of the bowel 3 years previously. He had been treated with multiple courses of chemotherapy including first cyclophosphamide, vincristine, doxorubicin, prednisolone, rituximab (R-CHOP), then rituximab, cisplatin, cytarabine, dexamethasone (R-DHAP), then rituximab, ifosfamide, carboplatin, etoposide (R-ICE) due to serial relapses. After an unsuccessful autologous stem cell transplant, he was eligible for CAR-T cells therapy. He presented with a critical illness, fever and infected abdominal tumoral mass leading to bowel obstruction. Treatment including intravenous filgrastim and broad spectrum antibiotherapy (piperacillin-tazobactam, imipeneme, metronidazole, gentamicin, fluconazole) was in run. A full blood count showed pancytopenia (haemoglobin concentration 7.9 g/dl, leukocytes $0.88 \times 10^9/l$ with 55% neutrophils and platelets $16 \times 10^9/l$). The neutrophils showed nonspecific toxic granulation but no anomaly of nucleus segmentation. Very few giant neutrophils were observed after careful examination of the blood film (around 2 per film, mosaic figure 1, column a). A bone marrow aspirate demonstrated hypercellular reactive granulopoiesis with occasional macropolycytes (3% of the neutrophils, mosaic figure 1, column b). Their diameter was roughly 20 μm . No giant band cells or metamyelocytes were found. No dysplastic features in other lineages and no abnormal lymphoid cells were observed (mosaic figure 1, column c).

Discussion

The diameter of a normal neutrophil varies from 10 to 12 μm . The term "giant" neutrophil or "macropolycyte" was first used by W.E. Cooke (from the Pathological Department of the Wigan Infirmary, UK, 1927) being applied to neutrophils with a diameter greater than 14 μm . Cooke described macropolycytes in two widely different conditions: acute pyogenic infections and megaloblastic anaemias. He asserted that macropolycytes were rarely found in infections, "perhaps twice or three times a year by anyone constantly examining blood films", but were frequently seen in megaloblastic anaemia, with diameters from 16 to 21 μm and hypersegmented nuclei [2]. Rare observations in healthy subjects were then reported [3-4]. More recently, macropolycytes were more confusingly reported in the PB from adults with various neoplastic or benign conditions. In the context of hematological neoplasms, they were encountered in chronic myeloid leukemia [1] and myelodysplastic syndromes, associated there with other dysplastic features (abnormal hypo pseudo-Pelger segmented nuclei, cytoplasmic hypogranulation) and becoming a key-finding for the assessment of dysplasia [5]. Benign disorders with scarce macropolycytes included viral infections [1], auto-inflammatory diseases, treatment using colony-stimulating factors [6] or methylprednisolone [7] or combination of viral infection and multiple drug effect [8]. Two pediatric cases were reported: a non-septic 17-month-old boy with Shwachman-Diamond syndrome receiving granulocyte colony-stimulating factor treatment, and a 12-year-old boy

with Kawasaki disease [9]. In the first case, macropolycytes disappeared after filgrastim was withheld, and in the second case after 4 days of high-dose intravenous immunoglobulin treatment.

As stated in a forward-thinking comment by Ian MacKay in 1939, macropolycytes may also occur occasionally in the PB from various contexts where there is a profound bone-marrow reaction caused by abnormal stimuli [4]. Our observation highlighted the possible occurrence of macropolycytes not only in the PB but also in the bone marrow, suggesting the production of giant neutrophils in case of stressed hematopoiesis, particularly in relationship with infection, neoplastic condition, chemotherapy and G-CSF treatment. In such context, macropolycytes should look like very large neutrophils without nucleus anomaly or dysplastic features. Such giant appearance might be linked to the production of tetraploid neutrophils during accelerated myelopoiesis, the neutrophils undergoing DNA duplication without cell division [9] and the number of lobes increasing proportionately. Corticosteroids were also proved to cause hyperdiploid neutrophils [7].

To conclude, macropolycytes are giant neutrophils rarely observed not only in the PB but also in the bone marrow, often in the context of a stressed granulopoiesis. They are closed to, but should be distinguished from, large hypersegmented neutrophils evoking megaloblastic anemia and dysplastic giant neutrophils related to myelodysplastic syndromes which.

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Figure

Mosaic image of macropolycytes (May-Grunwald-Giemsa stain, magnification x1000). Column a: blood, column b-c: bone marrow, bar scale 20 μm). Oversized macropolycytes reached up to 20 μm , and coexisted with usual sized neutrophils and metamyelocytes in the bone marrow.

Conflit d'intérêt: aucun.

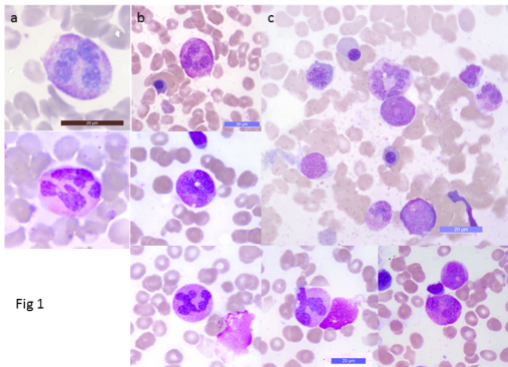


Fig 1