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Morphologically abnormal neutrophil granulocytes in COVID-19 cases

MEDISINEN I BILDER

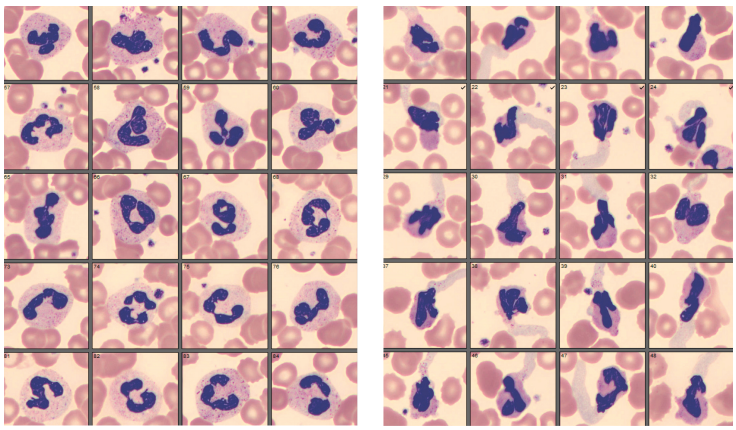
INGER ANNE TVEIT

E-mail: inger.anne.tveit@sshf.no
Department of Pathology
Sørlandet Hospital, Arendal
Inger Anne Tveit, MSc., biomedical laboratory scientist in haematology and coagulation.
The author has completed the ICMJE form and declares no conflicts of interest.

HEGE ZAAR NIELSEN

Department of Pathology
Sørlandet Hospital, Arendal
Hege Zaar Nielsen, MSc., biomedical laboratory scientist in haematology and coagulation.
The author has completed the ICMJE form and declares no conflicts of interest.

Inger Anne Tveit and Hege Zaar Nielsen have made equal contributions to this article.



The image on the left shows a blood smear with normal neutrophil granulocytes, stained with May-Grünvald-Giemsa stain. It was taken from a patient with COVID-19 on the day of admission. The image to the right was taken five days later and shows that all the granulocytes have developed a notably abnormal morphology. A few days later, the cell image had normalised again.

Today's haematology instruments are programmed to identify a number of abnormal findings in blood cells. When abnormal morphology is detected, the instrument will prepare and stain blood smears and perform automated cell classification, based on 200

individual leukocytes that are pre-divided into subgroups.

The instruments did not alert us to abnormal morphology of the blood samples taken five days after admission; however, these were examined microscopically for training purposes. The morphology of the granulocytes was striking. The amount of cytoplasm in the neutrophil granulocytes in the blood smear had decreased significantly, and they contained no vacuoles and few granules. The structure (segmentation), size and colour intensity of the cell nucleus appeared to be unchanged, however. In all the neutrophil granulocytes examined microscopically, a blue-coloured protuberance from the cytoplasm was observed, which in many cases constituted a large part of the cells' total volume. In some instances, granules could also be observed in the protuberance. All of the neutrophil granulocytes had the same abnormal morphology.

Blood smears from a further five patients with COVID-19 were followed up, and we found the same phenomenon in two of these patients. The observations in the three with pathological blood smears were made at approximately the same point of time in the disease course – 3–4 weeks after onset of symptoms. The degree of severity of the disease in the three patients varied. The only obvious common denominator was hospital admission and treatment for COVID-19. Two of the three patients were on ventilators during their hospitalisation. All three had neutrophilia and lymphopenia. The lymphocytes had a normal appearance and were not activated.

The neutrophil granulocytes constitute the first-line defence against pathogens (1). The ability to form so-called neutrophil extracellular traps (NETs) has recently been described for this cell group. This is a process whereby the cells form a meshwork of fibres with nucleated chromatin and proteins to enclose the pathogen for destruction, known as NETosis (2). Histological images have been published of neutrophil granulocytes infiltrated in the pulmonary capillaries of COVID-19 patients that may possibly be linked to this process (3). Severely ill patients with COVID-19 may develop acute respiratory distress syndrome (ARDS), and this may lead to a higher level of neutrophil extracellular traps in plasma (3).

The striking cell image observed in all of the neutrophil granulocytes in the three different patients may possibly be connected to ongoing NETosis. Granulocytes have a short half-life and are produced continuously in bone marrow. This may explain why the cell image normalised only days later.

REFERENCES:

1. Iba T, Hashiguchi N, Nagaoka I et al. Neutrophil cell death in response to infection and its relation to coagulation. J Intensive Care 2013; 1: 13. [PubMed][CrossRef]

2. Brinkmann V, Reichard U, Goosmann C et al. Neutrophil extracellular traps kill bacteria. Science 2004; 303: 1532–5. [PubMed][CrossRef]

3. Barnes BJ, Adrover JM, Baxter-Stoltzfus A et al. Targeting potential drivers of COVID-19: Neutrophil extracellular traps. J Exp Med 2020; 217.–e20200652. [PubMed]

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