

8. Davidov M. I., Dyabkina O. V. Acute diseases of the scrotum organs of non-traumatic genesis in school-age children. *Medical Almanac*. 2016;2(42):87-90.
9. Axelrov M. A., Minaev S. V., Razin M. P., Yusupov S. A., Tsap N. A. [et al.] Treatment of cryptorchidism in pediatric surgical practice: a multicenter study. *Urology Herald*. 2023;11(1):13-25.
<https://doi.org/10.21886/2308-6424-2023-11-1-13-25>
10. Adhikari S., Bhatta O. P., Bhetwal P., Awasthi S. Encysted spermatic cord hydrocele: A case series. *Int. J. Surg. Case Rep.* 2024;118:109619.
<https://doi.org/10.1016/j.ijscr.2024.109619>

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NETOSIS AS A PROCESS INVOLVED IN THE CONSOLIDATION OF ANEURYSMAL BONE CYSTS IN CHILDREN USING HEMOSTATIC AGENTS

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НЕТОЗ КАК ПРОЦЕСС, УЧАСТВУЮЩИЙ В ЗАЖИВЛЕНИИ АНЕВРИЗМАЛЬНОЙ КОСТНОЙ КИСТЫ У ДЕТЕЙ ПРИ ПРИМЕНЕНИИ ГЕМОСТАТИЧЕСКОГО ПРЕПАРАТА

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The study investigating the excessive formation of neutrophil extracellular traps (NETs) in neutrophils culture obtained while treatment of aneurysmal bone cysts using «Haemoblock», a hemostatic agent (Pul-Sar, Istra, Russian Federation), as a stimulator has been conducted. One hundred twenty-eight children with aneurysmal bone cysts (ABC) aged 6 to 15 years were included in the study. Sixty-three of the patients a clinical comparison group, underwent intralesional resection followed by alloplasty. Sixty-five of the patients made up a main clinical group who underwent minimally invasive surgery; 35 patients (A) and 30 children were treated by puncturing and administered a hemostatic agent (B).

Ex vivo excessive NET generation was evaluated in neutrophil culture isolated from blood obtained during cyst puncturing and from peripheral venous blood in all children of the main clinical group. Neutrophils isolated from cysts had a statistically significantly increased ability to form extracellular traps compared to neutrophils from peripheral venous blood in response to stimulation by «Haemoblock», a hemostatic agent. Neutrophils in these patients formed mainly filamentous NETs.

Thus, a modulating NETs formation plays a main role in providing intercellular interaction and proliferation of cells, including fibroblasts, leading to the closure of the cavity of aneurysmal bone cysts in children.

Keywords: aneurysmal bone cyst, netosis, neutrophil extracellular traps, hemostatic agent, children

Проведено исследование выраженности образования нейтрофильных внеклеточных ловушек (НВЛ) в культуре нейтрофилов, полученной при лечении аневризмальных костных кист при использовании в качестве стимулятора гемостатического раствора «Гемоблок» (Пуль-Сар, Истра, Российская Федерация). Всего в исследование

вошло 128 детей с аневризмальными костными кистами (АКК) в возрасте от 6 до 15 лет. Из них 63 ребенка были оперированы радикально с проведением внутриочаговой резекции и последующей аллопластики, которые составили группу клинического сравнения. В основную клиническую группу вошло 65 детей: оперированные по методике малоинвазивного оперативного вмешательства (А) – 35 детей и оперированные с проведением пункции и введением гемостатического препарата (В) – 30. У всех детей в основной клинической группе оценивали выраженность образования НВЛ *ex vivo* в культуре нейтрофилов, выделенных из крови, полученной при пункции кисты, и из периферической венозной крови.

Нейтрофилы, выделенные из кист, обладали статистически значимо высокой способностью к формированию НВЛ в сравнении с нейтрофилами из периферической венозной крови в ответ на стимуляцию гемостатическим препаратом «Гемоблок». Нейтрофилы у этих пациентов формировали в основном нитевидные НВЛ.

Таким образом, моделированное формирование НВЛ играет ведущую роль в обеспечении межклеточного взаимодействия и пролиферации клеток, в том числе фибробластов, приводя к закрытию полости аневризмальной костной кисты в детском возрасте.

Ключевые слова: аневризмальная костная киста, нетоз, нейтрофильные внеклеточные ловушки, гемостатик, дети

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ABC – aneurysmal bone cyst
CRL – Central Research Laboratory
EOC – electron-optical converter

NETs – neutrophil extracellular traps
PVB – peripheral venous blood

An aneurysmal bone cyst (ABC) is a destructive local benign lesion of the bone tissue represented by multiple cystic cavities and/or a blood-filled cavity predominantly located in the metaphysis [1]. The lesion was first described by H. L. Jaffe and L. Lichtenstein in 1942 based on clinical, X-ray, and histological investigations. There are several theories for ABC development as a destructive process due to vascular defects [2]. As a result of hemodynamic disorders and impaired outflow of interstitial fluid in the metaphyseal zone increase in intraosseous pressure is registered, leading to a fluid-filled cavity formation [3]. There is also a theory that the aneurysm is a result of trauma in anamnesis [4].

The clinical picture depends on the site of the bone cyst, the size of the lesion, and the type and degree of bone structure destruction [5–7]. While the process progresses, it is the local «swelling» of the bone, persistent pain, dysfunction of the affected limb, the development of contractures in the allied joints, impaired support function, such as limping and changes of the limb shape at the site of the lesion [8]. In X-ray, ABCs are usually located centrally or eccentrically concerning the bone axis [9].

Three stages of the disease are distinguished with X-ray: active (the osteolysis phase, lasting about one year and accompanied by increasing the size of the lesion and thinning of the cortical plates), passive (the delimitation phase, lasting up to 6–8 months when the cyst lost its activity decreasing in its size due to the compaction of the peripheral part of the bone) and the regenerative phase (come up in 2 years from the disease onset).

The new function of neutrophil leukocytes, the development of neutrophil extracellular traps (NETs), has been relatively recently described. The process is called

NETosis. It is accompanied by the release of extracellular DNA associated with histones and the content of leukocyte granules (enzymes and antibacterial proteins) [10]. NETs leading physiological role is capturing and destroying infectious agents [11]. However, the recent studies have demonstrated the role of NETosis in other physiological and general pathological processes, such as thrombosis [12] and wound healing [13]. Undoubtedly, NETosis can play a specific role in ABC evolution, but, unfortunately, we have found no such publications.

The purpose of this study is to evaluate *ex vivo* excessive generation of NET in neutrophil culture isolated from blood obtained while puncturing during the healing process of the cystic cavity in comparison with the excessive formation of neutrophil extracellular traps by neutrophils of peripheral venous blood using «Haemoblock», a hemostatic agent, as a stimulator in ABCs treatment.

Material and Methods. A retrospective analysis of medical records data and X-ray examinations of children treated in the Traumatology and Orthopedic Department at the Omsk Regional Clinical Children's Hospital from 2012 to 2023 was carried out. One hundred twenty-eight patients with ABC aged 6 to 15 years were included in the study. Sixty-three of the 128 patients, a group of clinical comparison, underwent intralesional resection followed by alloplasty. Sixty-five children were included in the main group with newer treatment approaches. Thirty-five patients of the 65 underwent minimally invasive surgery (subgroup A), and 30 children were treated using puncture and administration of a hemostatic agent (subgroup B).

The anatomic locations for the lesions were presented as follows: proximal humerus – 21 (16.4 %); proximal femur – 19 (14.8 %); ischium – 9 (7 %); proximal tibia –

17 (13.3 %); distal tibia – 18 (14.1 %); proximal fibula – 16 (12.5 %); distal fibula – 14 (10.9 %); calcaneus – 14 (10.9 %). Sixty-eight (53.1 %) of the 128 patients were male, and 60 (53.1 %) were female.

Diagnostic Kasirsky needle puncture using Triton IN ND 500/75 for invasive pressure monitoring (Ural Optical-Mechanical Plant, Ekaterinburg, the Russian Federation) to determine ABCs activity level was performed for all patients under anesthesia mask exposure with EOC control. It was registered that intraosseous pressure was 300–450 mm Aq at the initial stage (osteolysis) in all children. Much lower values of intraosseous pressure up to 250–300 mm Aq were recorded during the further development of the bone cyst and its transition to the second stage. Values 100–250 mm Aq were registered 3–4 months later in the recovery stage. Upon intraosseous pressure determination in ABC puncture treatment, the blood in test tubes was sent to the Central Research Laboratory (CRL) of the Omsk State Medical University to be investigated for NETosis and neutrophil traps.

The manipulation was completed by administering «Haemoblock» (Pul-Sar, Istra, the Russian Federation), a hemostatic agent, into the cavity in a volume equal to $\frac{1}{4}$ of the resulting volume of the cyst calculated in a routine X-ray examination in full size. Repeated punctures were performed three months later. When three or more stages of puncture treatment of the ABC were performed, and the cyst recovery was slow, intralesional resection of the affected site was performed, followed by filling the defect with an allograft.

If the ABC was inactive, the open intralesional resection of the cavity, followed by the replacement with bone straw and spongiouse bone chips, was performed. Since 2017, this surgery has been minimally invasive. A 6 mm incision is made in the cyst projection. A wide trocar with a 5 mm shortened «leg» is inserted, curettage of the cavity is carried out via the trocar using a Volkmann spoon, and the cavity is packed with crushed bone straw and spongiouse bone chips until the cyst cavity is filled.

Ex vivo excessive NETs generation was evaluated in neutrophils culture isolated from blood while cyst puncturing (ABC subgroup) and from peripheral venous blood (PVB subgroup) in all children of the main clinical subgroup B (n=30). Blood samples for ABC and PVB subgroups were taken simultaneously during the intervention. Neutrophils were isolated from heparinized blood using a Ficoll-verografin double-density gradient. When isolation was completed, the concentration of cells in Hank's solution was adjusted to 5000 cells per 1 μ l. Then, 1 part of Haemoblock was added to 10 parts of neutrophils, and the neutrophils were exposed for 30 minutes at 37 °C. Wet mount slides were prepared, and the results were visualized using fluorescence microscopy with an excitation filter with a wavelength range between 450–480 nm and an emission filter with a wavelength of 515 nm. In a sample, the ratio of the cells was calculated: of intact neutrophils, the bright green cells with an unstained nucleus; of activated neutrophils, the cells with the bright green surface structures and a stained red-orange nucleus; of early NETosis cells, the cells with bright green surface structures and an enlarged red-orange nucleus with a visualized release of a nuclear substance in at least one location; the cloud-like NETs, the unstructured homogeneous NETs located diffusely around a NETosis originated cell in the shape

of a «cloud», exceeding a cell size by more than two times; of filamentous NETs, the red-orange structured filamentous NETs, two times larger than the size of the cell.

Statistics data processing was carried out using the software Statistica 12.0 (StatSoft, USA). The data distribution in the groups was assessed using the Shapiro – Wilk test. The results are presented as a median and the interquartile range Me (Q1–Q3). The Mann – Whitney test was used to calculate the statistical significance of differences for independent samples. The Pearson χ^2 test was used to assess the qualitative indicators. A p-value<0.05 was considered statistically significant.

Results and Discussion. Neutrophils of the main clinical group (subgroup B) in the ABC subgroup formed the filamentous NETs statistically significantly more often than neutrophils of the PVB subgroup (p=0.0000; Mann – Whitney U-test). The median and interquartile range ratios of the filamentous NETs in ABC and PVB subgroups were 38.5 (28.9–41.1) and 7.7 (5.4–12.9) respectively (Fig. 1).

At the same time, neutrophils of both subgroups formed a tiny number of cloud-like NETs, a median, and the interquartile range were 0.8 (0.0–1.9) in the PVB subgroup and 1.2 (0.7–2.0) in ABC one, respectively. Neutrophils in the PVB subgroup in 10 cases out of 30 did not form the cloud-like NETs; and 7 cases out of 30 in the ABC subgroup. There were no statistically significant differences in the ratio of cloud-like NETs compared to PVB and ABC subgroups (p>0.05; Mann – Whitney U-test). In a neutrophil sample after «Haemoblock» exposure, the percentage of early NETosis cells was statistically significantly more often recorded in the ABC subgroup than in the PVB subgroup (p=0.0000; Mann – Whitney U-test). The median and interquartile range of the early NETosis cells proportion in the neutrophil sample in ABC and PVB subgroups after stimulation were 23.0 (20.8–25.0) and 16.6 (12.8–19.0) respectively (Fig. 2). Activated neutrophils in ABC subgroup were statistically significantly less than in PVB subgroup 13.9 (7.2–22.8) and 22.4 (12.0–29.2) respectively (p=0.0207; Mann – Whitney U-test). Enhanced ability of neutrophils to form an extracellular trap observed in the ABC subgroup under «Haemoblock» exposure on isolated neutrophils impacted the ratio of intact cells in the sample. In the ABC subgroup intact neutrophils were statistically significantly fewer compared to the PVB subgroup 25.7 (17.0–29.9) – 52.8 (47.7–59.3) respectively (p=0.0000; Mann – Whitney U-test) (Fig. 2).

Thus, neutrophils isolated from ABC blood had an increased ability to form extracellular traps compared to neutrophils from peripheral venous blood in response to «Haemoblock» exposure (Fig. 3).

Neutrophils from patients with ABC formed mainly filamentous NETs. Moreover, early NETosis cells were more frequently noted in a neutrophils sample of the ABC subgroup. The ability of neutrophils of the PVB subgroup to form extracellular traps was statistically significantly lower than in the ABC subgroup ($\chi^2=60.6$; df=4; p<0.0000).

As opposed to the processes with a systemic inflammatory response studied previously, for example, in the case of TB in children [14], peripheral blood neutrophils did not form extracellular traps spontaneously without exposure to an external stimulator. This reaction is predictable because ABC genesis is an aseptic, localized

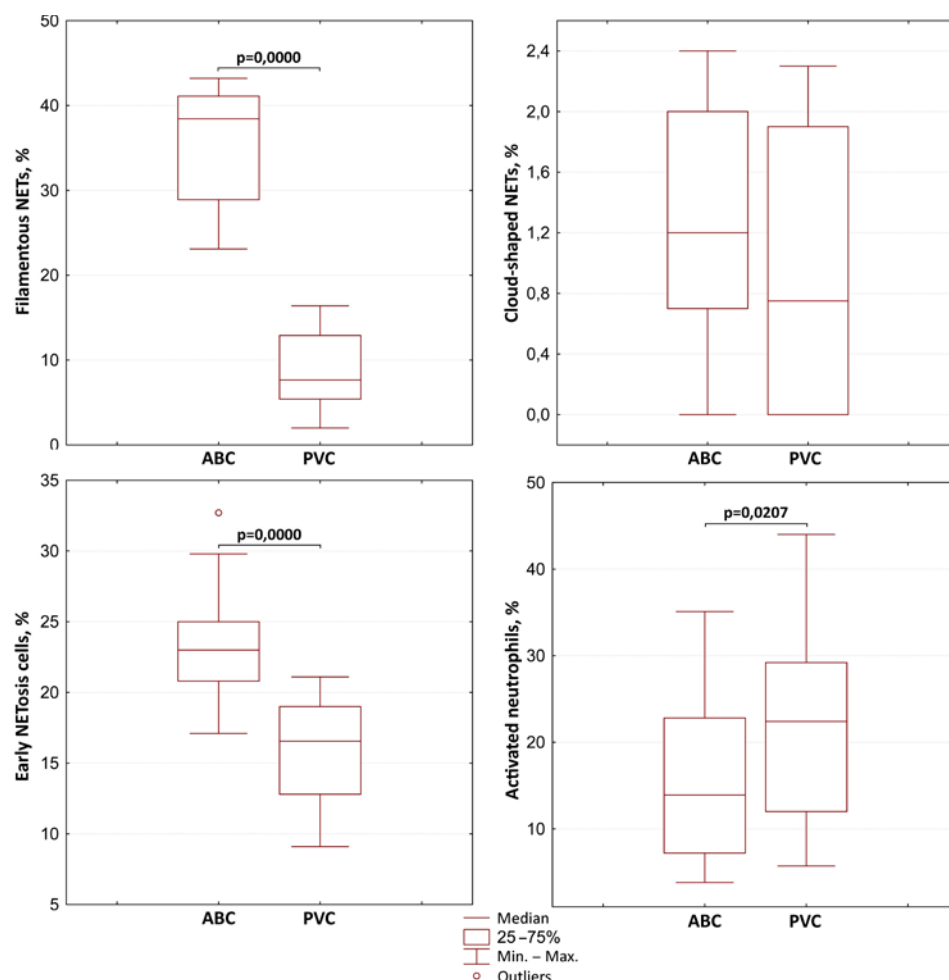


Fig. 1. Ratio of filamentous NETs, cloud-shaped NETs, early NETosis cells, and activated neutrophils in a sample of isolated neutrophils obtained from peripheral venous blood (PVB) and from the blood of the aneurysmal bone cyst (ABC) after stimulation with «Haemoblock», a hemostatic agent

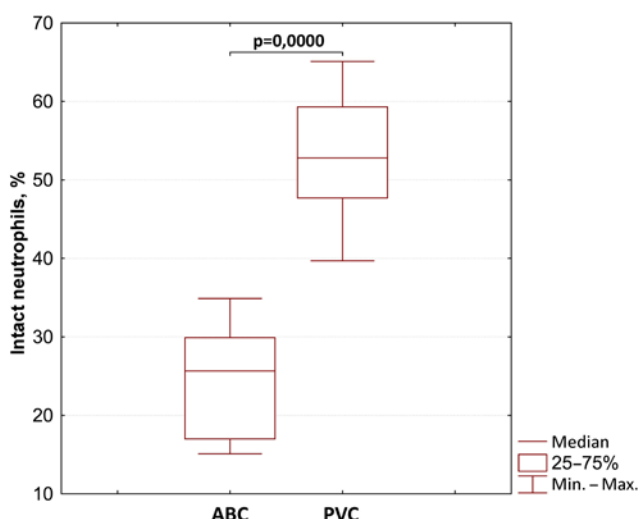


Fig. 2. Ratio of intact neutrophils in a sample of isolated neutrophils segregated from PVB and from blood of an ABC after «Haemoblock» stimulation

process. In the study above neutrophils were exposed to NETosis nonspecific antigen stimulator (Lactobacillus reutri, L. acidophilus, L. rhamnosus, and Bifidobacteri-

um longum), which caused a more significant number of NETs formation. However, in the present study, the neutrophil culture was incubated with «Haemoblock», a hemostatic agent, which contains an incomplete silver salt of polyacrylic acid containing silver nanoparticles. Its main mechanism of action is blood clotting with plasma proteins (mainly albumin) [15]. At the same time, the drug components' impact on immune cells is contrastively described. Polyacrylic acid inhibits interleukin-8 production but activates the production interleukin-10 by macrophages [16], which ultimately suppresses NETosis [17].

On the other hand, nanoparticles can act as activators for NETosis and apoptosis, and gold nanoparticles coated with polyacrylic acid cause a pro-inflammatory response [18]. The results indicate that only neutrophilic leukocytes isolated from the aneurysmal bone cyst generated NETs in response to the incubation with a hemostatic agent. This fact may be explained by the fact that neutrophils segregated from an ABC have

already had a pronetotic phenotype stipulated by their long-term presence in the lesion with abnormal hemocirculation, and, as a consequence, a different cytokine profile and the endothelium peculiarities. The impact of a hemostatic agent on this particular group of neutrophils leads to NETs formation. This is consistent with the evidence of J. A. Fraser et al., who demonstrated various effects of silver nanoparticles on different subpopulations of neutrophils [19]. Therefore, NETs appearance in the ABC cavity is considered an additional matrix for platelet adhesion [20]. In case of no infectious process, NETs can play a modulating role, providing intercellular interaction and cell proliferation, including fibroblasts, leading to ABC cavity closure as in wound healing [21]. In the meantime, in the presence of immunopathological processes and NETs impaired clearance carried out by macrophages, NETs themselves can act as a damaging agent, effecting by their serine proteases on the proteins of the intercellular matrix [22], leading to a longer or ineffective healing process of ABC. At the same time, in our study neutrophils generated only filamentous NETs and almost no cloud-like NETs, probably associated with the immunopathological process development [23].

Conclusion. Neutrophils isolated from ABC, having an increased ability to form NETs, can probably play

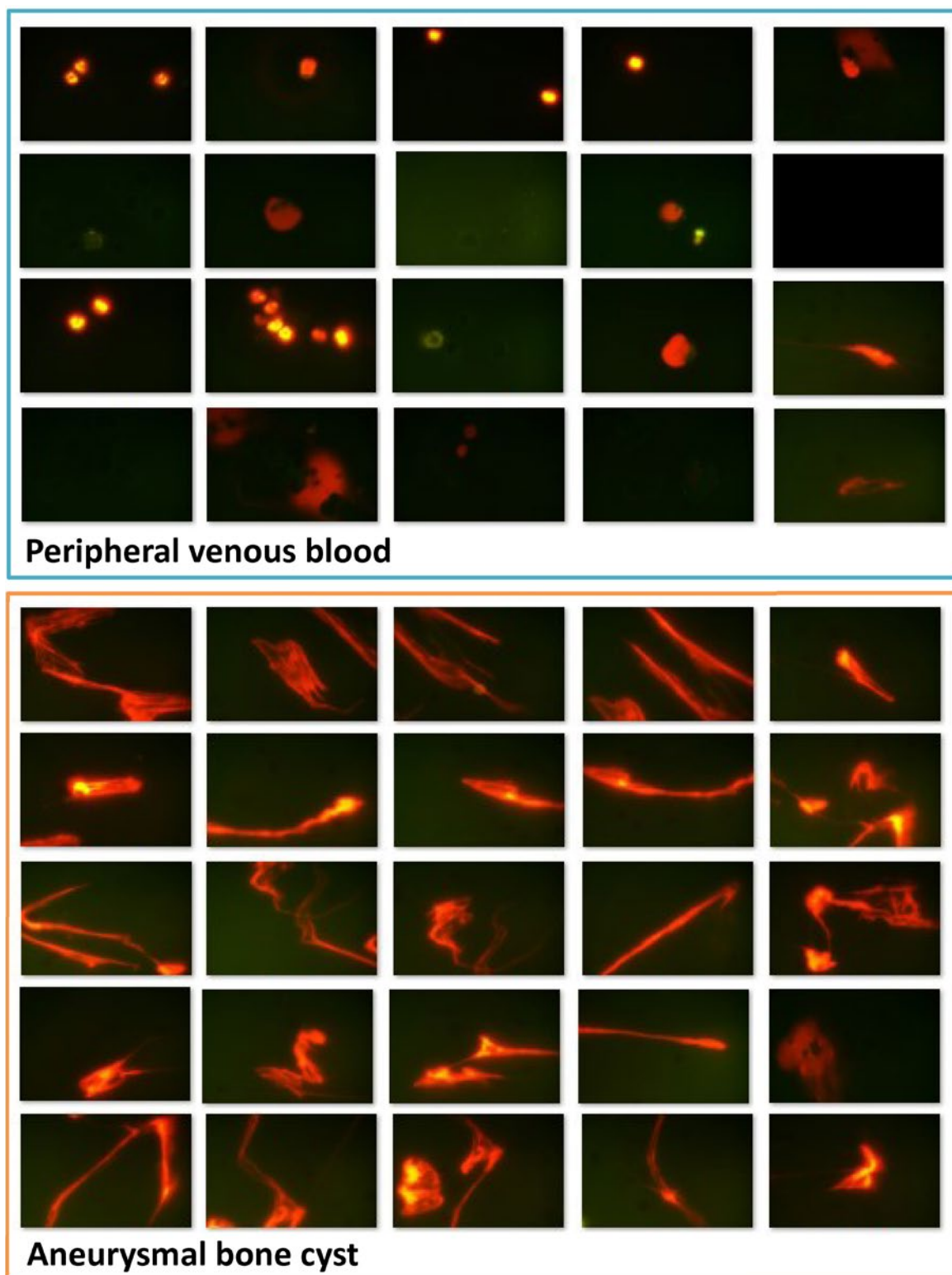


Fig. 3. Examples of visual fields of an isolated neutrophils sample segregated from peripheral venous blood and blood from an aneurysmal bone cyst after stimulation with «Haemoblock», a hemostatic agent. Luminescence microscopy, x1000

a modulating role, providing intercellular interaction and proliferation of cells, including fibroblasts, leading to the closure of the cyst cavity after «Haemoblock» exposure used in cyst treatment. While examining the

blood samples obtained from a cyst cavity and analyzing neutrophil traps, it has been detected that NETs formation is a positive dynamic process subsequently stipulated as a substrate for osteoblasts formation.

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References

1. Rogozhin D. V., Konovalov D. M., Bolshakov N. A., Talalaev A. G., Kozlov A. S. [et al.] Aneurysmal bone cyst in children and adolescents. *Pediatric Hematology/Oncology and Immunopathology*. 2017;16(2):33-39. <https://doi.org/10.24287/1726-1708-2017-16-2-33-39>
2. Mascard E., Gomez-Brouchet A., Lambot K. Bone cysts: unicameral and aneurysmal bone cyst. *Orthop. Traumatol. Surg. Res.* 2015;101(1 Suppl.):119-127. <https://doi.org/10.1016/j.otsr.2014.06.031>
3. Yashavnta K. C., Nalini K. B., Menon J., Patro D. K. Aneurysmal bone cyst of medial end of clavicle in a child, a rare case report. *Indian J. Surg. Oncol.* 2014;5(2):158-160. <https://doi.org/10.1007/s13193-014-0306-7>
4. Marie-Hardy L., El Sayed L., Alves A., Brunelle F., Ouchrif Y. [et al.] Percutaneous alcohol-based sclerotherapy in aneurysmal bone cyst in children and adolescents. *Orthop. Traumatol. Surg. Res.* 2020;106(7):1313-1318. <https://doi.org/10.1016/j.otsr.2019.12.024>
5. Erol B., Topkar M. O., Caliskan E., Erbolukbas R. Surgical treatment of active or aggressive aneurysmal bone cysts in children. *J. Pediatr. Orthop. B.* 2015;24(5):461-468. <https://doi.org/10.1097/BPB.0000000000000173>
6. Hauschild O., Lüdemann M., Engelhardt M., Baumhoer D., Baumann T. [et al.] Aneurysmal bone cyst (ABC): treatment options and proposal of a follow-up regime. *Acta Orthop. Belg.* 2016;82(3):474-483.
7. Subramanian S., Kemp A. K., Viswanathan V. K. Bone Cyst. 2022. In: StatPearls. Treasure Island (FL): StatPearls Publishing, 2024.
8. Muratori F., Mondanelli N., Rizzo A. R., Beltrami G., Giannotti S. [et al.] Aneurysmal Bone Cyst: A Review of Management. *Surg. Technol. Int.* 2019;35:325-335.
9. Hetaimish B. M., Alshaya O. S. Pediatric aneurysmal bone cyst in the ischial region. *Saudi Med. J.* 2016;37(7):799-803. <https://doi.org/10.15537/smj.2016.7.13945>
10. Tilley D. O., Abuabed U., Zimny Arndt U., Schmid M. [et al.] Histone H3 clipping is a novel signature of human neutrophil extracellular traps. *Elife*. 2022;11:e68283. <https://doi.org/10.7554/eLife.68283>
11. Schultz B. M., Acevedo O. A., Kalergis A. M., Bueno S. M. Role of Extracellular Trap Release During Bacterial and Viral Infection. *Front Microbiol.* 2022;13:798853. <https://doi.org/10.3389/fmicb.2022.798853>
12. Zhou Y., Xu Z., Liu Z. Impact of Neutrophil Extracellular Traps on Thrombosis Formation: New Findings and Future Perspective. *Front Cell Infect. Microbiol.* 2022;12:910-908. <https://doi.org/10.3389/fcimb.2022.910908>
13. Jiménez-Alcázar M., Kim N., Fuchs T. A. Circulating Extracellular DNA: Cause or Consequence of Thrombosis? *Semin. Thromb Hemost.* 2017;43(6):553-561. <https://doi.org/10.1055/s-0036-1597284>
14. Sabbatini M., Magnelli V., Renò F. NETosis in Wound Healing: When Enough Is Enough. *Cells*. 2021;10(3):494. <https://doi.org/10.3390/cells10030494>
15. Mordyk A. D., Zolotov A. N., Novikov D. G., Romanova M. A., Kirichenko N. A. [et al.] Netose-forming ability of neutrophils in children with latent tuberculosis infection with a positive test with recombinant tuberculosis allergen. *Questions of practical pediatrics*. 2023;18(5):7-12. <https://doi.org/10.20953/1817-7646-2023-5-7-12>
16. Hemostatic drug «Hemoblock». Available at: <http://gemosfera.ru/instrukciya-po-primeneniyu-gemoblok>. Accessed March 18, 2024.
17. Batool F., Özçelik H., Stutz C., Gegout P. Y., Benkirane-Jessel N. [et al.] Modulation of immune-inflammatory responses through surface modifications of biomaterials to promote bone healing and regeneration. *J. Tissue Eng.* 2021;12:20417314211041428. <https://doi.org/10.1177/20417314211041428>
18. Hahn S., Giaglis S., Chowdhury C. S., Hösli I., Hasler P. Modulation of neutrophil NETosis: interplay between infectious agents and underlying host physiology. *Semin. Immunopathol.* 2013;35(4):439-453. <https://doi.org/10.1007/s00281-013-0380-x>
19. Keshavan S., Calligari P., Stella L., Fusco L., Delogu L. G. [et al.] Nano-bio interactions: a neutrophil-centric view. *Cell. Death Dis.* 2019;10(8):569. <https://doi.org/10.1038/s41419-019-1806-8>
20. Fraser J. A., Kemp S., Young L., Ross M., Prach M. [et al.] Silver nanoparticles promote the emergence of heterogeneous human neutrophil sub-populations. *Sci. Rep.* 2018;8(1):75-86. <https://doi.org/10.1038/s41598-018-25854-2>
21. Zhou Y., Xu Z., Liu Z. Impact of Neutrophil Extracellular Traps on Thrombosis Formation: New Findings and Future Perspective. *Front Cell. Infect. Microbiol.* 2022;12:908-910. <https://doi.org/10.3389/fcimb.2022.910908>
22. Jiménez-Alcázar M., Kim N., Fuchs T. A. Circulating Extracellular DNA: Cause or Consequence of Thrombosis? *Semin. Thromb Hemost.* 2017;43(6):553-561. <https://doi.org/10.1055/s-0036-1597284>
23. Vorobjeva N. V., Chernyak B. V. NETosis: Molecular Mechanisms, Role in Physiology and Pathology. *Biochemistry (Mosc)*. 2020;85(10):11781190. <https://doi.org/10.1134/S0006297920100065>

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