Internal MedicineToday
Gonabad University of Medical Sciences
May 2023. Vol 29. Issue 3

Case Report

Platelet Satellitism Around Neutrophils in a Four-year-old Girl with Urinary Tract Infection: A Case Report

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Citation Zamani H, Ghorbani M, Taghdiri A, Moshari J. [Platelet satellitism around neutrophils in a four-year-old girl with urinary tract infection: A case report]. Internal Medicine Today. 2023; 29(3): 163-167

:https://doi.org/10.22034/imtj.2023.29.3.163

Received: 16 Mar 2022
Accepted: 20 Apr 2023
Available Online: 30 May 2023

Key words:
Platelet satellitism,
Platelet,
Pseudothrombocytopenia,
Urinary infection

ABSTRACT

Aims Platelet satellitism is a rare in vitro phenomenon that is considered one of the causes of pseudothrombocytopenia. This phenomenon is almost always observed in peripheral blood smears (PBS) prepared from blood samples containing EDTA anticoagulant and at ambient temperature, although it is not visible at lower temperatures and in blood samples treated with other anticoagulants. Failure to conduct a PBS may lead to misdiagnosis of thrombocytopenia. In this case, the platelet count of a 4-year-old child was checked in the laboratory for platelet satellitism.

Materials & Methods The patient's blood samples were collected separately with EDTA and sodium citrate anticoagulants, and the platelets were counted with a cell counter. At the same time as the platelet count was performed by the device, the PBSs were also analyzed. No bleeding symptoms were detected in the patient.

Findings The platelet count in the sample with EDTA anticoagulant was 85×109/L, and in the PBS prepared from this sample, the platelet satellitism was observed only around neutrophils. Nonetheless, there was no platelet satellitism in the sample prepared with sodium citrate anticoagulant, and the patient's platelet count increased to 242×109/L.

Conclusion Platelet satellitism is a rare phenomenon that can lead to laboratory error by inducing pseudothrombocytopenia. This condition should be considered in thrombocytopenia cases without clinical symptoms since it may exert adverse effects on the patient's care process by performing inappropriate therapeutic interventions.

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Introduction

Platelet satellitism is a rare phenomenon in the laboratory environment, which refers to the accumulation of platelets in the form of rosettes or multiple bundles around white blood cells (WBCs) [1, 2]. This platelet aggregation is mainly detected around neutrophils and sometimes also around other blood cells such as monocytes, lymphocytes, eosinophils, or basophils [3]. This phenomenon is almost always observed in peripheral blood smears prepared from blood samples containing EDTA anticoagulant and at room temperature, while it is not visible at lower temperatures and in blood samples prepared with other anticoagulants such as heparin or sodium citrate [4, 5].

To date, a precise and specific mechanism has not been described for platelet satellitism. Nevertheless, it is believed that immunological and non-immunological mechanisms play a role in the occurrence of this phenomenon [1,6]. Several theories and potential mechanisms have been proposed in the literature. One such hypothesis refers to an immunological mechanism stating that IgG autoantibodies in a patient's serum form an immune complex with hidden antigens on the platelet membrane glycoprotein IIb/IIIa complex. These antigens do not appear until the calcium ion is removed from the environment by EDTA anticoagulation and the membrane is spatially deformed. These immune complexes are absorbed by the surface of neutrophils or other leukocytes through binding to the Fcγ receptor and eventually lead to the accumulation of platelets in a rosette-like form around the leukocytes [1, 4, 5, 7]. On the other hand, the adhesion of platelets to neutrophils mediated by thrombospondin or other platelet alpha granule proteins, such as P-selectin, has been proposed as a non-immunological mechanism [1, 2].

Platelet satellitism is usually observed in healthy people; nonetheless, some cases have been reported in various pathological conditions, including infectious diseases. However, it has not yet been specifically linked to any particular drug or disease [5,8]. This phenomenon can lead to a false decrease in platelet counts by autoanalyzer, resulting in a misdiagnosis of thrombocytopenia. If this condition is not diagnosed correctly, unnecessary diagnostic and treatment measures may be taken and exert negative effects on the patient's care process [2]. In this case report, we describe platelet satellitism in a patient with a urinary tract infection, and with a review of the literature, we discuss possible mechanisms to better understand its nature.

Case Report

The patient is a 4-year-old girl with no specific clinical history who went to the doctor due to a high fever and urinary tract infection. Physical examinations revealed the absence of splenomegaly and lymphadenopathy. Moreover, the child did not have any clinical symptoms caused by thrombocytopenia, such as petechiae, purpura, easy bruising, epistaxis, and bleeding gums. Complete blood cell (CBC) counts in EDTA anticoagulation performed by hematology autoanalyzer demonstrated red blood cell (RBC) (4.47×1012/L), WBC (13.3×109/L), and platelet (Plt) (85×109/L) counts (Table1). Due to the observation of thrombocytopenia in CBC, peripheral blood smear (PBS) was prepared from a blood sample containing EDTA anticoagulant and Wright _ Giemsa staining was performed. This PBS examination illustrated that the platelet satellitism only around neutrophils, and platelet aggregation was not observed around other types of leukocytes (Figure 1).

Table 1. Laboratory values of hematological parameters of the patient's blood sample with EDTA anticoagulant

C.B.C	Result
WBC	13.3×10^9/L
RBC	4.47×10^{12}/L
Hemoglobin	11.8 g/dL
Hematocrit	35.2 %
MCV	78.7 fL
MCH	26.4 pg
MCHC	33.5 g/dL
Platelet	85×10^9/L
MPV	7.2 fL

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CBC: Complete blood count; WBC: white blood cells; RBC: red blood cells; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; MPV: mean platelet volume

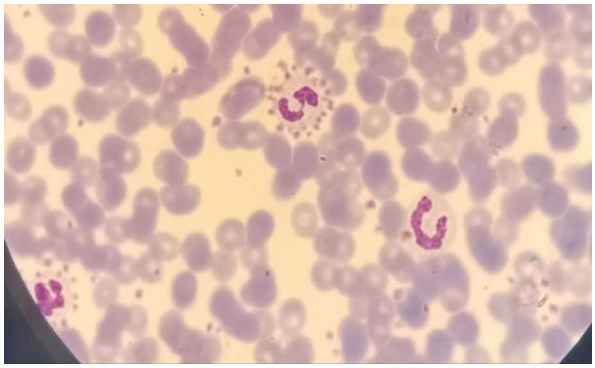

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Figure 1. Platelet satellitism around three neutrophils

Following that, another sample was obtained with sodium citrate anticoagulant, and in the PBS examination prepared from this blood sample, no

platelet accumulation was observed around the leukocytes. Furthermore, the patient's platelet count increased to 242×10^9/L after correction due to dilution in sodium citrate. It is worth noting that all analyses were performed by Mindray BC5800 - full automated cell counter. Finally, other primary CBC parameters were reported for the patient, along with a modified platelet count. After successful treatment of the infection and as the patient recovered, platelet satellitism was no longer observed in the smear prepared from a blood sample containing the anticoagulant EDTA.

Discussion

Platelet satellitism is a rare phenomenon in vitro, referring to the accumulation of platelets in the form of rosettes or multiple bundles around leukocytes [1, 2]. Although this phenomenon is often observed around neutrophils, it has also been seen around other blood cells, such as monocytes [4], lymphocytes [9], eosinophils [10], or basophils [11]. In addition, in some cases, the presence of platelet satellitism has been reported around several types of cells at the same time and even platelet phagocytosis [12]. This phenomenon is almost always observed at room temperature and in blood samples containing EDTA anticoagulant, while it is not seen at lower temperatures and in blood samples prepared with other anticoagulants, such as heparin or sodium citrate [4, 5].

The pathophysiology of the platelet satellitism has not yet been determined definitively and clearly. Nevertheless, it is believed that immunological and non-immunological mechanisms play a role in the occurrence of this phenomenon, and in this regard, several possible hypotheses and mechanisms are proposed [4, 6]. Numerous studies have pointed to hidden antigens (cryptantigens) on platelets. These hidden antigens are located on the glycoprotein IIb/IIIa complex of the platelet membrane. These antigens appear if calcium ions are removed from the environment by EDTA anticoagulation and the membrane changes in shape spatially, causing antibodies to access these antigens [5, 13]. Now, accordingly, one of the proposed hypotheses suggests an immunological mechanism that IgG autoantibodies present in the patient's serum form an immune complex with these antigens appearing on the glycoprotein IIb/IIIa complex of the platelet membrane. These immune complexes are connected to the surface of neutrophils or other leukocytes through binding to the Fcγ receptor and eventually lead to the accumulation of platelets in a rosette-like form around leukocytes, especially in the presence of EDTA. The reason for the presence of these types of autoantibodies has not yet been determined [1, 4, 7]. In addition, the adhesion of platelets to neutrophils via thrombospondin or other platelet alpha granule proteins, such as P-selectin, has been proposed as a non-immunological mechanism by Christopoulos and Mattock [14].

Platelet satellitism was first reported by Field and MacLeod in 1963, and since then, approximately 100 cases have been reported in different age groups. The satellite phenomenon of platelets is usually observed in healthy people; however, some cases have been reported in patients with vasculitis, lupus, urinary infections, asthma, chronic lymphocytic leukemia, hepatocellular carcinoma, and chronic alcoholism. Nevertheless, it is still not related to any specific drug or disease [1, 4, 6, 8]. Valentina Vidranski et al. reported platelet satellitism in a 73-year-old female patient who had a urinary tract infection. In the stated case, platelet satellitism continued even after the successful treatment of the disease. However, our case was a 4-year-old child whose platelet satellitism was no longer observed after the successful treatment of the disease and in subsequent tests [8].

Although hematology auto analyzers have made great advances and increased reproducibility and accuracy in platelet counts, they may still have difficulty diagnosing pseudothrombocytopenia. In many cases of platelet satellitism, platelet aggregates are mistakenly counted as WBCs by these auto analyzers, which can therefore lead to the report of Pseudothrombocytopenia by these devices. If this error is not correctly diagnosed and this low number of platelets is mistakenly reported, it can result in significant time and financial costs for both the patient and medical team due to needless additional testing. Furthermore, it can lead to inappropriate decisions and therapeutic interventions, such as aspiration, bone marrow, blood transfusion, surgery, and even splenectomy, in which case it may cause serious problems and complications for the patient [8, 12]. Therefore, according to this article, hematologists and laboratory staff should be aware of this phenomenon as one of the causes of pseudothrombocytopenia. Moreover, platelet satellitism underscores the importance of PBS investigation in platelet count reporting to avoid misdiagnosis of thrombocytopenia [1].

The platelet satellitism can also lead to errors in the differential counting of WBC differential (Diff) by cell counter devices. Therefore, in cases where we encounter thrombocytopenia and the overall WBC count is performed by the autoanalyzer without presenting WBC Diff, we must first suspect the satellite phenomenon of platelets. To correct pseudothrombocytopenia due to the platelet satellitism,

resampling in tubes containing sodium citrate anticoagulant is recommended. The sample obtained should not exhibit platelet aggregation, and the device count should also show more platelets. In this case, for the final report, the platelet count obtained with sodium citrate anticoagulant should be multiplied by 1.11 due to dilution in citrate [8]. Another suggested solution to determine the correct count of platelets in these cases is to take a sample from the patient next to the cell counter, in which case, immediately after taking a sample from the patient, the blood sample should be immediately transferred to the CBC tube with EDTA anticoagulant and be analyzed by an electronic counter [15]. In addition, for the correct count of platelets in these cases, 20 mg/mL of kanamycin can be used, which is added to the blood collected with EDTA anticoagulant, and an automatic platelet count is then performed [6].

Conclusion

If thrombocytopenia is observed in a patient's CBC, this thrombocytopenia should be confirmed or rejected by examining PBS since in case of incorrect diagnosis of thrombocytopenia, unnecessary diagnostic measures and therapeutic interventions may be performed and have negative effects on the patient's care process. If platelet aggregation is observed during PBS examination, the diagnosis of pseudothrombocytopenia should be considered. The platelet satellitism is a rare yet significant phenomenon in the laboratory environment since, after that, low and unusual platelet counts are obtained by electronic counters and it is considered one of the causes of pseudothrombocytopenia. In the event of encountering this phenomenon, resampling with another anticoagulant, such as sodium citrate or heparin should be performed to determine the patient's exact platelet count. Considering that in the present study, platelet satellitism was diagnosed by examining PBS, this research, like other similar studies, emphasizes the importance of examining PBS along with examining platelet counts and histograms of hematology auto analyzers. These investigations help to provide a detailed account of the patient's platelet count and prevent misdiagnosis of thrombocytopenia.

Ethical Considerations

Compliance with ethical guidelines

This case report has been approved by the Ethics Committee of Gonabad Medical Sciences University with the ethical code (IR.GMU.REC.1403.167). It should be noted that informed consent was obtained from the patient's parents for both participation and publication of the case details, and all personal information has been removed or anonymized to ensure the confidentiality and privacy of the patient.

Funding

This research has been funded by the Gonabad University of Medical Sciences

Authors' contributions

Dr. Jalil Moshari, as the attending physician, was responsible for the clinical examination, diagnosis, initial treatment, overall management, and follow-up of the patient. Hashem Zamani, the first author, collected the patient's clinical data and conducted the literature review, and together with Arian Taghdiri prepared the initial draft of the manuscript. Mohammad Ghorbani, as a PhD in hematology, performed the analysis of the laboratory findings and identified platelet satellitism as the underlying cause of the patient's thrombocytopenia. He also critically reviewed the preliminary draft and provided substantial revisions to enhance the scientific rigor and quality of the manuscript. All authors have read and approved the final version of the manuscript and affirm that they are accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part are appropriately investigated and resolved.

Conflicts of interest

The authors declare that they have no conflict of interest.

Acknowledgments

Thanks to the dear patient's family and Mr. Ebrahimi, Director of Medical and Paramedical Complex of Gonabad ACECR who helped study this case.

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