

CASE REPORT

Pseudothrombocytopenia: a Case of Maternal-Induced Neonatal Platelet Phagocytosis and Platelet Satellitism Phenomenon

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SUMMARY

Background: The phenomena of platelet phagocytosis and platelet satellitism (PS) are rare *in vitro* observations, with an estimated occurrence of 0.008%. These phenomena can be identified in blood smears utilizing ethylenediaminetetraacetic acid (EDTA) as an anticoagulant, manifesting as neutrophils engulfing platelets and platelets clustering around neutrophils to form satellite-like structures. These occurrences may result in pseudothrombocytopenia (PTCP), potentially complicating clinical diagnosis and treatment decisions.

Methods: This particular case study involved measuring whole blood samples from a pregnant woman and her neonate using EDTA-K₂ and sodium citrate anticoagulants. Blood smears were prepared and stained with Wright's stain to observe the morphology and count of platelets and leukocytes under oil immersion microscopy. Moreover, we investigate the potential pathophysiological mechanisms underlying these phenomena in both the mother and the infant.

Results: The platelet counts in EDTA-K₂ anticoagulated samples from both the mother and the neonate were significantly lower than those in sodium citrate anticoagulated samples. On EDTA-K₂ blood smears, neutrophils engulfing platelets and the platelet satellitism phenomenon were observed, with a high proportion of phagocytic cells, whereas the sodium citrate-treated whole blood samples showed no evidence of phagocytosis or platelet satellitism.

Conclusions: The manifestation of EDTA-dependent pseudothrombocytopenia (EDTA-PTCP) extends beyond aggregation and may include engulfment and adhesion. Sodium citrate anticoagulant can partly correct the low blood cell counts resulting from EDTA-PTCP. Furthermore, EDTA-PTCP can be maternally transmitted to neonates, causing neonatal pseudothrombocytopenia. To the best of our knowledge, this case constitutes an exceptionally rare occurrence of concurrent platelet phagocytosis and PS phenomena in both the mother and the infant. (Clin. Lab. 2026;72:xx-xx. DOI: 10.7754/Clin.Lab.2025.250755)

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KEYWORDS

neutrophil phagocytosis, platelet satellitism, ethylenediaminetetraacetic acid (EDTA), neonate, complete blood count

INTRODUCTION

EDTA is recommended by the International Committee for Standardization in Hematology as the anticoagulant of choice for complete blood counts due to its minimal impact on blood cell morphology and counts [1]. It is widely used in clinical testing [2]. However, in some patients, using EDTA-K₂ as an anticoagulant leads to in

vitro platelet aggregation, satellitism, and engulfment by neutrophils [3]. This can potentially cause blood analyzers to inaccurately identify platelets, resulting in counts lower than their actual value, known as ethylenediaminetetraacetic acid-dependent pseudothrombocytopenia (EDTA-PTCP) [4,5].

In pregnant women, the unique physiological state can induce a range of hematological changes, complicating the recognition and diagnosis of EDTA-PTCP. Moreover, maternal factors inducing neonatal phagocytosis and PS phenomena have been scarcely reported [6], it should always be excluded in newborns with isolated thrombocytopenia to avoid erroneous interpretation of platelet and leukocyte count, unnecessary laboratory investigation of false positive antiplatelet antibodies and needless platelet transfusions. This paper details a case of neonatal phagocytosis and PS induced by maternal factors, aiming to enhance clinical awareness and vigilance regarding these phenomena.

CASE PRESENTATION

The patient, a 31-year-old woman, at 28 weeks and 1 day into her first pregnancy, attended a routine prenatal examination on June 6, 2024, at our hospital to closely monitor the health of both the mother and the developing fetus. During this examination, various tests were conducted, and among them, the complete blood count results (Figure 1a) were largely normal, but the equipment flagged immature granulocytes and left shift. It was also found that the leukocyte scatterplot indicated an increased and significantly displaced neutrophil region. To investigate further, a smear microscopy examination was performed on the patient's whole blood sample. The smear microscopy examination revealed neutrophils engulfing platelets (Figure 1b), with a high proportion of phagocytizing cells along with the PS phenomenon (Figure 1c).

On August 29, as the expected due date approached, the pregnant woman returned to our hospital in anticipation of delivery. Given the abnormal findings of neutrophil phagocytosis and PS in the previous EDTA-K₂ anticoagulated whole blood test, the medical team decided to take a more comprehensive approach to blood analysis this time. Both EDTA-K₂ and sodium citrate [7] anticoagulated blood were collected for complete blood count analysis. The choice of using two different anticoagulants was based on the understanding that different anticoagulants can sometimes affect the appearance and behavior of blood cells differently. The results (Table 1) showed comparable leukocyte totals, neutrophil totals, neutrophil percentages, red blood cell counts, and hemoglobin concentration for both anticoagulant samples but revealed significantly lower platelet counts in EDTA-K₂ anticoagulated blood than in sodium citrate anticoagulated blood. Continuing the blood smear reviews in both anticoagulants revealed persistent neutrophil platelet phagocytosis and satellitism in the EDTA-

K₂ sample, but no such phenomena in the sodium citrate samples (Figure 2).

On August 30, a healthy baby girl was delivered vaginally. The neonate's complete blood count using EDTA-K₂ anticoagulated blood showed mild thrombocytopenia, but other results were normal (Table 1), and her leukocyte scatterplot resembled her mother's. Microscope examination confirmed neutrophils engulfing platelets and PS in the neonate's sample as well. A subsequent sample using sodium citrate anticoagulated blood corrected the thrombocytopenia, and no phagocytosis or satellitism was observed upon full smear review (Figure 2).

DISCUSSION

The phenomena of platelet phagocytosis and PS are rare in vitro observations. They are detectable in blood smears using EDTA as an anticoagulant. They manifest as neutrophils engulfing platelets and platelet clusters around neutrophils forming satellite-like structures. These phenomena were first reported in 1963 by Field and MacLeod, and to date about 100 cases have been reported [8]. Typically, the phenomena are described in relation to neutrophils, with rare reports involving eosinophils, basophils, monocytes, and lymphocytes. In agreement with previously published data, we found that platelet phagocytosis and PS occurred only around neutrophils and only in samples anticoagulated with EDTA.

This case report elaborates on the phenomena of neutrophil phagocytosis and PS discovered during pregnancy and traced into the neonatal period. Through the analysis of whole blood samples anticoagulated by both EDTA-K₂ and sodium citrate from the mother and her newborn, it was found that the use of EDTA-K₂ led to neutrophil phagocytosis of platelets and the appearance of PS, whereas the use of sodium citrate did not result in these abnormalities. This connection illustrates that EDTA-K₂ anticoagulant is a crucial factor leading to the phenomena and that sodium citrate can partially correct the low blood cell counts caused by EDTA-PTCP. This is of great significance in clinical laboratory tests, as incorrect results due to inappropriate anticoagulants can lead to misdiagnosis and improper treatment.

Currently, EDTA-PTCP is recognized as the most prevalent cause of PTCP, and it frequently presents as platelet aggregation. The conformational change of GP IIb/IIIa, a glycoprotein complex on the platelet membrane, plays a critical role in this process. EDTA-K₂ acts on the glycoproteins on the platelet membrane, altering their conformation. This change exposes cryptic antigenic epitopes that can interact with pre-existing EDTA-dependent platelet autoantibodies of the IgG class [9-11]. Once these autoantibodies bind to the exposed epitopes, they trigger a series of reactions that lead to platelet aggregation or the observed phagocytosis/satellite phenomena. The GP IIb/IIIa protein is high-

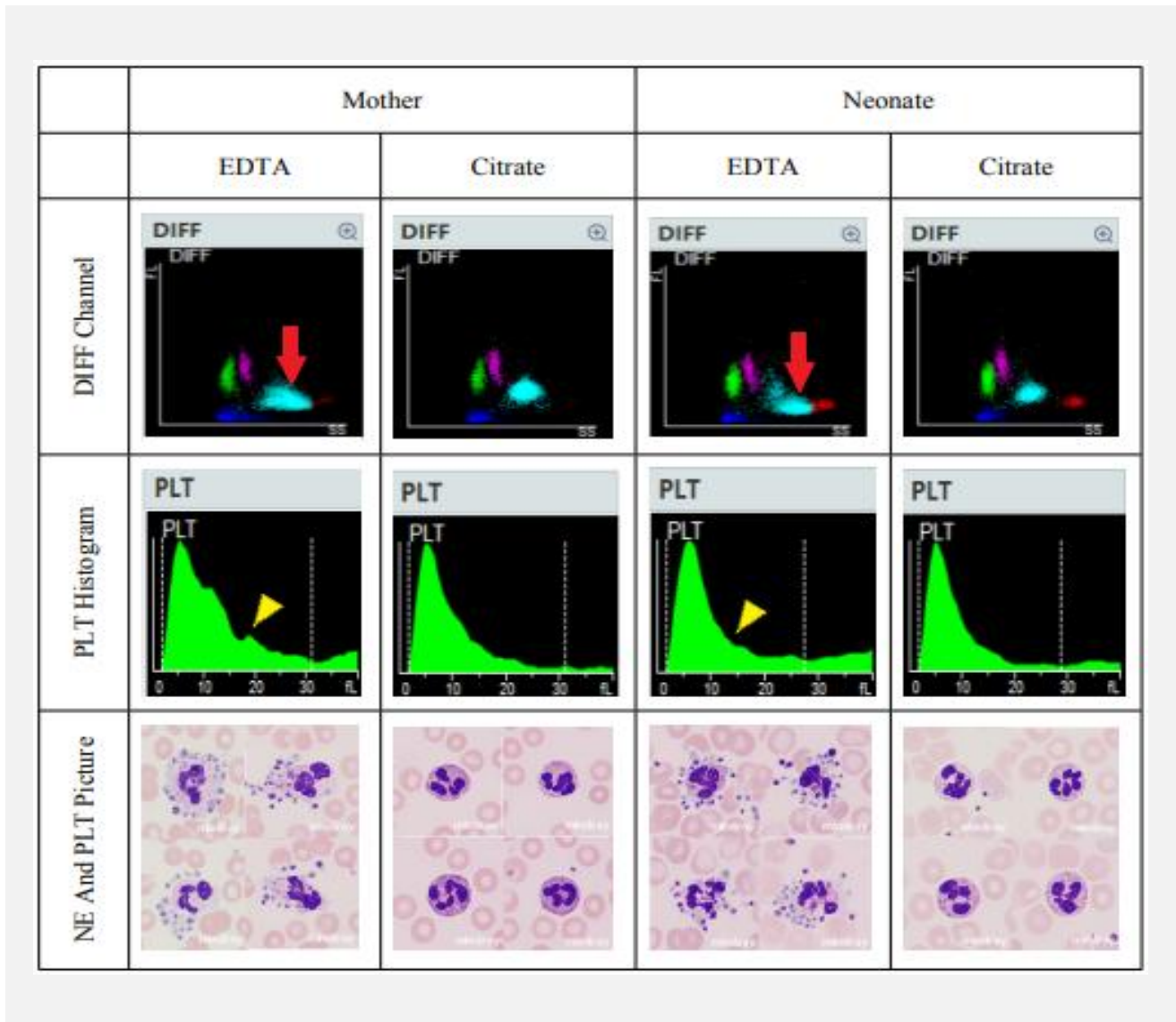


Figure 2. Comparison of instrument parameters and cellular images with two anticoagulants in the mother and neonate.

DIFF Channel (➡): A rightward shift in the neutrophil region on the DIFF scatter plot indicates abnormal cellular morphology.
PLT Histogram (▲): Left-sided elevation in the PLT histogram suggests platelet aggregation interference.

that pregnant women are more prone to developing EDTA-dependent platelet antibodies due to immune tolerance imbalance, which leads to increased autoantibody levels, complement system activation, and hormone-mediated immunomodulatory alterations. However, owing to technical constraints within the laboratory setting, maternal-neonatal platelet-specific antibody assays were not performed at this stage, thereby deferring their analysis for further investigation and validation. But other studies have documented that the maternal anti-platelet autoantibodies causing EDTA-PTCP are indeed typically of the IgG class, and importantly, IgG antibodies possess the ability to cross the placenta

[9,13,14]. When the newborn's blood is exposed to EDTA-K₂, these transferred antibodies bind to the platelet membrane glycoproteins. This binding triggers an immune response in the newborn that is similar to that in the mother, ultimately leading to neutrophil phagocytosis and PS. Another relevant study [6] on transient thrombocytopenia in newborns induced by maternal factors also explored this potential cause. The findings of that study are consistent with this current one, further validating the role of maternal antibody transfer in causing such phenomena in neonates under EDTA-K₂ anticoagulation. This knowledge is essential for accurate diagnosis and appropriate management of thrombocyto-

penia-related conditions in neonates.

CONCLUSION

In clinical practice, faced with abnormal alerts from routine blood tests and unusual blood cell morphology, the influence of EDTA-K₂ anticoagulant should be considered. In cases of suspected EDTA-PTCP, immediate preparation of peripheral blood smears for microscopic evaluation is imperative. Upon identification of morphological abnormalities (e.g., platelet aggregation, neutrophil phagocytosis or PS), subsequent testing should utilize sodium citrate-anticoagulated specimens (blue-top vacutainer) for hematological analysis, while EDTA-anticoagulated samples (purple-top vacutainer) must be excluded from repeat testing to preclude artifactual thrombocytopenia. Moreover, for hematological evaluations of pregnant women and newborns, more comprehensive strategies should be developed to secure maternal and neonatal health.

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Consent Declarations:

Patients enrolled in this study have provided their signed informed consent, explicitly consenting to the use of their data for the purposes of the research and being fully aware that their personal information will be handled with strict confidentiality.

Declaration of Interest:

The authors declare that they have no conflict of interest.

References:

- Lin J, Luo Y, Yao S, Yan M, Li J, Ouyang W, Kuang M. Discovery and Correction of Spurious Low Platelet Counts due to EDTA-Dependent Pseudothrombocytopenia. *J Clin Lab Anal* 2015 Sep;29(5):419-26. (PMID: 25425098)
- Dima F, Salvagno GL, Danese E, Veneri D, Lippi G. An unusual case of sodium citrate-dependent artifactual platelet count. *Interv Med Appl Sci* 2019 Oct 7;11(3):193-6. (PMID: 36343287)
- Lorubbio M, Ognibene A. Isolated case of platelet satellitism around white blood cells and phagocytosis by neutrophils and monocytes. *Pract Lab Med* 2022 Jan 14;29:e00264. (PMID: 35097180)
- Bao Y, Wang J, Wang A, Bian J, Jin Y. Correction of spurious low platelet counts by optical fluorescence platelet counting of BC-6800 hematology analyzer in EDTA-dependent pseudothrombocytopenia patients. *Transl Cancer Res* 2020 Jan;9(1):166-72. (PMID: 35117170)
- Sousa SM, Sousa TM, Silva CF, Mendes CC. Pseudothrombocytopenia: a case of platelet satellitism and phagocytosis by neutrophils. *Platelets* 2020 May 18;31(4):541-3. (PMID: 31516057)
- Tomicic M, Sotonica Piria T, Bingulac-Popovic J, Babic I, Stimac R, Vuk T. Transient pseudothrombocytopenia (PTCP) in the neonate due to the mother. *Transfus Clin Biol* 2022 Aug; 29(3):257-60. (PMID: 35718061)
- Vidranski V, Laskaj R, Sikiric D, Skerk V. Platelet satellitism in infectious disease? *Biochem Med (Zagreb)* 2015 Jun 5;25(2):285-94. (PMID: 26110042)
- Bizzaro N. Platelet satellitosis to polymorphonuclears: cytochemical, immunological, and ultrastructural characterization of eight cases. *Am J Hematol* 1991 Apr;36(4):235-42. (PMID: 1901444)
- Chiurazzi F, Villa MR, Rotoli B. Transplacental transmission of EDTA-dependent pseudothrombocytopenia. *Haematologica*. 1999 Jul;84(7):664. (PMID: 10406916)
- Koju S, Vaidhya N, Twitwi R, Shankhadev R, Pote N. Platelet Satellitism in a Patient with Bronchial Asthma. *Kathmandu Univ Med J (KUMJ)* 2022 Apr-Jun;20(78):240-2. (PMID: 37017174)
- Ghariani I, Braham N, Hamzaoui S, Bekir L. Platelet satellitism in autoimmune hemolytic anemia. *Curr Res Transl Med* 2017 Apr-Jun;65(2):61-4. (PMID: 28619392)
- Berkman N, Michaeli Y, Or R, Eldor A. EDTA-dependent pseudothrombocytopenia: a clinical study of 18 patients and a review of the literature. *Am J Hematol* 1991 Mar;36(3):195-201. (PMID: 1899964)
- Kortnerink JJ, Boersma B, Schoorl M, Porcelijn L, Bartels PC. Pseudothrombocytopenia in a neonate due to mother? *Eur J Pediatr* 2013 Jul;172(7):987-9. (PMID: 23229187)
- Ohno N, Kobayashi M, Hayakawa S, Utsunomiya A, Karakawa S. Transient pseudothrombocytopenia in a neonate: transmission of a maternal EDTA-dependent anticoagulant. *Platelets* 2012;23(5):399-400. (PMID: 21988316)