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ФЕНОМЕН ЛОЖНОЙ ТРОМБОЦИТОПЕНИИ. АЛГОРИТМ РЕШЕНИЯ ДИАГНОСТИЧЕСКОЙ ПРОБЛЕМЫ И ОПИСАНИЕ КЛИНИЧЕСКОГО СЛУЧАЯ

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False Thrombocytopenia Phenomenon. Algorithm for Diagnostic Problem Solution and Description of Clinical Case

Резюме

Лабораторные методы исследования активно применяются клиницистами для уточнения и установления диагноза, но часто возникают случаи, которые сбивают с толку практикующих врачей и заставляют проводить широкий дифференциально диагностический поиск. Выявление тромбоцитопении в общем анализе крови требует тщательного обследования пациента, соотношения результатов анализа с клинико-анамнестическими данными и критического отношения к лабораторным показателям. Одним из ложных диагностических феноменов, затрудняющих правильную интерпретацию снижения числа тромбоцитов, является псевдотромбоцитопения, ассоциированная с применением консерванта этилендиаминтетрауксусной кислоты. В данной статье представлен клинический случай пациентки с ЭДТА-ассоциированной псевдотромбоцитопенией, до выявления которой были проведены полный сбор жалоб и анамнеза, физикальный осмотр, дополнительные методы обследования, изучен обширный дифференциально-диагностический ряд.

Ключевые слова: *этилендиаминтетрауксусная кислота, ЭДТА, тромбоцитопения, псевдотромбоцитопения, ложная тромбоцитопения, лабораторный феномен, дифференциальная диагностика*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

Medical practitioners often face the problem of false diagnostic phenomena. Laboratory research methods are actively used by clinicians to clarify and establish a diagnosis. But there often occur some cases that are confusing and force to carry out a wide differential diagnostic search. The detection of thrombocytopenia in the complete blood count requires careful examination of the patient, the ratio of the analysis results with clinical and anamnestic data and a critical relation to laboratory indicators. One such phenomenon is pseudotrombocytopenia associated with using of the preservative ethylenediaminetetraacetic acid in a complete blood count. This article presents a clinical case of patient with EDTA-associated pseudotrombocytopenia, before the detection of which a complete collecting of complaints and history, physical examination, additional survey methods were carried out, an extensive differential diagnostic series was studied.

Key words: *ethylenediaminetetraacetic acid, EDTA, pseudotrombocytopenia, false thrombocytopenia, laboratory phenomenon, differential diagnosis*

Conflict of interests

The authors declare no conflict of interests

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EDTA — ethylene diamine tetraacetic acid, PTP — pseudothrombocytopenia, CVD — cardiovascular diseases, NAFLD — non-alcoholic fatty liver disease

Relevance

EDTA-dependent or EDTA-associated pseudothrombocytopenia is a laboratory phenomenon which causes diagnostic errors mostly related to the detection of significant thrombocytopenia. The term "EDTA-induced pseudothrombocytopenia" is more commonly used in foreign scientific literature.

M.J. Mant (1975) and R. Manthorpe (1981) were the first to describe EDTA-associated pseudothrombocytopenia in their studies. At that time this event had the prevalence of approximately 1.2 % in the population; however, as new clinical cases emerged, the importance of this issue has increased. It has been demonstrated that EDTA-dependent PTP is more common among inpatients then outpatients [2]. In 1991, N. Berkman et al. have published the study of 18 inpatients with EDTA-associated pseudothrombocytopenia; they also analyzed 34 cases described in the literature at that time. Authors concluded that this phenomenon occurred in patients with autoimmune diseases, malignancies, liver pathology, and atherosclerosis [8]. Modern sources present different data about the EDTA-associated PTP. The study of K.A. Papayan et al. has demonstrated that this phenomenon is equally prevalent both in patients with chronic diseases and the healthy population. The condition prevalence is 1:1000, and it is not associated with hemorrhages and thromboses [1]. The data of A.S. Polyakov et al. demonstrate that the incidence of false EDTA-associated thrombocytopenia is 20 % among examined healthy persons and 50 % in patients with various pathologies [2], which confirms the high rate of PTP detection in the population. The widespread use of automatic hematological analyzers, where ethylene diamine tetraacetic acid is essential as a blood stabilizer, has led to the rare application of manual platelet count in the prepared blood smear and, consequently, to more frequent EDTA-PTP reporting [1].

The pathogenesis of EDTA-dependent PTP is poorly understood; however, specific antibodies exist that cause platelet aggregation in the EDTA blood tube. EDTA is a preservative widely used in laboratory diagnosis for venous blood stabilization. This substance can suppress platelet aggregation due to the formation of weakly dissociating complexes with calcium ions — this leads to the attenuation of calcium interaction with platelet membrane receptors and calcium shut-off from the blood coagulation process [1].

So, what is the role of EDTA in false thrombocytopenia? EDTA causes calcium ions to bind in the venous blood — this leads to the dissociation of two subunits of the glycoprotein IIb/IIIa receptor on the platelet membrane. Thus, the receptor conformation changes, and the previously closed epitope (area for specific antibody binding) is exposed. This leads to platelet activation and aggregation in the tube with EDTA [1]. Besides, such reactions have been described for other anticoagulant preservatives, e.g. heparin sodium, sodium citrate [5]. However, the studies of false thrombocytopenias available mostly concern the EDTA use. The mechanism of EDTA-dependent platelet aggregation may be presented as follows (Fig. 1).

Currently no unified clinical guidelines exist for the diagnosis of EDTA-dependent pseudothrombocytopenia. According to the literature data, specific criteria can be defined for the diagnosis of EDTA-dependent false thrombocytopenia (Table 1).

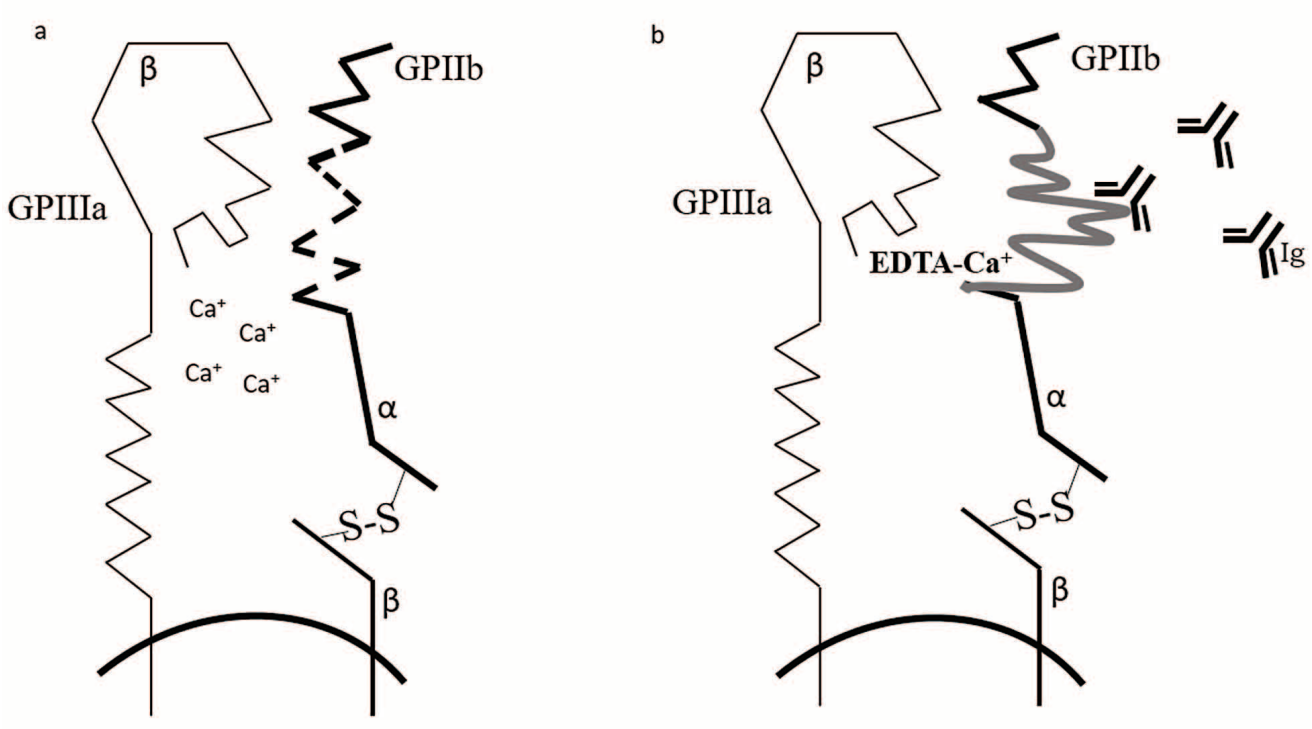

Figure 1. *The structure of the GP IIb/IIIa receptor on the platelet surface before reaction with EDTA (a) and the change in the conformation of the protein site by EDTA with the outcrop of a previously hidden epitope and specific antibodies bind with it (b). EDTA, ethylenediaminetetraacetic acid; Ca+, calcium ions*

Table 1. *Diagnostic criteria for EDTA-associated pseudotrombocytopenia. EDTA, ethylenediaminetetraacetic acid*

Diagnostic criteria for EDTA-associated pseudotrombocytopenia	
The number of platelets in the complete blood count	<100×10^9/L
In blood samples with using EDTA we find in repeated tests	Progressive platelet count reduction over time
When calculating the number of platelets in a blood smear according to Fonio	Normal platelet count
Manifestations of hemorrhagic syndrome	There are no any symptoms
Indicators of other formed blood elements, hematocrit level	In the normal range
The average volume of platelets	In the normal range

Our proper clinical observation is presented as a clinical case study.

Clinical case study

The female patient N., 62 years old, was invited by the general practitioner for standard laboratory and instrumental investigations (according to the Order of the Ministry of Health of the Russian Federation dated April 27, 2021 No. 404N, On approving the procedure for prophylactic medical examination and periodic screening examination of specific adult groups) to the polyclinics at place of residence. The complete venous blood count (February 1, 2023) demonstrated the platelet count of 41×10^9/L (reference range 180-400×10^9/L) with normal counts for other blood cells (red blood cells 4.2×10^{12}/L, white blood cells 8.4×10^9/L), as well as the normal hematocrit level — 44.0 %. The patient was

referred by the general practitioner to the hematologist. Before the hematologist counseling, the patient applied to the private laboratory individually for repeated blood collection: the venous blood count (February 3, 2023) demonstrated the platelet count of 17×10^9/L, with the laboratory comment of "confirmed by smear". Other blood cell counts and the hematocrit level were normal.

The patient asked for a second opinion in another hospital, where she was counseled by another general practitioner. The physical examination results were as follows: the general condition was satisfactory, without active complaints. The patient was overweight, but with normal constitution. Anthropometric data: height 164 cm, weight 75 kg, body mass index (BMI) 27.89 kg/m^2, waist circumference 86 cm. The skin color was physiological, and the skin was moderately humid. Visible mucous membranes were clear; no rash and signs of cutaneous hemorrhagic syndrome were detected. Cardiac borders were not enlarged. Pulmonary auscultation revealed vesicular breathing with no rales; the respiratory rate (RR) was 16/min. Cardiac auscultation revealed regular rhythm, clear cardiac tones, and no murmurs. Blood pressure (BP) was 125/80 mm Hg; the heart rate (HR) was 72/min; the pulse was symmetric, of satisfactory filling. The abdomen was soft and non-tender on palpation. The liver and spleen were not palpated; based on percussion results, no enlargement was noted. Bowel habits and urination were normal. Neurological examination revealed normal motor and sensory patterns. According to the patient, she did not have any epistaxis, gum bleeding or other evident hemorrhages. History: the patient underwent the surgery for the congenital heart disease — patent ductus arteriosus ligation via an open access at the age of 6. The patient had been suffering from essential hypertension since the age of 45; currently BP was controlled within the target values (130/80 mm Hg). The patient had been suffering from type 2 diabetes mellitus for 4 years; she took oral hypoglycemic therapy (metformin 1,500 mg). The patient was sick with the mild novel coronavirus infection twice (in November 2021 and September 2022). The family history was positive for cardiovascular diseases (CVD) (essential hypertension and two myocardial infarctions in a father; essential hypertension, acute cerebrovascular accidents, type 2 diabetes mellitus in a mother; early hypertension in a sister) and malignancies (high-grade gastric adenocarcinoma in a father). The patient was highly treatment-compliant, constantly taking hypotensive (enalapril, indapamide), oral hypoglycemic (metformin) and hypolipidemid (atorvastatin) drugs. The allergy history was negative. No new drugs or dose adjustments were introduced within a year; the latest vaccination was 6 months ago with a vector-based vaccine for the novel coronavirus (SARS-CoV-2) infection prophylaxis.

The venous blood was collected using a Vacutainer with the ethylene diamine tetraacetic acid (EDTA) preservative, and the capillary blood was collected from the finger with a dry glass capillary without preservatives in the laboratory of the second hospital. The capillary blood smears were prepared for Phonio platelet count. The venous blood was also collected for the D-dimer, coagulation panel, and biochemistry parameters. Urinalysis, fecal occult blood test, ultrasound of the abdominal cavity and kidneys were also monitored.

The following results were obtained (February 8, 2023): the platelet count in the venous blood collected with a Vacutainer with the EDTA preservative in the automatic analyzer was 11×10^9/L. A clear trend to successive platelet count decrease in the venous blood tests was observed (first test 41×10^9/L, second test 17×10^9/L, third test 11×10^9/L; the private laboratory confirmed the EDTA use as a preservative for the complete blood count), which is one of the criteria for EDTA-dependent pseudothrombocytopenia (Fig. 2).

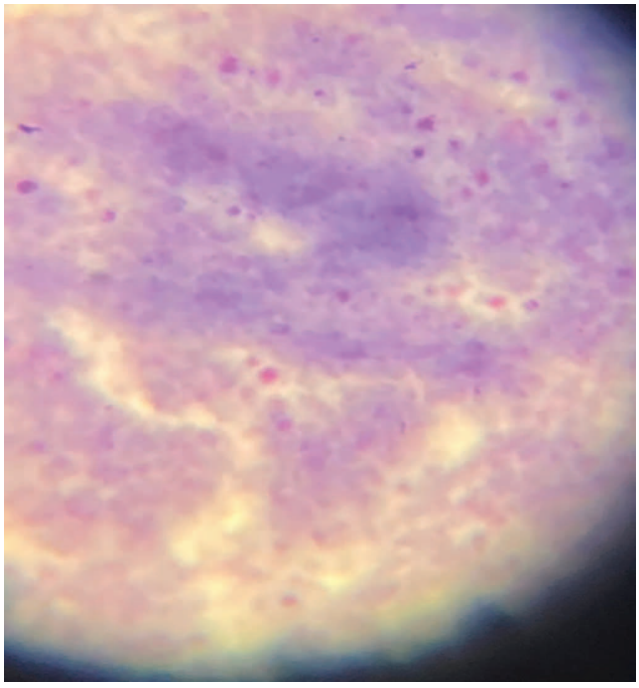

Figure 2. *Venous blood pattern in test tube (08.02.23) using EDTA of Patient N. Aggregated platelets reacted with preservative are visible as violet bands*

The platelet count in the capillary blood (Phonio method) was 372×10^9/L.

The coagulation panel parameters were normal: prothrombin time 9.9 seconds (9.0–14.0); prothrombin index 105.5 % (70.0–120.0); international normalized ratio (INR) 0.94 (0.80–1.20); activated partial thromboplastin time (APTT) 23.9 seconds (22.0–34.0); fibrinogen 3.9 g/L. The D-dimer level (February 8, 2023) was 74.4 ng/mL. The HbA1c level was 6.5 %. The serum creatinine level was 76 μmol/L; estimated glomerular filtration rate (GFR) based on the CKD-EPI equation (2021) was 72.4 mL/min/1.73 m^2. The urinalysis (February 8, 2023) was normal. The fecal occult blood test was negative.

Ultrasound of the abdominal cavity and kidneys (February 8, 2023) revealed fatty liver and diffuse parenchymal changes of the pancreas.

To confirm the diagnostic hypothesis, previous results of the patient tests were analyzed. In 2021, low platelet count was also detected in the complete blood count performed at the polyclinics at place of residence on November 15, 2021 (72×10^9/L), with a decreasing trend with the repeated count on December 3, 2021 (15×10^9/L). The private laboratory has detected the platelet count within the normal limits on December 14, 2021 (182×10^9/L). The preservative name used in the private laboratory at that time could not be established. After receiving the normal test result, the patient did not seek medical attention regarding this issue. All platelet count changes are presented using a time scale (Fig. 3).

Based on the data obtained, the following clinical diagnosis was established: Grade II essential hypertension. Controlled hypertension. Abdominal obesity. Complicated family history (CVD). Dyslipidemia. Left ventricular hypertrophy. Type 2 diabetes mellitus; target HbA1c level ≤7.0 %. Risk grade 3 (high). Target BP <130/<80 mm Hg. Non-alcoholic fatty liver disease (fibrosis stage to be defined). EDTA-associated pseudothrombocytopenia.

The diagnosis of EDTA-associated pseudothrombocytopenia was consequently confirmed by the hematologist.

The patient was recommended to monitor the complete blood count, with the platelet count to be determined using the Phonio method (without EDTA) 3 months later, and to test the coagulation panel / D-dimer 6 months later.

The patient gave written consent for data publication.

Discussion

The presented clinical case demonstrates the importance of detecting the EDTA-dependent pseudothrombocytopenia. The diagnostic search due to duplicate thrombocytopenia results with a decreasing trend coupled with the absence of hemorrhagic syndrome made us think about impaired platelet hemostasis with normal plasma factor levels, which could explain the absence of hemorrhages. The coagulation panel results were within

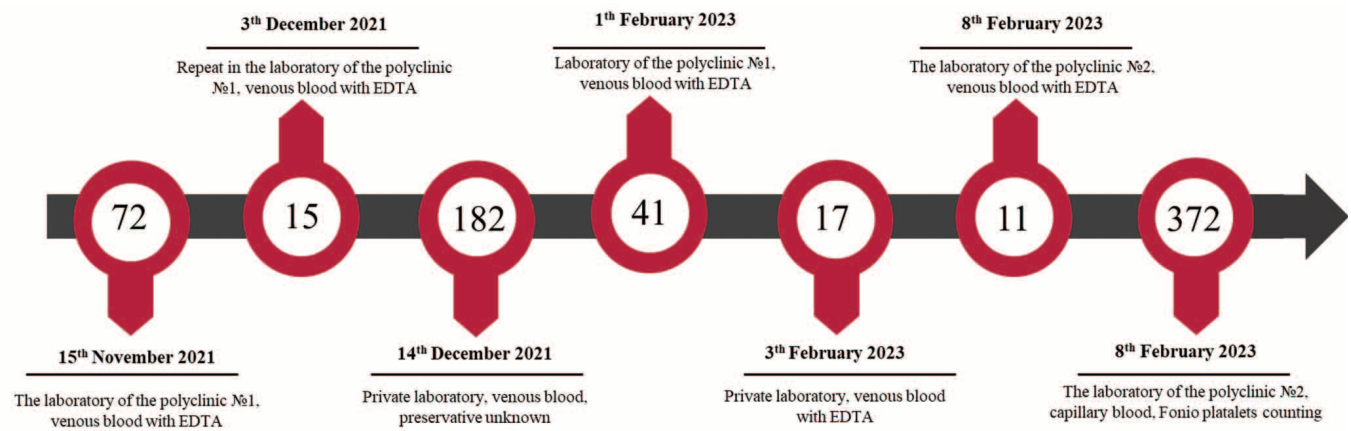

Figure 3. *The changes in the patient's blood platelet count over time, the number inside the circle corresponds to the number of platelets X $\times10^9$/L. EDTA, ethylenediaminetetraacetic acid; polyclinic № 1 — a medical institution at the place of residence; polyclinic № 2 — is a medical institution where patient N. went for a second opinion*

normal limits. The differential diagnosis was made with the following conditions: idiopathic thrombocytopenic purpura, drug- or vaccine-induced thrombocytopenia, severe liver pathology, malignancies [9]. The diagnostic search in thrombocytopenia is represented in the tabular form (Table 2).

However, the history, physical examination, laboratory and instrumental investigations did not confirm the hypothesis.

The examination of the comorbid patient (abdominal obesity, diabetes mellitus, essential hypertension) detected the signs of non-alcoholic fatty liver disease (NAFLD).

Table 2. *Differential diagnostics of various thrombocytopenia types*

The differential diagnostics of thrombocytopenia			
Group of disorders		**Disease/condition**	**Mechanism of development**
True pathology	Hereditary thrombocytopenia	Glantzman's thrombasthenia; the May-Hegglin anomaly; Wiskott-Aldrich syndrome; Bernard-Soulier syndrome; grey platelet syndrome; Fanconi anemia; congenital amegakaryocythemia	Mutations of platelet genes that change their morphology: micro- and macroformes (giant platelets), changes in platelet granules (gray cells due to decrease in a-granules), as well as leukocyte inclusions
	Acquired immune thrombocytopenia	Primary immune thrombocytopenia — idiopathic thrombocytopenic purpura (Verlhof's disease)	Production of autotrombocytic IgG antibodies against various complexes on the platelet surface, predominantly against glycoprotein IIb/IIIa. T-cell immune link imbalance
		Secondary immune — against the background of diseases: systemic lupus erythematosus, antiphospholipid syndrome, chronic viral hepatitis, HIV, rheumatoid arthritis, autoimmune thyroiditis, lymphoproliferative diseases, drug-induced TP, acute leukemia, myelodysplastic syndrome	Cross-pathogenetic reactions — heterogeneity of disorders in various immune units — immune dysregulation and autoaggression as a mechanism for the development of the underlying disease, followed by the formation of several clones of autoantibodies against platelets
	Acquired not immune thrombocytopenia	Consumption thrombocytopenia: DIC syndrome, thrombotic thrombocytopenic purpura (Moschkowitz's disease), hemolytic-uremic syndrome, thrombotic microangiopathies against the background of diseases with endothelial damage — heart defects, vascular atherosclerosis, diabetes mellitus	Intravascular thrombus formation, vascular occlusion, enhanced platelet destruction
		Platelet sequestration (Gaucher's disease, lymphomas, cirrhosis)	Increased platelet deposition in enlarged spleen with portal hypertension (splenomegaly)
		Hemodilution	In patients after massive blood loss and infusion therapy with platelet-free media
		Insufficient platelet production: aplastic anemia, acute and chronic myelo- and lymphoproliferative diseases, thrombocytopenia induced by chemo- and radiation therapy.	In aplastic anemia — due to fat infiltration in the bone marrow; in acute leukemia, chronic lympho- and myeloproliferative diseases, metastases to the bone marrow — due to suppression of the growth by the tumor substrate; in myelodysplastic syndrome — megakaryocytopoiesis disorder; in chemo- or radiation therapy, alcohol consumption — direct toxic effect on platelets
False pathology		EDTA-dependent pseudotrombocytopenia	Formation of platelet aggregates in a blood smear under the action of a preservative anticoagulant — EDTA

There are some data indicating the spontaneous or induced platelet aggregation in patients with NAFLD, concomitant hypertension and obesity, as well as in patients with isolated NAFLD. WIth that, patients demonstrate increased mean platelet volume with their decreased counts in the blood count due to aggregation [3]. One of the reasons for false platelet count decrease in such patients is the phenomenon of EDTA-associated or EDTA-dependent thrombocytopenia, which was confirmed in our patient. G. Trindade et al. (2021) described a clinical case of EDTA-induced pseudothrombocytopenia in a patient with hepatosplenic Mansoni schistosomiasis [7]. The accumulated clinical data presume the important role of hepatic and splenic diseases in the pathogenesis of false PTP phenomenon.

In our clinical case the patient had a history of two confirmed novel coronavirus infection episodes. The American Society for Clinical Pathology studies have demonstrated that novel coronavirus (COVID-19) infection plays a role in the development of both transient PTP (within 3 weeks in a patient with acute severe COVID-19 pneumonia) and 9-month PTP that persisted after recovery in a 60-year-old male patient. Anti-nucleocapsid and coronavirus spike protein antibodies persisted in the blood of the patient for the whole period (9 months), which allowed the investigators to propose the association of EDTA and IgG/IgM to SARS-CoV-2. EDTA-pseudothrombocytopenia is also possible as a result of seroconversion due to the large-scale vaccination [6].

Thus, the causes of EDTA-dependent PTP in our patient could be variable, including non-alcoholic fatty liver disease due to diabetes mellitus or a prior coronavirus infection.

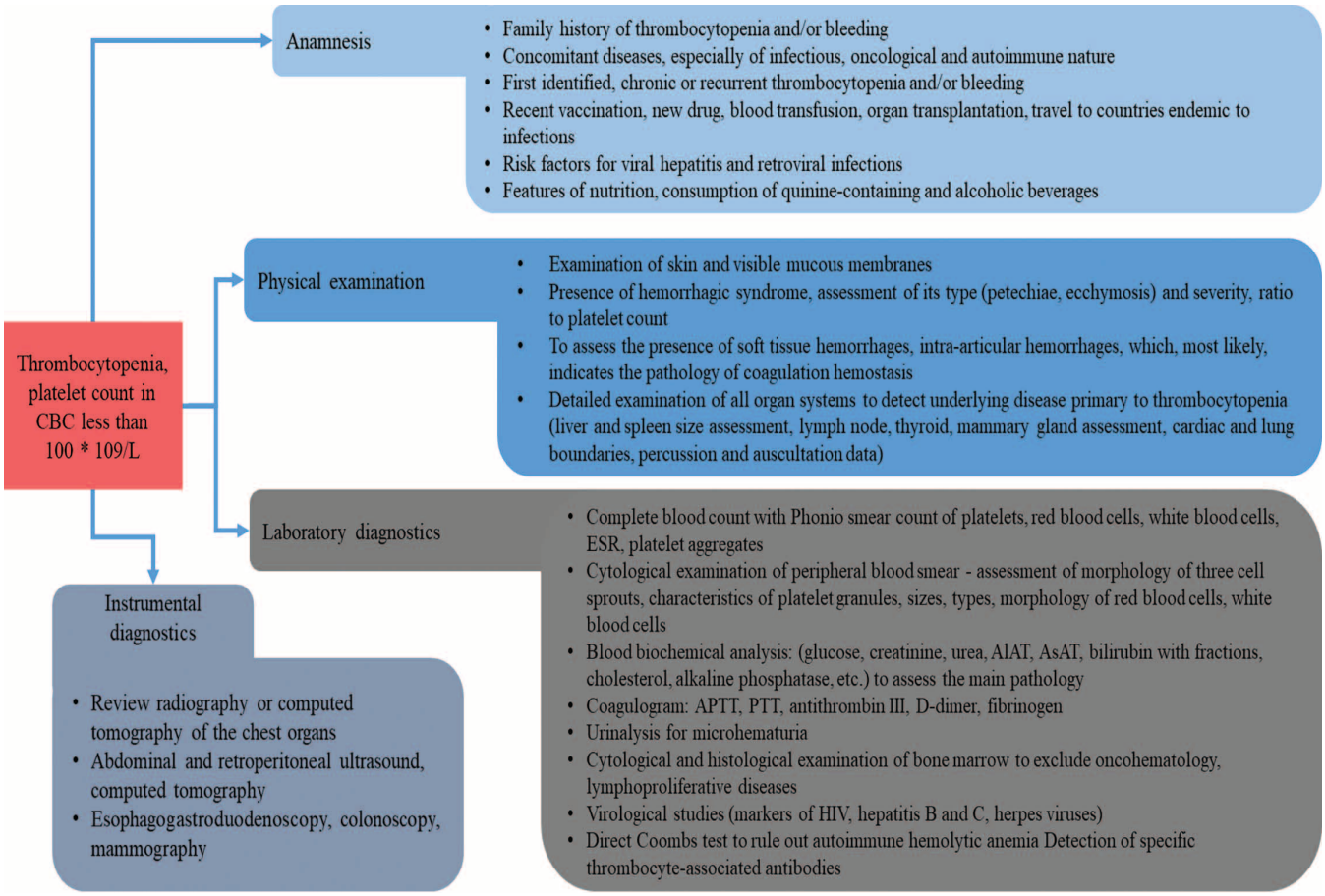

Figure 4. *Physician tactics when thrombocytopenia is detected in a complete blood count*

Note: CBC — complete blood count; ESR — erythrocyte sedimentation rate; AlAT — alanine aminotransferase; AsAT — asparagine aminotransferase; APTT — activated partial thromboplastin time; PTI — prothrombin index; HIV — human immunodeficiency virus

The study concerning the association of EDTA-associated thrombocytopenia and a genetic feature (fibrinogen platelet receptor gene polymorphism) has demonstrated the absence of statistically significant results regarding the value of this marker after the analysis of a limited patient group — further studies are required. Authors A.S. Polyakov and E.V. Goncharova have concluded that this laboratory phenomenon should not be considered a predictive factor for any diseases, though patients with pseudothrombocytopenia of this origin require periodic screening of blood parameters [2]. On the other hand, the author data confirm the high mortality level in patients with EDTA-PTP, as well as the fact that this phenomenon is an independent risk factor of malignancies [10].

M. Nagler et al. described an interesting observation that histograms of both platelets and white blood cells can change in patients with EDTA-dependent pseudothrombocytopenia. They demonstrated the activation of lymphocytic cells in response to EDTA-associated platelet aggregation in a clinical case of the patient with suspected acute leukemia. The automatic analyzer may count platelet aggregates as white blood cells, which leads to distorted complete blood count results. The authors ask for thorough evaluations of white blood cell and platelet histogram patterns, which can help to establish EDTA-dependent pseudothrombocytopenia and avoid treatment errors [11].

Currently it is impossible to establish the exact disease cause, though it is feasible to monitor the existing chronic diseases (essential hypertension, type 2 diabetes mellitus) with repeated blood tests.

Below is the physician tactics in cases of thrombocytopenia (Fig. 4).

Conclusion

The detection of thrombocytopenia in the complete blood count requires wide differential diagnosis. A large number of pathologies are accompanied by true thrombocytopenia. The treatment tactics should be initially determined with the correspondence of the laboratory data obtained to the clinical signs, which is the main difference of true pathology from the false phenomenon.

The presented clinical case demonstrates the importance of detecting laboratory phenomena in the outpatient setting.

It is necessary to inform attending physicians and laboratory personnel about the prevalence of false diagnostic phenomena and tactics upon their detection. The evaluation of the platelet count using hematological analyzers is a rather quick and cheap method, though it requires using an anticoagulant [12]. If the laboratory uses the EDTA anticoagulant preservative, it is feasible to inform the specialists about possible dependent thrombocytopenia and further tactics. After obtaining low platelet count in the automatic analyzer, one should count the platelets in the blood smear using the Phonio method, which is the reference and available method for the diagnosis of this condition.

The interdisciplinary interactions of clinical and laboratory physicians (or lab technicians, if the latter are missing), discussion of doubtful diagnostic cases, and mutual decisions are really important to confirm laboratory phenomena.

Besides, the correct diagnosis in the presented clinical case was determined by the correct interrogation, history collection, and physical examination of the patient, which helped to avoid tactical errors. Laboratory and instrumental diagnostic methods often yield artifacts which do not fit into the clinical pattern and history; they should always be critically evaluated by the attending physician. A serious hematological diagnosis was suspected in this patient, which could affect her quality of life, lead to increased anxiety and depression before the laboratory phenomenon verification.

Accounting for the modern availability of medical information and possibilities of self-examinations and interpretations of the data obtained by patients, the clinical physicians have to constantly enhance their knowledge not only about widespread pathologies, but also rare conditions, including laboratory phenomena.

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Список литературы / References:

1. Папаян К.А., Цветкова Т.Г., Андреева Э.Ф. и др. Значение своевременной диагностики ЭДТА-ассоциированной псевдотромбоцитопении в клинической практике. FORCIPE. 2018; 1(1): 4-8. doi:616-097:616.151.5:612.12:615.273.5:616.15-07:616.155.294.
   Papayan K.A., Tsvetkova T.G., Andreeva E.F. et al. Significance of timely diagnosis of EDTA-associated pseudotrombocytopenia in clinical practice. FORCIPE. 2018; 1(1): 4-8. doi: 616-097:616.151.5:612.12:615.273. 5:616.15-07:616.155.294 [in Russian].
2. Поляков А.С., Гончарова Е.В., Бологов С.Г. и др. Современное состояние проблемы ЭДТА-ассоциированной псевдотромбоцитопении, значение в патогенезе полиморфизма в гене тромбоцитарного рецептора к фибриногену. Сборник трудов к 90-летию стернальной пункции. Гены и клетки. 2016; 11(3): 123-128.
   Polyakov A.S., Goncharova E.V., Bologov S.G. et al. Current state of the problem of EDTA-associated pseudotrombocytopenia, meaning in pathogenesis of polymorphism in the fibrinogen platelet receptor gene. Collection of works on the 90th anniversary of sternal puncture. Genes and cells. 2016; 11(3): 123-128. [in Russian].
3. Баженова Н.М. Агрегационная способность тромбоцитов у пациентов с гипертонической болезнью в сочетании с неалкогольной жировой болезнью печени на фоне ожирения. Гастроэнтерология. 2018; 52(4): 216-221. doi:10.22141/2308-2097.52.4.2018.154141.
   Bazhenova N.M. Aggregation capacity of platelets in hypertensive patients in combination with non-alcoholic fatty liver disease against the background of obesity. Gastroenterologia. 2018; 52(4): 216-221. doi: 10.22141/2308-2097.52.4.2018.154141 [in Russian].
4. Shimasaki A., Kato T., Ozaki Y. Studies of platelet aggregation in six cases of EDTA-dependent pseudothrombocytopenia. The Japanese journal of clinical hematology.1994 Jun; 35(6): 529-34. PMID: 8078186.
5. Narasimha A., Kumar H., C. S. B. R. Prasad. Anticoagulant induced artefacts in peripheral blood smears. Indian journal of hematology and blood transfusion. 2008 Jun; 24(2): 43-8. doi: 10.1007/s12288-008-0027-6.
6. Bereczki D., Nagy B., Kerenyi A. et al. EDTA-Induced Pseudothrombocytopenia up to 9 Months after Initial COVID-19 Infection Associated with Persistent Anti-SARS-CoV-2 IgM/IgG Seropositivity. Laboratory medicine. American Society for Clinical Pathology. 2022 Mar 7; 53(2): 206-209. doi: 10.1093/labmed/lmab050.
7. Trindade G., Pereira T.A., Caporali J. et al. EDTA-dependent pseudothrombocytopenia in patients with hepatosplenic schistosomiasis mansoni: a clinical management alert. Transactions of the Royal Society of Tropical Medicine and Hygiene. 2021 Oct 1; 115(10): 1168-1173. doi: 10.1093/trstmh/trab034.
8. Berkman N., Michaeli Y., Or R. et al. EDTA-dependent pseudothrombocytopenia: a clinical study of 18 patients and a review of the literature. American journal of hematology. 1991 Mar; 36(3): 195-201. doi: 10.1002/ajh.2830360307.
9. Меликян А.Л., Пустовая Е.И., Егорова Е.К. и др. Дифференциальная диагностика тромбоцитопений. Онкогематология. 2017; 12(1):78-82. doi:10.17650/1818-8346-2017-12-1-78-87.
   Melikyan A.L., Pustovaya E.I., Egorova E.K. et al. Differential diagnosis of thrombocytopenia. Oncohematology. 2017; 12(1):78-82. doi: 10.17650/1818-8346-2017-12-1-78-87 [in Russian].
10. Ohashi-Fukuda N., Inokuchi R., Sato H. et al. Poorer prognosis with Ethylenediaminetetraacetic acid-dependent pseudothrombocytopenia: a single-center case-control study. Medicine. 2015; 94(15): e674. ISSN 0025-7974 DOI: 10.1097/MD.0000000000000674.

11. Nagler, M., Keller, P., Siegrist, D. et al. A case of EDTA-dependent pseudothrombocytopenia: simple recognition of an underdiagnosed and misleading phenomenon. BioMed Central Clinical Pathology. 2014; 14(19): doi: 10.1186/1472-6890-14-19.
12. Минникова А.И. Аналитические возможности гематологических анализаторов в оценке тромбоцитов (обзор литературы). Клиническая лабораторная диагностика. 2012; 3: 32-33. doi: 615.471.03:616.155.25-074.
Minnikova A.I. Analytical capabilities of hematological analyzers in platelet assessment (literature review). Clinical laboratory diagnostics. 2012; 3:32-33. doi: 615.471.03:616.155.25-074 [in Russian].