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Case Report

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The Importance of Pseudo Thrombocytopenia Due to Platelet Cold Agglutination before Surgery, What Should We Do? A Case Report

Mohammad Ghorbani[1,2], Amin Solouki[3], Farhang Soltani[4], Amir Moayedpour[5], Zahra Khoshnegah[6]

[1]Laboratory Hematology and Transfusion Medicine, Department of Medical Laboratory Sciences, Faculty of Allied Medicine, Gonabad University of Medical Sciences, Gonabad, Iran
[2]Laboratory Hematology and Transfusion Medicine, Department of Pathology, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran
[3]Department of Hematology and Blood Banking, School of Allied Medical Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Department of Internal Medicine, Gonabad University of Medical Sciences, Gonabad, Iran
[5]Islamic Azad University of Medical Sciences, Mashhad, Iran
[6]Department of Hematology and Blood Banking, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran

Corresponding Author: Zahra Khoshnegah, Department of Hematology and Blood Banking, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran
E-mail: Zkhoshnegah@gmail.com

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ABSTRACT

Platelet cold agglutination (PCA) is a rare in-vitro phenomenon caused by Immunoglobulin M (IgM) autoantibodies, which results in Ethylenediaminetetraacetic Acid (EDTA) independent pseudo thrombocytopenia (PTCP). Its diagnosis is made based on the peripheral blood smear (PBS) examination and pre-test warming blood sample.

Here, a case of PTCP secondary to PCA is presented. He was first admitted for pre-surgical tests but his platelet count was low. His blood was taken with EDTA and sodium citrate anticoagulant to rule pre-analytical error out. Then his sample warmed up and the test was run again with Mindray BC-6000 automated cell counter. Moreover, the rheumatologic tests were done for him.

His platelet count was 23×10^9/L at first, and PBS showed many platelet aggregates. The low platelet count was not correct with Sodium Citrate or re-sampling with EDTA so platelet satellitism and improper sampling were ruled out. By warming the sample up to 37◦C, the Platelet count rose to 216×10^9 / L. The rheumatologic tests were negative except for HLA-B27 which was positive.

Finally, he was diagnosed with PCA which is due to a cold antibody (clinically insignificant). This diagnosis is important for the prevention of recurrent tests, unnecessary platelet transfusion, and other problems. Here these conditions will be discussed.

Keywords: Platelet; Thrombocytopenia; Pseudo thrombocytopenia; Cold agglutination; Platelet cold agglutination

INTRODUCTION

Thrombocytopenia defined as a low platelet count less than 150×10^9 / L is classified into three groups: mild thrombocytopenia (100 to 150 × 10^9/L), moderate thrombocytopenia (50 to 99×10^9/L), and severe thrombocytopenia (less than 50×10^9/ L)[1]. Nevertheless, some patients may be diagnosed with spurious thrombocytopenia, also known as pseudo-thrombocytopenia (PTCP). The presence of PTCP has been reported in several diseases such as colorectal cancer and the emerging coronavirus disease 2019 (COVID-19) [2-5].

The difference between real thrombocytopenia and PTCP is crucial and challenging in daily practice. Otherwise, the misdiagnosis of thrombocytopenia inevitably results in over-treatment and further unnecessary assessments. PTCP may be secondary to various causes such as anticoagulation administration, cold antibodies, and human sampling error [6]. One of the causes of PTCP is platelet cold agglutinins (PCA) which results in a spurious decrease of the platelet counts[5].

PCA may happen with any of the anticoagulants such as EDTA, citrate, or heparin. Therefore, platelet clumping does not usually resolve with repeated sampling and replacement of anticoagulants [7]. In this regard, the examination of PBS in patients with thrombocytopenia reveals the platelet clumping condition[6]. Here a case of a 26-year-old male is presented as a candidate for orthopedic surgery diagnosed with PTCP secondary to PCA.

Case presentation

A 26-year-old man was admitted to the library for pre-surgical tests to undergo orthopedic surgery. He had no remarkable medical history. The complete blood count (CBC) in an EDTA tube showed Red Blood Cell (RBC): 5.71×10^{12}/L, White Blood Cell (WBC):6.7×10^{9}/L, and platelet count: 23×10^{9}/L, which his platelet count was low. For the low platelet evaluation, the PBS was examined, and many platelet aggregates were observed (Figure 1). At first, sampling was repeated with EDTA anticoagulant, to rule out pre-analytical errors and probably improper sampling. However, the results were the same in both CBC and PBS examination. Then, the anticoagulant was changed into citrate, and the results was not changed (Table 1). According to repeated results, the diagnosis of platelet satellitism was ruled out. Finally, to assess the cold platelet agglutination, the CBC tube was incubated at 37°C for 30 min, and immediately sample was analyzed by Mindray BC-6000 automated cell counter. As a result, the platelets rose to 216×10^{9} / L. The patient was referred to the rheumatologist, he ordered complementary laboratory tests such as rheumatoid factor, wright, 2-mercaptoethanol, thyroid stimulating hormone, the anti-double stranded DNA, antinuclear antibody, erythrocyte sedimentation rate, and C-reactive protein. The results were also normal. However, the human leukocyte antigen-B27 (HLA-B27) was positive.

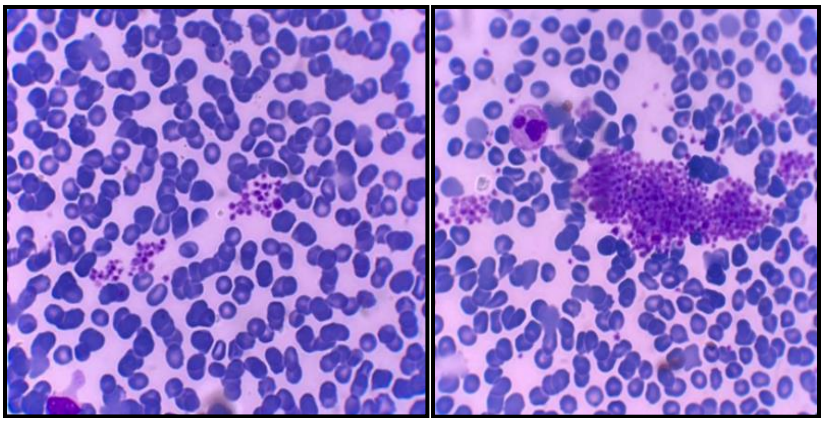

Figure1. Platelet aggregations in peripheral blood smear in two samples containing EDTA (left) & citrate (right) anticoagulants

Table 1.The results of CBC analysis in different samples of inpatient with pseudo thrombocytopenic. Sample 1: EDTA anticoagulation; Sample 2: repeated with EDTA anticoagulation; sample 3: With citrate sodium anticoagulation, sample 1,2,3 analyzed in the room temperature; sample 4: analyzed after placing the sample at 37 °C for 30 min

	Repeated Sampling				
	Sample 1	Sample 2	Sample 3	Sample 4	Reference Interval
RBC ($\times10^{12}$/L)	5.71	5.98	5.93	5.81	4.2-6.2
WBC($\times10^{12}$/L)	6.51	6.42	6.23	6.61	4-11
PLT ($\times10^{9}$/L)	***23***	***24***	***22***	***216***	***150-450***
Hb (g/dL)	17.6	17.5	17.4	17.8	11.5-18
HCT (%)	51.3	51.1	51.2	51.1	35-54
MCV (10^{-15} L)	88	87.4	87.5	87.9	77-96
MCH (10^{-12} g)	30.2	30.4	30.1	30.6	26-32
MCHC (g/dL)	34.8	34.7	34.4	34.8	30-36

Abbreviations: RBC – red blood cells; Hb – hemoglobin; HCT – hematocrit; MCV - mean corpuscular volume; MCH - mean corpuscular hemoglobin; MCHC - mean corpuscular hemoglobin concentration; PLT – platelets; WBC – white blood cells

DISCUSSION

PTCP may be associated with EDTA-dependent antibodies or EDTA-independent antibodies, and pre-analytical errors[8]. Statistically, PTCP accounts for 15.3% of all thrombocytopenia[9]. Therefore, the misdiagnosis of thrombocytopenia may lead to performing unnecessary procedures like splenectomy in Immune Thrombocytopenic Purpura (ITP) patients, and avoidable invasive diagnostic tests such as bone marrow biopsy and redundant platelet transfusions with its associated adverse effects [1, 6, 10, 11]. Among various causes of PTCP, PCA does not usually resolve with repeated sampling and anticoagulant replacement unlike other etiologies[6]. PCA-associated IgM autoantibodies do not affect platelet function and have no clinical significance due to they are unable to have a function and react at body temperature. However, when the blood sample with cold agglutinin remains at room temperature and tests are delayed, IgM type antibodies are activated [12-14]. This leads to platelet clumping and aggregation, and consequently PTCP. This phenomenon is temperature-dependent and relates neither to the sampling nor the type of anticoagulant. To obtain an accurate platelet count, the continuous high temperature (37°C) must be maintained from the time of sampling until analyzed in the laboratory and tests should be performed quickly without delay. In the presented patient, the pre-warming method was conducted by placing the CBC tube at 37°C for 30 min. Consequently, the PLT count was normal (216×10^{9}/L).

CONCLUSION

In patients with thrombocytopenia, the detected thrombocytopenia should be confirmed with the PBS examination. If the platelet aggregation was observed in the PBS, the PTCP should be considered as one of the differential diagnoses. To determine the accurate platelet count in PTCP patients, repeated sampling, anticoagulation replacement, and pre-warming method in case of PCA must be done.

Informed Consent

It should be noted that the informed consent was obtained from the patient for his data publication.

Conflict of Interest

None declared.

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