SHORT COMMUNICATION

Multicoagulant resistant pseudothrombocytopenia

Nausheen Waseem,[1] Bashir Hanif,[2] Jawaid Jabbar[3]

Abstract

Pseudo thrombocytopenia is the estimation of low platelet counts by a Haematology analyzer despite of shortage in platelets. EDTA-induced pseudo thrombocytopenia, commonly seen in clinical practice, occurs mainly due to the anti-platelet antibodies. Pseudo thrombocytopenia is seen in normal healthy individuals and other disorders like cardiovascular, liver, autoimmune diseases and malignancy. We are presenting a case of multi-coagulant resistant dependent thrombocytopenia. The purpose of this letter is to review approaches to pseudo thrombocytopenia. The case has coagulant resistant dependent thrombocytopenia in association with Anasarca and was a known case of cardiomyopathy with severely dilated left atrium, left ventricle and right atrium.

Keywords: Pseudo platelet aggregation, Multicoagulant resistant thrombocytopenia, Pseudo thrombocytopenia.

DOI: https://doi.org/10.47391/JPMA.03-390

Introduction

A 50-year-old male clinically presented to Tabba Heart Institute's cardiac emergency with tachypnoea and anasarca on 10th of Jan 2019. He had a history of dilated cardiomyopathy for the last two years. Complete blood count (CBC) revealed a platelet count of 51×10^3/mm^3, and the patient was referred to the step-down unit. A platelet count history of previous six months was normal. There was no abnormal finding in the physical examination other than generalized oedema, with normal biochemical tests showing the absence of any viral or bacterial infection. Complete blood count was performed; the patient had thrombocytopenia, but no findings were suggesting bleeding diathesis such as petechiae, purpura and ecchymosis on physical examination. Platelet count was detected initially as 36×10^3/mm^3 when CBC was re-evaluated by re-warming tubes containing EDTA, at 37 degree centigrade after taking samples in Na- citrate / lithium- heparin, and the patient had clustered platelets on the peripheral blood smear. At the same time the Analyzer showed a low count. The patient platelet counts were re-evaluated by taking a blood sample in a syringe; the manual platelet count showed value of 175×10^3/mm^3.

The integrity of the vessel wall depends upon platelets. Defect in the primary homeostasis and bleeding may cause low platelets, but without any clinical significance, if there is thrombocytopenia, it may cause diagnostic failure.[1-10] Pseudothrombocytopenia should be considered if patients do not have any identified haematological disease,e family history or bleeding tendency identified. Platelets agglutination or vitro clumping of platelets falsely measure low platelet counts by haematology analyzer. It is presumed, that an immune mediated response induces PLT clumping, due to the presence of anti-PLT auto-antibodies. The knowledge of PTCP is very important for diagnostic accuracy and for avoiding unnecessary treatment. We present a case with multi coagulant-dependent PTCP and introduce a diagnostic measurement that may help to avoid this problem. Majority of the agglutinins will react strongly at room temperature or low temperatures so some are temperature independent or reacted mostly at 37°C. Falsely low PLT counts resolved after warming blood sample tubes at 37°C.

The PLT clumps are not only anticoagulant and temperature dependent but also time dependent.[7] The processing of PLT specimen should be done immediately after sample collection for accurate estimation. Anticoagulant-dependent PTCP is an in-vitro phenomenon characterized by falsely low PLT counts due to anti platelet antibodies which cause platelet clumping in blood samples collected in anticoagulant tubes. Anticoagulants as (EDTA ,citrate, or oxalate) have a chelating effect on calcium ions and the low temperature effects the platelet membrane glycoprotein complex IIb /IIIa[5,7] which exposes the epitope of glycoprotein IIb that is normally hidden in the glycoprotein complex IIb/IIIa[10,4] (Figure-1 and 2). In case of heparin, PTCP is caused by platelet endothelial, and monocyte-activating antibodies that target multi molecular complexes of PLT factor IV and heparin.[3] These anti-PLT auto antibodies which are against platelet belong to the class of immunoglobulins i.e. IgG, IgM, or IgA.[7] These antibodies may exist temporarily or permanently. Other diseases with haematological origin (viral infections, neoplastic diseases, and autoimmune diseases) and drug abuse[8]

[1,3]Laboratory, [2]Department of Cardiology, Tabba Heart Institute, Karachi, Pakistan.

Correspondence: Jawaid Jabbar. Email: jawaid.jabbar@tabbaheart.org

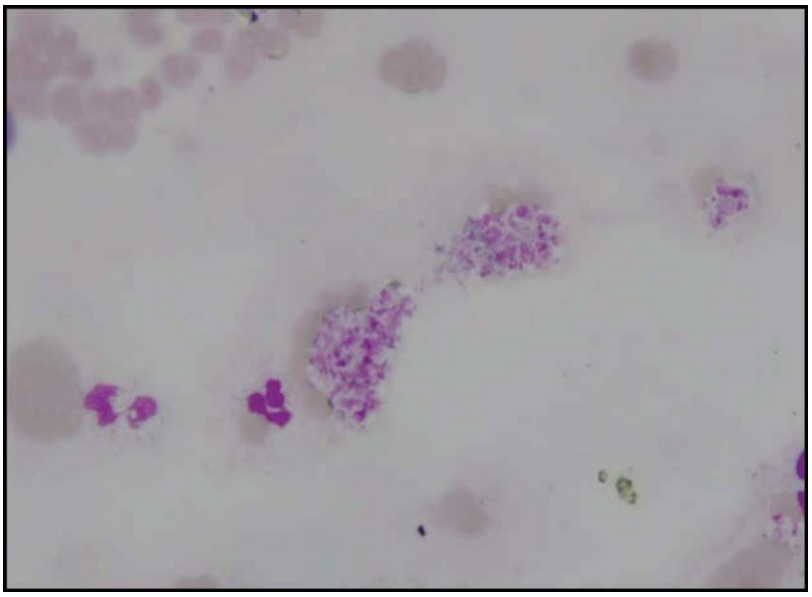

Figure-1: Platelet clumps in EDTA tube.

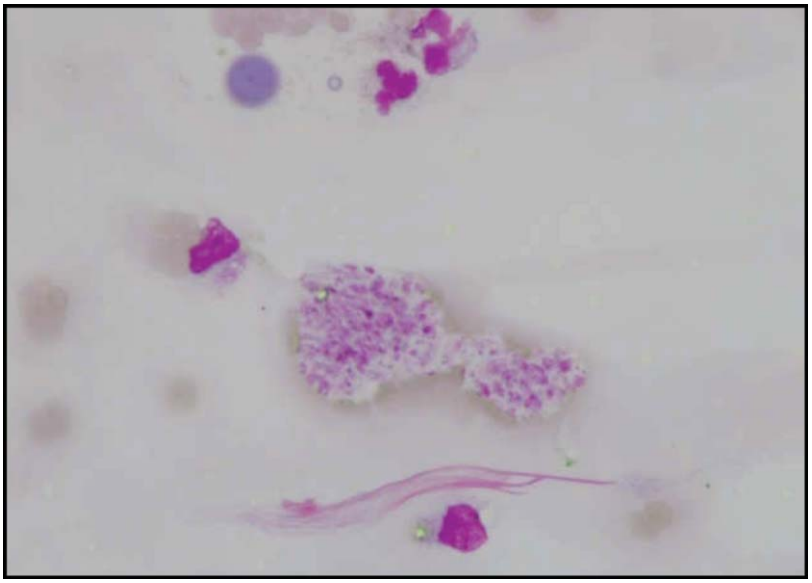

Figure-2: Platelet clumps in Na citrate tube.

may also cause cold agglutination. Pseudo thrombocytopenia if unrecognized leads to incorrect diagnosis, inappropriate treatment and debilitating iatrogenic disease. Haematology analyzer which is on automation mode counts platelets more accurately and quickly than the manual methods. SYSMEX XN analyzer recognizes platelets based on their size. Therefore, the clumps cannot be identified as platelets.[5] Thus, it may lead to a falsely low PLT number measured by haematology analyzer.

Method

Laboratory should take the following steps in the investigation of platelet clumping until a non-clumping smear is obtained. Check the blood draw method (e.g., finger prick versus venipuncture versus line draw) and exclude collection method related clotting.

Step 1. Blood sample collected in EDTA. (If clumping persists, continue to Step 2).

Step 2. Then the blood sample collected in Na citrate. (If Step 2 is not possible, proceed to Step 3).

Step 3. Obtain a sample in Lithium Heparin if clumping still present, then do Step 4.

Step 4. Obtain a sample in Na Fluoride if clumping still present, then do Step 5.

Step 5. Obtain a sample in ammonium oxalate, and count platelets utilizing a Newbauer chamber, if available, as per described methods above.

Note: The Steps 3, 4 & 5 are reserved for the rare instances if Steps 1 and 2 do not resolve the platelet clumping.

Conclusion

Modern haematology analyzer shows flagging of platelet clumps and laboratory technologists do manual verification by examining peripheral blood smear under the microscope. The CBC reports of platelet counts of samples that show platelet clumps can be a challenge. We have to give a report of the CBC sample which shows platelet clumps in the following format. i.e. If an instrument shows low platelet count and smear shows clumps after processing in all the anticoagulant tubes, a comment has to be stated, that for accurate estimation a fresh sample in a syringe is required for doing manual count in Newbauer chamber.

Disclaimer: None.

Conflict of Interest: None.

Funding Disclosure: None.

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