

Case Report

Ethylenediaminetetraacetic Acid (EDTA) - Dependent Pseudo thrombocytopenia: A 3 Case Comparative Study

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ABSTRACT

Ethylenediaminetetraacetic acid (EDTA) is a commonly used anticoagulant in sampling tubes designed for determination of complete blood counts. EDTA-dependent pseudo thrombocytopenia (PTCP) is the phenomenon of a spurious low platelet count due to EDTA-induced aggregation of platelets which are frequently not included in the platelet window of auto-analysers. We report 3 cases of EDTA induced pseudothrombocytopenias which were otherwise healthy with non specific symptoms that were resolved to a certain extent by subsequent collection in the Heparin tube and with complete resolution by collection in Sodium Citrate tube.

Keywords: Pseudo-thrombocytopenia, Peripheral blood smear, Platelet clumping, EDTA.

INTRODUCTION

EDTA-dependent pseudothrombocytopenia is a rare phenomenon with an incidence of approximately 0.1% in the general population. ⁽¹⁾ EDTA-PTCP is solely an in vitro effect without any clinical relevance. ⁽²⁾ EDTA-PTCP may generate significant costs and discomfort to the patient due to needless diagnostic testing, unnecessary platelet transfusions (SDP/RDP) and even with-hold of emergency treatments. ^(3,4) Visual evaluation of blood smears is regarded as gold standard for detection of EDTA-PTCP, but only a limited amount of smears will be performed in routine laboratories. A simpler approach for detection of EDTA-PTCP is to inspect the histograms and flags of hematology analyzers, although using former models of hematology analyzer suggest some false-positive and false-negative results. ^(5,6)

MATERIALS AND METHODS

The study was carried out by collection of blood in EDTA, Heparin and Sodium Citrate tubes respectively. The samples were run in automated hematology cell (5 part differential Siemens Advia 2120i), and peripheral smears prepared by using Fields stain.

RESULTS

We encountered 3 cases of EDTA-dependent pseudo thrombocytopenia showing similar results.

The blood of three patients was collected in three tubes each containing different types of anticoagulants: EDTA, Heparin and Sodium Citrate. The three blood samples were run in fully automated 5 Part Differential Hematology Cell Counter. (5 part differential Siemens Advia 2120i)

Case 1: 20 year old male presented with intermittent fever of mild grade since 5

days. His physical and systemic findings were unremarkable. Complete blood count revealed a platelet count of $23 \times 10^3 / \text{uL}$, the peripheral smear of which showed many platelet clumps (with the remaining values being within the normal range). A subsequent blood sample was drawn in Heparin and Sodium Citrate tubes which revealed platelet counts of $1.0 \times 10^3 / \text{uL}$ and $2.16 \times 10^3 / \text{uL}$ respectively.

Case 2: 30 year old female presented with non specific complaints of fatigue and weight loss with normal physical and systemic examination. The CBC revealed $13 \times 10^3 / \text{uL}$, $1.63 \times 10^3 / \text{uL}$ and $3.23 \times 10^3 / \text{uL}$ platelet counts in EDTA, Heparin and Trisodium Citrate respectively with the remaining values being normal.

Case 3: 19 year old male was referred to our hospital in view of low platelet count

reported in a private lab. The patient had non-specific symptoms and was otherwise healthy. The CBC revealed $18 \times 10^3 / \text{uL}$, $1.3 \times 10^3 / \text{uL}$ and $2.60 \times 10^3 / \text{uL}$ platelet counts in EDTA, Heparin and Trisodium Citrate respectively with the remaining values being normal.

Table 1.summarizes the platelet counts of the three cases with respective anticoagulants.

The peripheral smears made from EDTA of all three cases showed many clumps (Figure 1 and 2), while the ones made from Heparin revealed clumps to a lesser extent comparatively and no clumps were seen on smears prepared from Sodium Citrate. Thus, establishing the diagnosis of EDTA-dependent pseudothrombocytopenia in all the 3 cases.

Table 1: Table demonstrating platelet counts of the three cases in respective anticoagulants.

Case Number	Platelet Count		
	EDTA	Heparin	Trisodium Citrate
Case 1	$23 \times 10^3 / \text{uL}$	$1.0 \times 10^3 / \text{uL}$	$2.16 \times 10^3 / \text{uL}$
Case 2	$13 \times 10^3 / \text{uL}$	$1.63 \times 10^3 / \text{uL}$	$3.23 \times 10^3 / \text{uL}$
Case 3	$18 \times 10^3 / \text{uL}$	$1.3 \times 10^3 / \text{uL}$	$2.60 \times 10^3 / \text{uL}$

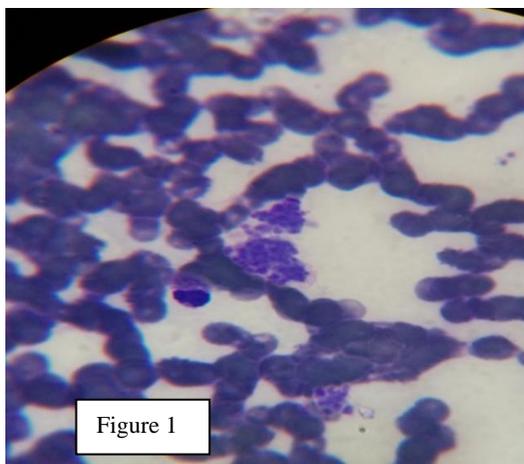


Figure 1

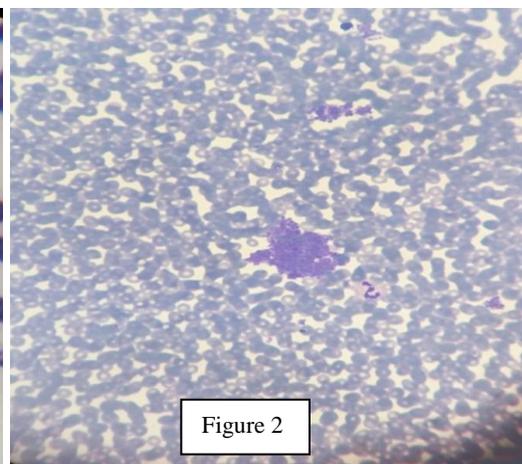


Figure 2

Figure .1 and .2 show platelet clumps on peripheral smears prepared from EDTA on 100x and 40x respectively.

DISCUSSION

EDTA induced PTP was first reported by Gowland *et al.* (7) when a patient reports for evaluation with an abnormally low platelet count in the absence of a history consistent with thrombocytopenia, pseudo thrombocytopenia should be suspected. (8) EDTA-dependent PTCP is the phenomenon of a spurious low platelet count due to the appearance of antiplatelet autoantibodies

that cause platelet clumping in blood anticoagulated with EDTA. (1,9) Antiplatelet autoantibodies (IgG&IgM) appear due to an alteration of the platelet surface glycoproteins (GPIIb/IIIa) when they are incubated with a calcium chelator such as EDTA. (8) Anticoagulants such as Heparin and Sodium Citrate are usually used for obtaining accurate platelet counts in EDTA-dependent PTCP patients. (9,10) Other

methods such as warming the sample to 37°C and addition of kanamycin have also been proposed. Most aggregating antibodies are cold reacting and are inhibited by incubation at 37°C, though in 20% cases PTP reportedly persists even at 37°C. ⁽²⁾ PTP has been found more frequently in patients on medication as well as severely ill patients, in association with autoimmune, neoplastic, atherosclerosis related and liver related conditions. ⁽¹¹⁾ Around 20% of cases with EDTA induced PTP show the phenomenon in Citrate anticoagulant as well (which was not the case in our study). ⁽²⁾

In our cases, we examined whether platelet clumping was prevented by the use of Sodium Citrate and Heparin as anticoagulants. While heparin failed in resolving pseudo thrombocytopenia completely (with few platelet clumps on peripheral smear), it did give better results compared to EDTA, and sodium citrate completely resolved the pseudo thrombocytopenia with no platelet clumps seen in the peripheral smear giving an accurate platelet value.

CONCLUSION

Given the widespread use of EDTA-containing vacutainers for blood collection, identification of PTCP requires a high index of suspicion after the identification of thrombocytopenia in the absence of a suggestive medical history. Examination of the peripheral blood smear provides evidence of PTCP in the form of platelet clumping. Our cases are examples of otherwise healthy individuals with non specific symptoms who, in light of their current conditions, were suspicious for EDTA-PTCP and were resolved by subsequent collection in the Trisodium Citrate tube. Nonetheless, an awareness of this particular condition is necessary, because its lack of recognition may lead subjects to unnecessary clinical or medical interventions like platelet transfusions which were not required at all.

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