



Pseudotrombocytopenia Caused by EDTA in Obstetrics and Perinatology - Case Report

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SUMMARY

Introduction: Clinically, the most important pseudothrombocytopenia is described in pregnant women and also in their newborns if blood sample is taken using EDTA.

Case report: Patient, 35 years old pregnant woman, 36 weeks of gestation, was admitted to Gynecological and Obstetrics Clinic in the CCS because of pregnancy monitoring. The EDTA thrombocytes result was $34.0 \times 10^9/L$ and patient was without any symptoms of bleeding tendency. Pseudothrombocytopenia was suspected. We decided to check it by examination of blood smear and incubating EDTA sample on $37^\circ C$ degrees for an hour. The platelets value on $37^\circ C$ degrees was $32.0 \times 10^9/L$. Blood smear showed a platelet aggregation. The platelet count with the Sodium Citrate was $253.0 \times 10^9/L$, with the Ammonium oxalate $266.0 \times 10^9/L$ and with Mg-sulphate $284.0 \times 10^9/L$. Newborn was healthy. The Complete Blood Count of newborn revealed normal parameters apart from a low platelet count $49.0 \times 10^9/L$. A blood smear was ordered and it revealed platelet aggregations. Platelet count of newborn blood sample taken on sodium-citrate was $189.0 \times 10^9/L$ which clearly indicated pseudothrombocytopenia.

Conclusions: Although PTP does not require clinical-therapeutic intervention, undiagnosed PTP can lead to therapeutic intervention (unnecessary administration of platelet concentrate) and seriously deteriorate both mother's and child's health. Therefore, the authors suggest examination of blood smear in every case when thrombocytopenia is diagnosed.

Keywords: pseudothrombocytopenia, EDTA, newborn, pregnant woman

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INTRODUCTION

Pseudothrombocytopenia is a phenomenon in which antibodies, present in the patients' blood react with platelets in blood sample anticoagulated with EDTA, causing agglutination and a spuriously low platelet count [1]. Although EDTA-dependent pseudothrombocytopenia has been practically and literally well-handled for more than 30 years, today it may also be unrecognizable.

Pseudothrombocytopenia most commonly occurs when using anticoagulant Ethylene Diamine Tetra Acetic acid (EDTA) in blood laboratory sampling. Clinically, the most important, pseudothrombocytopenia occurs in pregnant women and in their newborns if blood sample is taken using EDTA [2]. Analyzation of platelets could be done from the newborn sample taken with another anticoagulant (ammonium oxalate, citrate) and tested immediately after sampling [2]. This condition in a newborn disappears after a month of birth [3,4,5].

CASE REPORT

Patient MT, 35 years old, obese pregnant woman 36 weeks of gestation who got pregnant naturally for the second time, was admitted to Gynecological and Obstetrics Clinic Clinical Centre of Serbia for monitoring pregnancy and delivery planning.

Previous natural pregnancy was due to the pelvic presentation of the fetus delivered by Cesarean section. The first child was born healthy.

During this second pregnancy was administered antihypertensive (methyl-dopa) and anticoagulant therapy (sirete fraxiparine) due to the comorbid clinical conditions hypertension and varices *cruris et femoris bilateralis*. In addition, laboratory values of platelets were monitored.

Due to obstetric reasons such as: pelvic presentation of the fetus, intrauterine growth restriction (IUGR) and reduced amounts of amniotic fluid (oligoamnion) has been determined to deliver a child with the Cesarean section at 36th week of gestation. The cardiotocography (CTG) record was within normal limits.

EDTA pseudothrombocytopenia was suspected considering that at the admission, the EDTA platelets (Plt) result was 34.0

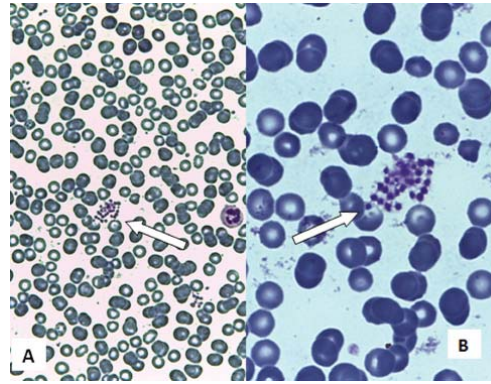


Figure 1. Peripheral smear sample of mother's blood taken on EDTA, A x 400 B x 1000

$\times 10^9/L$ (MPV 16, 9fl) and patient was without any symptoms of bleeding tendency. We decided to check it by examining blood smear and incubating EDTA sample on 37°C for 1 hour. The Plt value on 37°C was 32.0 $\times 10^9/L$ and blood smear showed a platelet aggregation (Figure 1).

Blood samples were simultaneously taken in four tubes containing four different types of anticoagulants; EDTA, Sodium Citrate (Na-citrate), Ammonium oxalate and Magnesium-sulfate (Mg-sulfate). The blood samples were run in fully automated Hematology analyzer Siemens ADVIA 2120i. The platelet count

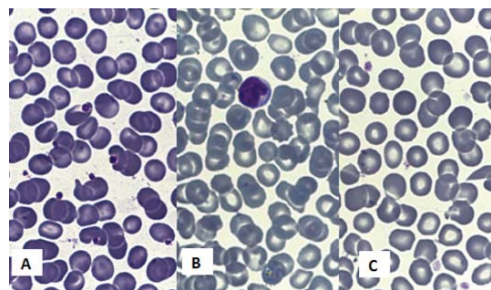


Figure 2. Peripheral blood smears taken on: A Na-citrate, B-Ammonium oxalate and C-Mg-sulphate

in the Sodium Citrate tube was 253.0 $\times 10^9/L$, in the Ammonium oxalate 266.0 $\times 10^9/L$ and in Mg-sulphate 284.0 $\times 10^9/L$. Blood smears on anticoagulants other than EDTA showed no agglutination (Figure 2).

Additionally, blood sample on EDTA was measured every 10 minutes from the moment of taking, and results were: 156.0 \times

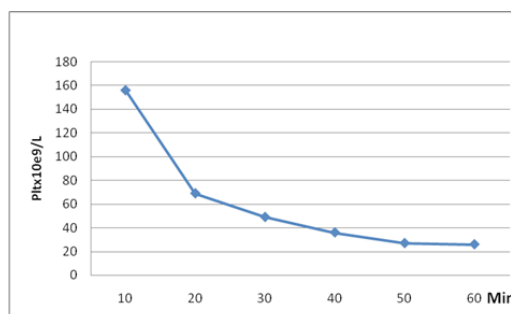


Figure 3. Mother's platelet values measured in a blood sample on EDTA every 10 minutes from the moment of blood sampling

10e9/L, 69.0 x 10e9/L, 49.0 x 10e9/L, 36.0 x 10e9/L, 27.0 x 10e9/L, and 26.0 x 10e9/L, respectively (Figure 3).

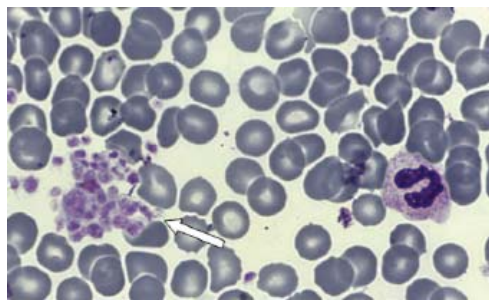
The decision was made to terminate the pregnancy with the Cesarean section so the patient was on prophylactic therapy with Low molecular weight heparin (LMWH) (Nadroparin-calcium, Fraxiparine®, 2850 i.j. / 0.3 ml sc). Because of the possibility of developing heparin-induced thrombocytopenia (HIT), antibodies to the heparin / PF4 complex were controlled and result was negative. HIT antibodies were determined by using PAGA Heparin / PF4 Antibody test kit, BioRad Switzerland.

Despite the results of the laboratory and the precise transfusiologists' diagnosis of the pseudothrombocytopenia, the surgical team requires preparing 2 pools of platelet concentrates. Due to the careful monitoring of transfusiologists, platelet concentrates were not administered to the patient.

Newborn was healthy boy (Apgar score 9, length 48 cm, body weight 2700 g, head circumference 35 cm).

The newborn's Complete Blood Count (CBC) results revealed normal parameters apart from a low platelet count 49.0 x 10e9/L (MPV 9,4 fl). He had no bleeding tendency. A blood smear was ordered and it revealed platelet aggregations (Figure 4).

Figure 4. Blood smear of the newborn's peripheral blood sample taken on EDTA



Newborn platelet counts from a blood sample taken from sodium citrate was 189.0 x 10e9 / L (MPV 7.3 fl), which made it clear that it was pseudothrombocytopenia. So, the baby was considered to have pseudothrombocytopenia and discharged from the hospital.

It has been advised that the baby's platelets should be controlled one month after birth due to the apparent elimination of the transplacental cause of pseudothrombocytopenia. Finally, during his last follow up visit, he was 2 months old and the baby's platelet count was normal, even in the presence of

EDTA. Literature data indicate the possibility of pseudothrombocytopenia in children born by mothers with pseudothrombocytopenia, as in our case. It is recommended that blood smear sample should be mandatory for that children.

DISCUSSION

Gowland and his team first reported in 1969 about PTP induced by EDTA (6).

EDTA induced alteration of surface glycoproteins (GP) enables binding of anti-platelet antibodies. This is the cause of agglutination. Platelet agglutinins could belong to all immunoglobulin classes (IgG, IgM, IgA) (7,8). Among these 20% of EDTA induced PTP show the agglutination in citrate anticoagulant as well. Oxalate and heparin have also been implicated in PTP (7, 9).

This phenomenon in a newborn disappears after a month of birth indicating transplacental transmission of plasma components (most likely IgG) leading to pseudothrombocytopenia of the newborn (10). Due to this phenomenon, concerning neonate with asymptomatic thrombocytopenia shall be proceeded with patterns as adults in order to avoid inappropriate and potentially harmful treatment decisions [3, 4, 5, 11].

In addition to enable better diagnostic and therapeutic approach needed for personalized medicine concept, it is necessary to include specialist of clinical transfusiology, clinical pharmacology and clinical immunology in every day practice. To acquire this level it is necessary to enlarge these specialists number.

CONCLUSION

Although PTP does not require clinical-therapeutic intervention, undiagnosed PTP can lead to therapeutic intervention (unnecessary administration of platelet concentrate) and seriously deteriorate both mother's and newborn's health. Therefore, the authors suggest examination of blood smear in every case when thrombocytopenia is detected and warn to respect multidisciplinary medical team work.

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Pseudotrombocitopenija izazvana upotrebom EDTA u akušerstvu i perinatologiji - prikaz slučaja

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KRATAK SADRŽAJ

Uvod: Pseudotrombocitopenija opisana kod trudnica, a takođe i u kod njihove novorođenčadi je klinički veoma važna. Najčešće se javlja ukoliko se za uzorkovanje krvi koristi EDTA.

Prikaz slučaja: Trudnica, 35 godina, 36 nedelja trudnoće, primljena je u Kliniku za ginekologiju i akušerstvo KCS radi praćenja trudnoće. Rezultat EDTA trombocita bio je $34.0 \times 10^9 / L$, a pacijentkinja je bez simptoma i znakova krvarenja što ja navelo na sumnju da se radi o EDTA pseudotrombocitopeniji. Nakon inkubacije EDTA-uzorka krvi na $37^\circ C$ u trajanju od 1 sata vrednost trombocita je bila $32.0 \times 10^9/L$. Na razmazu periferne krvi uočeni su agregati trombocita. Broj trombocita u epruveti sa natrijum citratom je bio $253.0 \times 10^9 / L$, sa amonijum-oksalatom $266.0 \times 10^9 / L$ i sa Mg-sulfatom $284.0 \times 10^9 / L$. Novorođenče je bilo zdravo. Rezultat krvne slike novorođenčeta imao je normalne parametre osim niskog broja trombocita $49.0 \times 10^9/L$. Ispitivanjem razmaza periferne krvi otkrivena je agregacija trombocita i kod novorođenčeta. Broj trombocita novorođenčeta u uzorku krvi na natrijum-citratu iznosio je $189.0 \times 10^9 / L$ što je bilo jasno da se radi o pseudotrombocitopeniji.

Zaključak: Iako PTP ne zahteva kliničko-terapijsku intervenciju, nedijagnostikovana PTP može dovesti do terapijske intervencije i ozbiljno pogoršati zdravstveno stanje i majke i deteta. Zbog toga, autori sugerišu kod svake trombocitopenije analizu razmaza periferne krvi i kod odraslih i kod dece.

Ključne reči: pseudotrombocitopenija, EDTA, novorođenče, trudnica

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