CASE REPORT

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Pseudothrombocytopenia in Obstetric Patients: Case Reports

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ABSTRACT Thrombocytopenia is defined as platelet count of less than 150x10^3/uL. During pregnancy, haemodilution and increased aggregation lead to physiological thrombocytopenia and it has no harmful effects on pregnancy. Pseudothrombocytopenia is defined as in vitro platelet clumping that results falsely low platelet counting by automated cell counters. Before diagnosis, we should exclude probable severe pregnancy-induced diseases leading to thrombocytopenia during pregnancy such as preeclampsia, gestational thrombocytopenia. It is important to avoid unnecessary intervention and treatment. Herein, we report three cases with profound artifactual thrombocytopenia during pregnancy.

Keywords: Pregnancy; pseudothyrombocytopenia; etylendiaminetetracetic ascit

Thrombocytopenia is defined as platelet count of less than 150x10^3/uL.[1] During pregnancy, haemodilution and increased aggregation lead to physiological thrombocytopenia and it has no harmful effects on pregnancy. In general, the leading cause of thrombocytopenia is diagnosed as gestational thrombocytopenia and similarly, it has no adverse maternal-fetal effects. Occasionally, thrombocytopenia can be a life threatening condition in pregnancy when is due to pregnancy-related hypertension spectrum (preeclampsia, eclampsia), HELLP syndrome, acute fatty liver of pregnancy, immune thrombocytopenic purpura (ITP), hemolytic uremic syndrome (HUS), thrombotic thrombocytopenic purpura (TTP), sepsis, malignancy or disseminated intravascular coagulapathy (DIC).[1,2] Pseudothrombocytopenia is another reason of iatrogenic thrombocytopenia.[3,4]

Pseudothrombocytopenia is defined as in vitro platelet clumping that results falsely low platelet counting by automated cell counters. The main reasons of pseudothrombocytopenia can be classified as a. Cumulation of thrombocytes due to Etylendiaminetetracetic ascit (EDTA) in blood hemogram tubes b. Platelet satellitism c. Giant platelets. EDTA, sodium citrate and heparine which are in blood specimen tubes and inhibit clotting blood samples by chelating calcium, are associated with pseudothrombocytopenia.[5] Before diagnosis, we should exclude probable severe pregnancy-induced diseases leading to thrombocytopenia during pregnancy. It is important to avoid unnecessary intervention and treatment.

Herein, we report three cases with profound artifactual thrombocytopenia during pregnancy.

CASE REPORTS

CASE 1

A 25-year-old woman with gravida 3 parity 2 was admitted to emergency obstetric clinic with complaints of uterine contraction and back pain. On clinical examination, body temperature (36.8°C), blood pressure (100/70 mmHg), hearth rate (92 pulse/min), oxygen saturation (98%) were normal. On pelvic examination, she had 7 centimeter of cervical dilatation and %80 cervical effacement. Ultrasound scan showed cephalic presentation, normal amniotic volume (single deepest vertical pocket: 36 milimeter) and anterior placenta. The estimated fetal weight was calculated as 2400 g; below 10 percentile. After her examination, blood samples were sent to the laboratory and the laboratory tests including biochemical [aspartate aminotransferase (AST), alanine aminotransferase (ALT) creatinine, uric aside, lactate dehydrogenase (LDH)] and coagulation parameters [activated partial thromboplastin time (aPTT), international normalized ratio (INR), prothrombin time (PT)] were within normal ranges except complete blood count (CBC). Laboratory findings demonstrated platelet counts of 5x10^3/uL and repeated CBC demonstrated similar platelet counts, a peripheral blood smear was sent to hematology department. It was seen that platelet clustering making it pseudothrombocytopenia and estimatedly platelet count was 100x10^3/uL (Figure 1, Figure 2). Peripheric smear was prepared from EDTA-contained blood tube. It was considered pseudothrombocytopenia and there was no transfusion indication. She had an uneventful normal vaginal delivery of a female infant. The newborn was healthy (2500 g, APGAR score 9, length 50 cm and head circumference 35 cm). On the first day after delivery, the complete blood count of the neonate revealed normal platelet count (269x10^3/uL). Her physical examination was completely normal. After delivery, the patient remained well and her postnatal sixth hour CBC control revealed pseudothrombocytopenia and hemoglobin level was 11.5 g/dL. On follow-up sonographic examination, there was no pathologic image suggesting haemorrhage. She was discharged from the hospital the next day. Informed consent form was obtained from the patient.

CASE 2

A 24-year-old woman with gravida 4, parity 2, abortus 1; and with no co-morbidities was admitted to emergency obstetric unit with complaints of uterine contraction and amnion fluid leakage. On her pelvic examination, she had 10 cm of cervical dilatation and 100% effacement. Her vital signs were completely normal (blood pressure 120/76 mmHg, hearth rate 86 pulse/min, body temperature 36.4 °C, oxygen saturation 98%). On ultrasonographic examination, there was no pathologic finding. Her preoperative basic blood samples were sent to the laboratory. Shortly after her admission to the hospital, she delivered a 3410 g, healthy female infant. After delivery, blood sam-

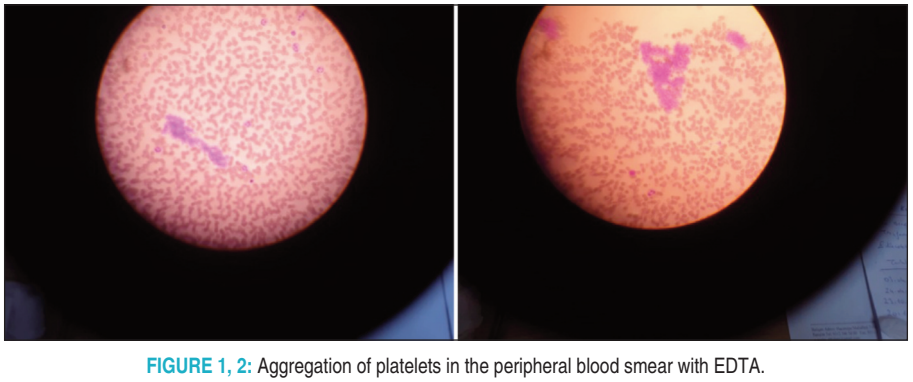

FIGURE 1, 2: Aggregation of platelets in the peripheral blood smear with EDTA.

ple results revealed normal parameters (AST, ALT, creatinine, uric aside, BUN, CRP, INR, aPTT, PT) except CBC. The platelet value in EDTA- tube was 33x10^3/uL. Peripheral blood smear was sent to the laboratory and the result was reported as 'clustering thrombocytes, calculated platelet count was estimatedly 75cx10^3/uL'. On follow-up examination after delivery, her vital signs were completely normal and she had no more bleeding tendency than expected. Control CBC revealed a normal hemoglobin level of 10.8 g/dL. The newborn's blood samples was investigated and no pathologic findings were observed regarding thrombocytopenia. After two days she was discharged from the hospital. Informed consent form was obtained from the patient.

CASE 3

A 29-year-old woman with Type 2 diabetes mellitus, chronic hypertension, morbid obesity and new-onset thrombocytopenia was referred to our hospital at 34th gestational week. She was hospitalized to regulate blood sugar level and to ascertain the etiology of thrombocytopenia. She was receiving alpha methyldopa tid and insulin treatment. Ultrasound scan showed that fetal growth was beyond than due to gestational age and dating to first trimester crown rump length (CRL) measurement. Her blood pressure was 160/90 mmHg, fasting blood glucose was 152 mg/dL on admission to the hospital. Routine blood samples (CBC, biochemistry, urine analysis, coagulation tests) were sent to the laboratory and revealed normal parameters apart from CBC and spot urine protein. The platelet value in EDTA-tube was 34x10^3/uL. A 24-hour urine was collected and the mean measured 24-hour urinary protein was 1.5 g. She had no complaints of headache, epigastric pain, diplopia. Control blood samples were sent after 6 hours; AST-ALT levels were below 35 U/L, and platelet counts were 35x10^3/uL and 32x10^3/uL, respectively. Peripheral blood smear was sent to the laboratory and result was reported as 'clustering thrombocytes, calculated platelet count was estimatedly 80x10^3/uL'. Recurrent late decelerations was observed following minimal uterine contraction on cardiotocography and she underwent cesarean section with fetal distress indication. A healthy boy was born, 2400 g/ 46 cm and with a 9 point Apgar score. Postoperative control CBC revealed low platelet count and biochemical parameters were within normal ranges. Preoperative was administered at a loading dose of 4g/h over 30 minutes and postoperatively followed by an infusion of 1g/h. Informed consent form was obtained from the patient.

DISCUSSION

EDTA-dependent pseudothrombocytopenia is a rare phenomenon, with in vitro platelet clumping that results falsely low platelet counting by automated cell counters. The estimated prevalence is 0.1% in general population, however this rate rises up to 2% in critical illnesses [sepsis, cardiac surgery, rubella, human immune-deficiecny virus (HIV) infection, malignancy] and with drug use and in hospitalized patients.[6] EDTA is a widely used chelator for hematological testing to avoid the presence of coagulum in blood samples. Specific pathophysiological pathway for EDTA-dependent pseudothrombocytopenia have been identified. In the low temperatures, EDTA leads to a structural change of glycoprotein IIb-IIIa complex, and EDTA dependent anti-platelet antibodies access and bind to glycoprotein IIb.[7] This binding results in platelet clustering and falsely low platelet counting by automated cell counters.

True diagnosis and management of pseudothrombocytopenia has clinical importance to avoid unnecessary intervention for diagnosis and treatment. In literature, platelet transfusion, splenectomy, bone marrow biopsy have been reported.[8] At this point, major criteria should be known to make a diagnosis, 1. Platelet count <100×10^3/uL. 2. No clinical signs of bleeding diathesis 3. Presence of clumps in EDTA samples 4. Time-dependent fall of platelet count.[9] It is important because there is no platelet transfusion indication for pseudothrombocytopenia.

Additionally, it should be kept in mind when making a differential diagnosis for thrombocytopenia in pregnancy. The main causes of life-threaten-

ing and pregnancy-related thrombocytopenia are HELLP syndrome and DIC. As in our cases, there is not enough time to reveal the certain etiology of thrombocytopenia in the course of active labor. Shortness of the time and to decide the delivery mode are stressful for specialist. As known, surgical bleeding can occur when platelet counts are less than 50×10^3/uL and 30×10^3/uL for vaginal delivery. Initially, to determine the etiology of thrombocytopenia, physical examination can help us. If there is no sign or symptoms of bleeding disorders, completely normal physical examination with lower platelet counts, laboratory is asked to confirm platelet counts with citrated tube or peripheral blood smear regarding to pseudothrombocytopenia. Other laboratory parameters can help us to rule out pregnancy-associate hypertension spectrum (preeclampsia, eclampsia), HELLP syndrome and DIC.

The second important point is the possibility of artifactual thrombocytopenia in newborns. In literature, Korterink et al., reported that this entity in a newborn is due to transplacental transmission of immunoglobulins and reverse after one month.[10] In our cases, we didn't determine neonatal thrombocytopenia. Obstetricians should inform pediatricians about maternal pseudothrombocytopenia before delivery. If transmission is revealed in a newborn, diagnostic peripheral blood smear is obligatory.

In conclusion, the etiological conditions of thrombocytopenia are in a spectrum from life-threatening, serious illness; to iatrogenic, artifactual laboratory defects in pregnancy. Before any intervention, blood smear should be interpreted for hemolysis, clustering and multidisciplinary management should be performed.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Betül Yakıştıran, Orhan Altınboğa;* ***Design:*** *Betül Yakıştıran,* ***Control/Supervision:*** *Turhan Çağlar, Orhan Altınboğa;* ***Data Collection and/or Processing:*** *Betül Yakıştıran;* ***Analysis and/or Interpretation:*** *Betül Yakıştıran, Orhan Altınboğa;* ***Literature Review:*** *Betül Yakıştıran;* ***Writing the Article:*** *Betül Yakıştıran, Orhan Altınboğa;* ***Critical Review:*** *Turhan Çağlar;* ***Materials:*** *Betül Yakıştıran,Turhan Çağlar.*

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