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Treatment of pregnant patient with disseminated intravascular coagulation (DIC) due to placental abruption – a case report

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Summary

A primigravid woman at 29th gestational week with placental abruption causing fetal death, that underwent instant cesarean section, developed a disseminated intravascular coagulation (DIC), revealed by hemoperitoneum and hematoma of the abdominal wall. After re-laparotomy and transfusion of blood, fresh plasma, and platelets, the patient was discharged from hospital on the 14th postoperative day completely recovered. To conclude, conservative surgical approach for DIC treatment is possible and safe. Novel antifibrinolitic drugs are recommended for obstetrical patients with DIC to enable a healthy subsequent pregnancy.

Key words: Placental abruption; DIC; Congenital thrombophilia; Antifibrinolitic drugs; Tranexamic acid; Desmopressin.

Introduction

Placental abruption is one of the most common causes of antepartum hemorrhage as well as the coagulation failure like disseminated intravascular coagulopathy (DIC). It is as the leading cause of maternal morbidity and mortality, despite modern improvement in obstetric practice [1].

Case Report

A primigravid woman aged 36 years was administered to Clinic for Gynecology and Obstetrics Clinical Center of Serbia at 29th gestational week due to uterine hyper-tonus and moderate to profuse hemorrhage that had begun two hours prior, suddenly, in the middle of the night. She complained of intermittent uterine contractions and headache lasting 24 hours.

After clinical and ultrasound examinations, fetal death and placental abruption were diagnosed. Blood pressure on admission was 120/70 mmHg and pulse was 96 bpm. Laboratory analysis showed altered glucose, creatinine, bilirubin, AST, LDH, creatinine kinase, uric acid, serum protein, and sodium levels. Other biochemical parameters were within the referral range.

Due to maternal vital indications, urgent cesarean section was performed. A dead (Apgar score 0) male fetus weighing 1,200 grams was delivered. A partial placental abruption was confirmed. During operation patient received ten IU oxytocin bolus, two blood pools (545ml), two doses of fresh frozen plasma (FFP), and ten doses of cryoprecipitate. Manual revision of uterine cavity was performed and uterus was sutured in two layers. Hemostasis was achieved and uterus was appropriately contracted. Before closing the abdomen sub-fascial drainage was established. At 75 minutes after cesarean section, diffuse bleeding with fresh light red blood on the abdominal wall and vaginal hemorrhage were registered. However, on clinical examination and palpation, uterus was adequately contracted. Ultrasound scan revealed anticipated size, clear contours, and empty cavity of the uterus. In the right adnexal region a hypo-echogenic area approximately 35mm in diameter was seen. This finding could correspond to free fluid (possibly blood) in the abdomen. Another a hypo-echogenic area approximately 20 mm in diameter was registered in the anterior abdominal wall between fascia and muscles. According to its ultrasound characteristics, it resembled a hematoma.

Laboratory analyses after caesarean section were altered and anemia was confirmed. Blood pressure was 116/68 mmHg and pulse 115 bpm. Therefore, despite therapy, the symptomatology worsened one hour later. Consequently, due to patient's vital indications, a re-laparotomy performed was straightaway. The operative findings confirmed diffuse intra- and retro-peritoneal hemorrhage with hematoma. Uterus was showing signs of Couvelair's syndrome, but the stitches on the uterine incision were intact with adequate hemostasis. A conservative approach was decided due to age and parity of the patient. Described hematomas were evacuated and revision of hemostasis was done. There was no visible active bleeding, either in the abdomen, or in the anterior abdominal wall. Nonetheless, because of the existing right infundibulopelvic ligament hematoma, a ligature was performed on the right ovarian artery. During surgery the patient received seven blood pools (1,700 ml), three doses of SSP (955 ml) and 25 doses of cryoprecipitate, 20 doses of platelets, and cell saver 1,775 ml.

Patient spent the following seven days in the intensive care unit. For the first three days she was on mechanical respiration due to impaired auscultator sound in the basal lung regions. Chest radiography showed pleuropericardial effusions. The patient was medically treated with oxygen, aminophylline, urbasone, lasix, enalapril, presolol, nifelat, bensedine, uterotonic treatment, and desmopressin.

Postoperatively, patient received uterotonic treatment (oxytocin and prostaglandin M15) and antibiotics daily. She also received treatment with anti-fibrinolitic tranexamic acid (one mg/kg/hour infusion) and emosint (desmopressin, DDAVP). She was given additional three blood pools (720 ml), two doses of SSP (455 ml)

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and five doses of crio-precipitate. On the tenth postoperative day clinical findings were significantly improved. Biochemical analyses were all in referral range. Coagulation factors stabilized: PT 12.9s, INR 1.10, aPTT 29.1s, D-dimer 13.1, AT III 108.8, and fibrinogen 3.3.

Patient was discharged from hospital on the 14th postoperative day, completely recovered with appropriately contracted uterus and laboratory data in referral range. On the control examination 21 days after surgery, all clinical and laboratory findings were normal, therefore the stitches were removed.

Six months later, as a part of detailed diagnostics made in order to discover the true etiology of described complications, a hematological examination was performed. Patient was diagnosed with congenital heterozygote thrombophilia type FII 20210A. She also had positive anti beta 2 GP I antibodies in low titer. Patient was advised that in case of pregnancy, antithrombotic therapy must be immediately begun. One year later patient became pregnant again. Throughout the whole pregnancy she was gynecologically and hematologicaly regularly controlled and received anticoagulant therapy. On the July 19th, 2013, the patient underwent a planned cesarean section and gave birth to a healthy child weighing 3050 grams. Postoperative course was uneventful for both mother and child.

Discussion

The most important causes of antepartum hemorrhage (vaginal bleeding from the 20th week of gestation until delivery) are placenta praevia and placental abruption, which together account for more than 50% of cases [1, 2]. Placental abruption is defined as premature separation of a normally sited placenta and occurs in one in 100 pregnancies. Risk factors include pre-eclampsia, blunt abdominal trauma, smoking, cocaine use, multiple pregnancies, increasing maternal age and parity, polyhydramnios, and previous history of abruption [2, 3].

Placental abruption can be easily diagnosed if it occurs in the lower part of the placenta and blood escapes through vagina. However, bleeding can occur at times between the placenta and the uterine wall and in that manner can remain concealed for significant time. The only symptoms apparent in these cases are sudden onset of abdominal pain, persistent abdominal pain, and marked uterine hyper-tonus. Maternal tachycardia with decreased blood pressure and fetal heart rate abnormalities are present. Hemorrhage can penetrate through the uterine wall and infiltrate the myometrium causing Couvelaire uterus. Maternal shock, acute renal failure, coagulopathy (DIC), and fetal demise are complications of most such cases [4]. Severe coagulation defects rarely occur unless the separation of the placenta is significant enough to result in fetal demise [5, 6].

Abruption is usually diagnosed clinically (hard, tender, irritable uterus; with or without bleeding). Ultrasonography can help in detecting retro-placental hematomas. Furthermore, CTG is non-reassuring in most cases [7]. Evaluation of blood count, hematocrit, coagulation profile, and biochemical parameters of renal and hepatic function should be done immediately. In the presented case the authors suspected placental abruption according to presence of bleeding and tetanic uterus. After ultrasound examination the exact diagnosis was confirmed [8].

If bleeding is light to moderate, management depends on the fetal condition; however, if bleeding is heavy (evident or hidden), delivery should be carried out as soon as possible. If vaginal delivery is not imminent, delivery by cesarean section should be carried out [5]. This is true especially in case of fetal death when only the benefit for the mother has to be taken into consideration. The present authors performed a cesarean section immediately after completing diagnostics [2].

Disseminated intravascular coagulopathy presents a complex coagulation disorder resulting from widespread activation of both the clotting and fibrinolytic systems. There is an excess of both thrombin and the plasmin [9]. Activation of the complement system has systemic manifestations of increased vascular permeability, hypotension, and even microangiopathic hemolysis. Systemic production of fibrin polymers causes fibrin thrombosis producing end-organ ischemia and necrosis [10].

Clinical signs and symptoms of DIC can include oozing from venipuncture sites and/or mucous membranes, red cell lysis from activation of the complement system, hemorrhage from coagulopathy, and possible uterine atony, hypotension from hemorrhage and/or bradykinin release, and oliguria from end-organ insult and hypovolemia/hypotension, PT < 60%, aPTT of more than 30 seconds, fibrinogen < 200 mg/ml, platelet count < 100,000/ml^3, fibrinogen split products (FSP) > 40 mg/ml, and antitrombin III activity of < 80% are all indicative of DIC [8, 9].

In the current treatment of severe obstetrical hemorrhage, first-line therapy includes transfusion of packed cells and fresh frozen plasma in addition to uterotonic medical management and surgical interventions [6, 11]. The present patient received significant amounts of transfused blood and blood derivates.

The most important treatment is elimination of underlying triggering mechanism. Even in the case of a pronounced clotting defect, significant bleeding occurs only when the anatomical integrity of the vascular system is disrupted [10]. Consequently, adequate hemostasis is essential for DIC treatment. Bilateral hypogastric artery ligation is proven to be effective if there is no active bleeding or infection [12]. The authors also proved that conservative treatment is safe and hysterectomy can be avoided.

Treatment of DIC consists of replacement of volume, blood products, coagulation components, cardiovascular, and respiratory support. The correction of clotting factors deficiencies (evident by prolonged PT/PTT) is done with FFP. Early fibrinogen replacement should be made in women who have low fibrinogen where worse outcomes can be expected. On the other hand, if the initial fibrinogen level is < 50 mg/ml, infusion of cryoprecipitate is strongly indicated. Hematocrit levels should be maintained with transfusion of packed erythrocytes, while platelet transfu-

sions should increase their count. In refractory cases, treatment with antithrombin III concentrate could be considered. Data suggest that the use of recombinant factor VIIa should be limited to bleeding that has not responded to an optimal transfusion strategy [13, 14].

Recently several novel therapies were described but are still not included as standard clinical therapies for DIC patients. Desmopressin is a synthetic vasopressin analogue that increases Von Willebrand's factor VIII blood concentrations and therefore adhesion, activation, and aggregation of platelets [13, 14]. Desmopressin proposed for both prevention and treatment of acute bleeds during pregnancy in women with congenital bleeding disorders [15].

Tranexamic acid is a synthetic derivative of the amino acid lysine that exerts its antifibrinolytic effect [16]. It is a competitive inhibitor of plasminogen and plasmin which reversibly blocks lysine binding sites on plasminogen molecules. In that manner, it inhibits the interaction of plasminogen and plasmin with lysine on the surface of fibrin. Although plasmin can still be formed under these circumstances, it is unable to bind to and degrade fibrin [17, 18].

It can be administered both orally and intravenously and it is eliminated through urine. Tranexamic acid is well tolerated [19]. Increased risk of thrombosis with the drug has not been demonstrated in clinical trials. It is still contraindicated in patients with a history of thromboembolic disease, and dosage reductions are recommended in patients with renal insufficiency. The drug crosses the blood-brain barrier and the placenta, but excretion into breast milk is minimal. Therefore it is a safe treatment postpartum [17, 18].

Tranexamic acid significantly reduced mean blood losses with statistically significant reductions in transfusion requirements [19]. Efficacy of tranexamic acid in the control of bleeding has also been reported in numerous studies regarding cesarean section, placental abruption or postpartum hemorrhage [16]. It the presented case, it was proven that tranexamic acid can be a beneficial treatment for obstetrical patients with DIC.

Literature data show that there is a strong connection between hematological disorders, especially congenital thrombophilia and dismal pregnancy outcomes as miscarriage, placental abruption, or peri-neonatal ischemic stroke [20].

Placental abruption should be considered if hard and painful uterus is found and especially if the patient is bleeding. Ultrasound scan should always be performed in order to determine both retro-placental hematomas and the fetal condition. If bleeding is heavy, delivery should be carried out as soon as possible. Conservative approach is possible and safe. Disseminated intravascular coagulopathy is a common complication of placental abruption. Treatment of DIC consists of replacement of volume, blood products, coagulation components, cardiovascular, and respiratory support. Novel drugs, as tranexamic acid and desmopressin, are good treatment for obstetrical patients with DIC and therefore the present authors recommend their use. Optimal treatment of pathological conditions that lead to DIC can enable a healthy subsequent pregnancy.

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