Resistant Idiopathic Thrombocytopenic Purpura in Pregnancy; A Case Report

GEBELİKTE REZISTAN İDİOPATİK TROMBOSITOPENIK PURPURA: BİR VAKA SUNUMU

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Summary

Objective: *The aim of the study was to investigate a case of resistant idiopathic trombocytopenic purpura in pregnancy.*

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Material and Method: *A case of resistant idiopathic trombocytopenic purpura in pregnancy was presented and delivered by cesarean section.*

Findings: *Most patients with resistant idiopathic trombocytopenic purpura in pregnancy have a response to corticosteroids or intravenous immune globulin, but improvement is often transient. Our case was successfully managed with administration of pulsed high-dose oral dexamethasone.*

Conclusion: *The treatment of resistant idiopathic trombocytopenic purpura in pregnancy with pulsed high-dose oral dexamethasone offers ease of administration, a low cost-therapeutic option with minimal side effects in patient.*

Key Words: Idiopathic thrombocytopenic purpura, Pregnancy, Dexamethasone, Cesarean section

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Özet

Amaç: *Bu çalışmada, gebelikte resistan idiyopatik trombositopenik purpura vakasını araştırmak ve uygun bir yöntemle tedavi etmek amaçlanmıştır.*

Çalışmanın Yapıldığı Yer: *Marmara Üniversitesi Tıp Fakültesi Kadın Hastalıkları ve Doğum Anabilim Dalı.*

Materyel ve Metod: *Gebelikte resistan idiyopatik trombositopenikpurpura vakası tedavi sonrası sezaryen ile doğurtuldu.*

Bulgular: *Gebelikte resistan idiyopatik trombositopenik purpuralı hastaların çoğu kortikosteroidlere veya intravenöz immun globulinlere cevap verirler ancak bu cevaplar çoğu kez geçicidir. Bu yazıda gebelikte resistan idiyopatik trombositopenik purpura vakası yüksek doz oral deksametazon ile başarılı şekilde tedavi edilmiştir.*

Sonuç: *Gebelikte resistan idiyopatik trombositopenik purpura vakalarının yüksek doz oral deksametazon ile tedavisi hasta için kolay uygulanabilen, ucuz ve diğer tedavi seçeneklerine oranla çok daha az yan etkileri olan bir tedavi yöntemidir. Klasik tedavilere direnç gösteren resistan vakalarda uygulanabilir.*

Anahtar Kelimeler: Resistan idiyopatik trombositopenik purpura, Gebelik, Deksametazon, Sezaryen

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Autoimmune thrombocytopenia, also termed idiopathic thrombocytopenic purpura, is the maternal platelet disorder that first prompted concern about fetal thrombocytopenia. The disorder is most common in women, and more than70% of women with autoimmune thrombocytopenia are of childbearing age (1). Platelet autoantibodies facilitate increased platelet destruction by the reticuloendothelial system, especially the spleen. Immunoglobulin antiplatelet autoantibodies cross the placenta and place the fetus at risk for thrombocytopenia and serious bleeding problems such as intracranial hemorrhage (2). Thus avoidance of fetal hemorrhagic complications became the central issue in the obstetric management of women with autoimmune thrombocytopenia.

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The route of delivery was considered to have great impact on fetal-neonatal hemorrhage in women with autoimmune thrombocytopenia, after neonatal intracranial hemorrhage was first reported 20 years ago in association with vaginal birth (3). Passage through the birth canal was proposed as the reason for bleeding in thrombocytopenic fetuses (4).

However, others suggested that cesaren birth should be reserved for fetuses known to be severely thrombocytopenic (5). This approach was attractive because the risk of neonatal bleeding is inversely proportional to the platelet count, and bleeding complications are rare with platelet counts >50,000 cells/mm^3 (6). Because most fetuses have higher platelet counts, the majority of cesarean deliveries could potentially be avoided.

Case Report

A 29-year-old pregnant woman, gravida 2, para 0, abortus 1 was newly diagnosed with thrombocytopenia when a routine complete blood cell count revealed a platelet count of 36,000/mm^3 at 30,5 weeks of gestation. The repeat platelet count 1 week later was 24,000/mm^3. A diagnosis of idiopathic thrombocytopenic purpura was established after other causes of thrombocytopenia were ruled out.

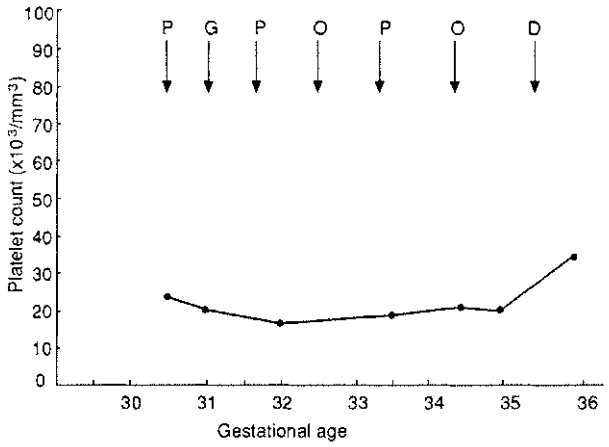
After the hematology consultation, oral prednisolone 1 mg/kg perday (total of 76 mg) was initiated. One week later no response was seen and intravenous IgG, 1 gm/kg was given. When she was at 32,5 weeks of gestation the repeat platelet count fell to 19,000/mm^3, and prednisolone 76 mg po was started again. Five days later the platelet count was 21,000/mm^3. The patient was treated with oral pulsed-dose dexamethasone 40 mg daily for 3 days only. Patient's platelet count rapidly increased to 34,000/mm^3. The patient tolerated the medication well. Patient's platelet count remained between 30.000 and 40.000 mm^3 without further treatment. Between the 32.5 and 36 weeks, patient was observed with NSTs, which were reactive. At 36 weeks of gestation NST became non-reactive, and the primigravid patient had a Bishop score of <5, and it was not appropriate for her to perform an elective induction. A cesarean section was therefore performed and a male infant with a weight of 3150 gm, Apgar score 9/10 was delivered.

At the preoperative period within a 2 hours time before the operation, 8 units of thrombocyte transfusion was started. Then, during the operation 4 units, and in the postoperative period another 4 units of thrombocyte transfusion was carried out.

At the second postoperative day the platelet count was 48,000/mm^3. In the early neonatal period, the infant's platelets were 372,000/mm^3. The neonatal course and maternal postoperative course were uncomplicated. On the third postoperative day the patient's platelet count fell down to 10.000/mm^3, and the patient was given 1 mg/kg po prednisolone. At the sixth day, when the platelet count still low 16,000/mm^3, prednisolon was increased to 2,5 mg/kg orally for 5 days.

Five days later, the platelets increased to 36,000/mm^3, it was decided to decrease the prednisolone dose to 48 mg daily. Meanwhile, the patient and her close relatives wanted to discharge from the hospital for social reasons. A meeting was made with the hematology clinics and they considered splenectomy for the patient. It was decided to follow the patient in the outpatient clinic on regular intervals.

The course of treatment during the pregnancy was shown in the figure below.



Changes in the platelet count after administration of prednisolone (P), intravenous immune globulin (G), and oral dexamethasone (D).

Discussion

Autoimmune thrombocytopenia can be difficult to distinguish from other causes of thrombocytopenia and is a diagnosis of exclusion. Although unexplained thrombocytopenia in pregnancy is often labeled as autoimmune thrombocytopenia, some women have other disorders, including incidental thrombocytopenia, preeclampsia, systemic lupus erythematosus, antiphospholipid syndrome, human immunodeficiency virus infection, disseminated intravascular coagulation, drug-induced thrombocytopenia, thrombotic thrombocytopenia, and pseudo-thrombocytopenia as a result of laboratory artifact.

Incidental thrombocytopenia of pregnancy describes a mild (usually >80,000 cells/mm^3 platelet count), common (up to 5%), asymptomatic thrombocytopenia that occurs during pregnancy (7). This accounts for >70% of thrombocytopenia in pregnant women (8). The cause of thrombocytopenia in these women is unclear but may be an acceleration of the physiologic pattern of increased platelet destruction (8). Women with incidental thrombocytopenia are healthy, not at risk for fetal thrombocytopenia or bleeding complications, and have no history of autoimmune thrombocytopenia (9). The only infant bom to a cohort of 756 women with incidental thrombocytopenia and a platelet count <50,000 cells/mm^3 had congenital bone marrow dysfunction (8). Others have confirmed the extremely low risk of fetal thrombocytopenia in women with incidental thrombocytopenia (TO).

Over the past few years several investigators have made convincing and eloquent arguments for the conservative management of women with incidental thrombocytopenia and autoimmune thrombocytopenia (11). Recommendations are to deliver by cesarean section only for obstetric indications, without determining the fetal platelet count. Nevertheless, same cases of thrombocytopenia are still managed with cordocentesis, fetal scalp sampling, and cesarean delivery (12). We share the universal desire to prevent the life-threatening morbidity of neonatal bleeding and intracranial hemorrhage. However, we propose that it is time to discard the routine use of these invasive tests and treatments.

In summary, the risk of serious fetal or neonatal hemorrhage is quite low in women with autoimmune thrombocytopenia and negligible in those with incidental thrombocytopenia. Fetal scalp sampling and cordocentesis lead to unnecessary cesarean sections. Finally and perhaps most important, it has not been shown that vaginal delivery causes hemorrhage in fetuses with thrombocytopenia or that cesarean delivery prevents it. These interventions in women with incidental thrombocytopenia and autoimmune thrombocytopenia are costly, potentially risky, and ineffective in the prevention of neonatal bleeding complications. Evidence docs not support the routine use of fetal scalp sampling, cordocentesis, and cesarean delivery in women with thrombocytopenia.

This case illustrates the potential usefulness of pulsed-dose oral dexamethasone for refractory idiopathic thrombocytopenic purpura in pregnancy. Other medications used in this setting (e.g., intravenous Rh immunoglobulin, danazol, vincristine, and colchicine) have undesirable effects in pregnancy and potential fetal risk. This dexamethasone regimen was described by Anderson (13). In that report, patients who had failed to maintain adequate platelet levels in spite of multiple treatment modalities (including high-dose prednisone in addition to splenectomy, intravenous IgG, or chemotherapy) all had significant improvement with pulsed-dose oral dexamethasone. This improvement in platelet levels persisted for >6 months of posttreatment follow-up, and no significant side effects were identified.

The principal concerns with the use of pulsed-dose dexamethasone are maternal immune suppression and maternal or fetal adrenal suppression. Immune suppression does not appear to be a clinical risk until the regimen has been used for 3 or less months. Clinical experience with repeated dosing of long-acting steroids in comparable cumulative doses suggests that any maternal or fetal adrenal suppression with pulsed-dose steroids is clinically insignificant in the first 3 months of the treatmant (14).

In addition to improvement in platelet status, this treatment also offers benefits because of its low cost and ease of dosing. The cost of intravenous IgG therapy approaches $120/per gm a day for the

medication alone. In contrast, dexamcthasone would cost < S5 per day. The benefits of oral dexamcthasone in terms of efficacy, cost, and ease of administration make it a reasonable if not preferred alternative.

Differential diagnosis for ITP include common disorders, such as autoimmune diseases, and lymphomas, which were exclucded in this case by negative tests for ANA (antinuclear antibody), anti DNA antibody, rheumatoid factor, normal lactad dehydrogenase, sedimentation rates, and normal abdominal ultrasound.

Future studies should pursue the efficacy and safety of pulsed high-dose oral dexamethasone as second-line therapy for those pregnant patients with idiopathic thrombocytopenic purpura who fail to respond to high-dose prednisone.

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