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Case Report

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Severe Immune Thrombocytopenic Purpura in a Patient at 33 Weeks of Gestation: A Case Report

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Abstract

Background: Immune thrombocytopenia (ITP) is an autoimmune condition that affects individuals of all ages, leading to a heightened risk of bleeding. ITP accounts for 5% of all pregnancy-related thrombocytopenia cases with an incidence of 1 in every 1,000 pregnant women. Several conditions can cause thrombocytopenia during pregnancy, making the diagnosis challenging. Current treatment of patients with ITP focuses on maintaining a safe platelet count rather than correcting it to normal levels.

Case Presentation: This article presents a case of a 26-year-old patient at 33 weeks of gestation with severe symptoms of thrombocytopenia, evidenced by a platelet count of 1000/mm^3. The patient experienced self-resolving episodes of gingival bleeding, vaginal bleeding, and petechiae on her abdomen, as well as on both upper and lower extremities, over a duration of three days. She was successfully managed with prednisolone and intravenous immunoglobulin (IVIG), resulting in favorable maternal and neonatal outcomes.

Conclusion: While there are currently no universally accepted guidelines for the treatment of ITP, expert consensus recommendations are available. Therefore, treatment should be individualized and closely monitored. A multidisciplinary team approach is essential for the effective management of ITP during pregnancy.

Keywords: Bleeding, Immune thrombocytopenia, Immunoglobulins, Platelet count, Prednisolone, Pregnancy, Purpura.
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Introduction

Immune thrombocytopenia or immune thrombocytopenic purpura, previously referred to as idiopathic thrombocytopenic purpura, is an autoimmune condition that targets both the adult and pediatric populations. It usually presents with a transient or a persistent thrombocytopenia which, depending on the severity, increases the risk of bleeding (1). ITP is classified into primary and secondary forms. Primary ITP is characterized by an isolated thrombocytopenia (less than 100×10^9 cells/L), with the absence of any other causes that may be associated with thrombocytopenia. It remains a diagnosis of exclusion.

On the other hand, secondary ITP is usually associated with an underlying disease or a drug-mediated thrombocytopenia (2). The distinction between primary and secondary ITP has a clinical importance due to their distinct nature and treatment options (2). ITP is usually classified into four phases: "Newly Diagnosed" ITP which occurs within 3 months from diagnosis, "Persistent" ITP which lasts between 3 and 12 months,

"Chronic" ITP which persists for more than 12 months, and "Severe" ITP characterized by bleeding symptoms that require treatment (2). ITP accounts for 5% of all pregnancy-related thrombocytopenia cases with an incidence of 1 in every 1,000 pregnant women (3).

ITP symptoms are similar in both pregnant and non-pregnant patients, with most cases being asymptomatic and mild, presenting with incidental thrombocytopenia during routine examinations (4). More rarely, ITP presents with clinical features including extensive petechiae and purpura, epistaxis, gingival bleeding, excessive bruises, prolonged bleeding from cuts, and hematochezia (4). Women who have a history of ITP before pregnancy are at a higher risk of developing a more symptomatic form of the disease once they become pregnant (4). A retrospective study by Webert K E et al of 92 patients who had 119 pregnancies over 11 years showed that patients with a previous diagnosis of ITP were more likely to require therapy than those who developed ITP for the first time during pregnancy (5).

ITP is mediated by antibodies that target many platelet surface glycoproteins including GP Ib/IX and GPIIb/IIIa (3). These autoimmune complexes trigger platelet destruction by the reticuloendothelial system of the spleen, followed by macrophage phagocytosis through Fcγ receptors (3). As a result, the bone marrow compensates by increasing the production of megakaryocytes which can be detected on bone marrow aspirate (3) and eventually in peripheral blood (4).

According to British Committee for Standards in Haematology General Haematology Task Force, treatment of patient with ITP aims to provide a safe platelet count rather than correcting it to normal levels (6, 7). The severity of the illness and the age of the patient must be accounted for in order to decrease the risk of bleeding and death (8). It has been shown that both bleeding risk and fatality rates increase with age (8) and that the risk of serious bleeding significantly rises when platelet counts fall below 30×10^9 cells/L (9). Accordingly, treatment should be reserved for patients with bleeding symptoms or platelet counts below 30×10^9 cells/L due to the potential toxicity associated with available treatment options (6, 10).

Universally accepted guidelines on the treatment of ITP still do not exist, as no randomized controlled trials have been published yet. However, an expert consensus is available. As a result, treatment must be individualized and closely monitored. Risk of hemorrhage should always be kept in mind when choosing the proper treatment. Therefore, ITP in pregnancy constitutes a prime example of a condition that requires a multidisciplinary collaboration among hematologists, obstetricians, neonatologists, and anesthesiologists (11-13).

Table 1 demonstrates the comparisons between the current treatment options for ITP. Steroids and IVIG remain the mainstay of therapy (14). Treatment can also be initiated if symptoms of thrombocytopenia begin to appear (epistaxis, petechiae, gingival bleeding, excessive bruises, prolonged bleeding from cuts, hematochezia), regardless of platelet level (15). Steroids are the first-line therapeutic agents for asymptomatic patients, with studies indicating a response rate of 70%. However, their use is associated with adverse effects including hypertension, Cushing's syndrome, and elevated intracranial and intraocular pressure (16). Dosage of administered prednisone is usually between 0.5 and 2 *mg/kg/day*, with a therapeutic response typically observed over several weeks (17).

Treating physicians revert to IVIG as the first-line treatment for symptomatic patients or when platelet levels fall below 10×10^9 (16). IVIG dosing has changed from 0.4 *g/kg/day* administered over 5 days to newer protocols that suggest the

Table 1. Treatment options for pregnancy induced ITP (17)

Treatment	Response rate (%)	Dosage	Time for response
Prednisone	70	0.5-2.0 *mg/kg/day*	Several days to weeks
IVIG	70	1000 *mg/kg/day*	1 to several days
Rituximab	40	100-375 mg/m^2	Several weeks
Intravenous anti-D	70	75 *µg/kg*	1 week
Romiplostim	80	1-10 *µg/kg*	More than 1 month
Eltrombopag	80	25-75 *mg/day*	More than 1 month
Splenectomy	80	-	-

administration of 1 *g/kg* over one or two infusions in 48 *hr* (18). The latest protocol leads to an elevation of platelet levels within a shorter time frame as adopted from the American Society of Hematology (17). Despite the quicker response, rare cases of thrombosis and renal failure have been reported (17). Some studies have shown that the combination of both corticosteroids and IVIG lead to a synergistic effect (18, 19).

The second-line treatment options available include Rituximab, thrombopoietin receptor antagonist (Romiplostim, Eltrombopag) (11, 19), intravenous anti-D, and splenectomy in pregnant women who are in their second trimester of pregnancy (20).

In this paper, a rare case of a 26-year-old pregnant patient is described who presented to our hospital with severe symptoms of ITP and a platelet count of 1000/mm^3. The condition was successfully managed, resulting in a good maternal and neonatal outcome.

Case Presentation

A 26-year-old female patient, with an obstetric history of Gravida 3 Para 1, and a known diagnosis of gestational hypertension controlled with Nifedipine, was referred to our institution (Saint George Hospital University Medical Center, Beirut, Lebanon) in 2019 at 33 weeks of gestation for a routine nonstress test (cardiotocography).

The patient reported self-resolving episodes of epistaxis for three days, gingival bleeding, and petechiae on her abdomen and both upper and lower limbs (Figures 1A, 1B, and 1C). She also reported one episode of vaginal bleeding and two episodes of diarrhea on the same day of presentation. She reported no experience of contractions, fluid leakage, headache, or epigastric pain. There was no history of trauma or recent initiation of a new medication prior to the onset of these symptoms. However, she had a history of one previous preterm delivery (spontaneous vaginal delivery) and one spontaneous miscarriage at an unknown gestational age. Her blood group was A+, and she had undergone a splenectomy due to a war-related trauma in 1993, when she was one year old. She was a non-smoker, denied alcohol consumption and had no known food or drug allergies. The patient was taking aspirin, Nifedipine, and multivitamins. The aspirin was prescribed for preeclampsia prophylaxis but was discontinued upon the diagnosis of ITP.

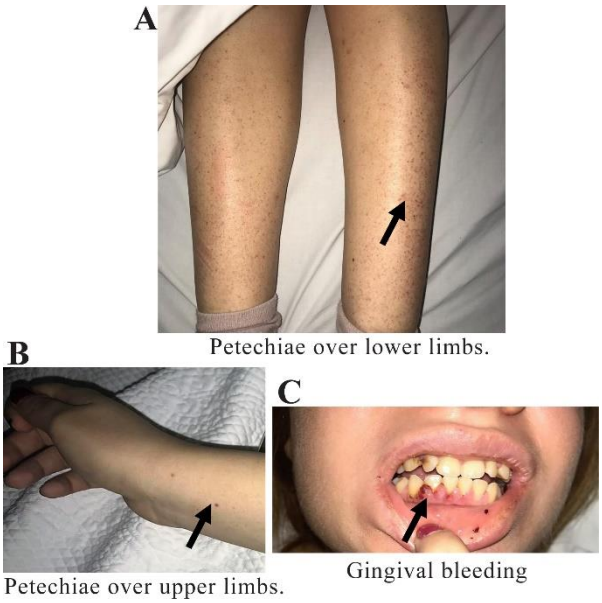

Figure 1. Clinical presentation of the patient

Upon arrival, her initial vitals were as follows: heart rate of 100 *bpm*, temperature of 36.6°*C*, and blood pressure of 145/90 *mmHg*. Laboratory tests and blood smear obtained upon presentation showed a platelet count of 1000/mm^3, which was repeated for confirmation, with no evidence of hemolysis or pancytopenia. Blood smear test confirmed thrombocytopenia with absence of platelet clumping on examination.

Following these results, the patient was admitted to the hospital, and a multidisciplinary approach was initiated, involving consultations with a hematologist, perinatologist, and a neonatologist to investigate her marked thrombocytopenia. Two units of platelets were transfused immediately, and 40 *mg* of dexamethasone per day were started in accordance with Bussel, JB et al and Mithoowani, S et al respectively (21, 22). The fetus was monitored using a nonstress test twice a day. The fetal ultrasound performed upon admission showed no abnormalities.

Inpatient management: Secondary thrombocytopenia was ruled out, as the patient had not initiated any new medications and exhibited no history of bruising or petechiae prior to pregnancy. HELLP syndrome, disseminated intravascular coagulation (DIC), preeclampsia, and acute fatty liver were ruled out by laboratory findings including normal liver enzymes, normal coagulation panel, and no proteinuria. The patient's blood smear indicated thrombocytopenia, characterized

by the presence of anisocytosis and the absence of abnormal white blood cells (WBC). Gestational thrombocytopenia was ruled out due to the significantly low platelet count. Additionally, congenital thrombocytopenia and pancytopenia were also excluded due to the normal platelet levels in the neonate after delivery. An immunoassay was conducted, yielding negative results except for the presence of immunity to hepatitis B and cytomegalovirus (CMV) (Table 2).

The diagnosis of immune thrombocytopenic purpura was confirmed. The patient received a daily dose of 40 *mg* of dexamethasone since the day of hospitalization, for a total of four days. Following this treatment, the platelet count increased to 20000/mm^3, but subsequently declined to 1000/ mm^3 two days later, showing a persistent grade 4 thrombocytopenia without any new bleeding episodes.

On day 9, IVIG was initiated along with a second course of dexamethasone, administered intravenously at a dose of 6 *mg* every 12 *hr* for a total duration of four days. During this treatment period, the platelet count increased from 5000/mm^3 on day 8 to 38000/mm^3 on day 10, before falling to 23000/mm^3 on day 13. Detailed platelet count values are presented in figure 2.

A second course of IVIG was administered on days 14 and 15, at a dosage of 1 *g/kg* per day over a 48-*hr* period. Platelet count rose above 50000/mm^3 for the first time during her hospitalization. During her stay, the patient received a total of 15 units of platelet transfusions. Throughout her treatment, no side effects of the given IVIG were noted; the patient reported no symptoms of headache, nausea, or vomiting. Additionally, there was no evidence of decreased urine output or any signs of acute kidney injury.

Table 2. Immunoassay results

Parameters	Results
HIV ag/ab	0.13 S/CO
HCV Ab	0.06 S/CO
HBs Ab	95.28 *mIU/mlH*
HBs antigen	0.17 S/CO
CMV IgG	87.5 *AU/ml* H
CMV IgM	0.32 Index
EBV IgM (VCA)	0.24 S/CO
EBV IgG (VCA)	41.89 S/CO
Direct coombs test	Negative
Indirect antiglobulin coombs test	Negative

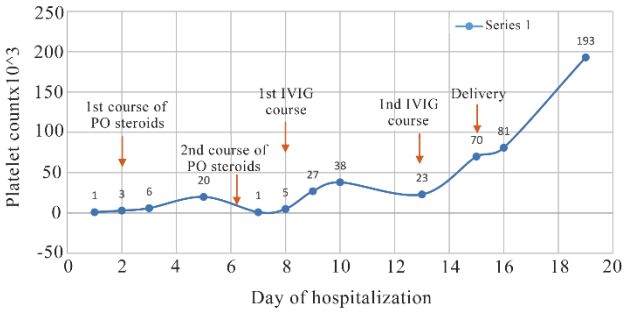

Figure 2. The platelet counts during the patient's hospital stay shown as days of hospitalization. The platelet count increased from 1000/mm^3 on the day of admission to 70,000/mm^3 on the day of delivery. This rise in platelet count was the result of steroid and IVIG treatments

It is important to note that the fetal ultrasound performed on day 9 of hospitalization (at 34 weeks and 6 days of gestation) revealed oligohydramnios with an amniotic fluid index (AFI) of 3. The estimated fetal weight (EFW) was 2453 *g*, which is at the 35th percentile. No gross congenital abnormalities or signs of thrombocytopenia were observed. The umbilical artery Doppler examination showed normal results. On day 15, AFI dropped to 1.8, showing severe oligohydramnios, while the EFW was 2628 *g* at the 36th percentile, with no signs of intracranial hemorrhage. Considering these factors, the team decided to perform a cesarean section at 35 weeks and 5 days, due to the presence of oligohydramnios and an increase in the platelet count to 50,000/mm^3. The major concern was that inducing labor could lead to further decrease in the platelet count. This would limit the patient's ability to benefit from locoregional anesthesia and the risk of postpartum hemorrhage could be increased.

Two units of packed red blood cells (RBC) and eight units of platelets were prepared prior to surgery. The cesarean section was performed under spinal anesthesia, with a Pfannenstiel incision. The placenta was extracted and sent to pathology. Estimated blood loss was within normal levels post Cesarean section. A living baby girl was born with an Apgar score of 8 at 1 *min*, 5 at 5 *min*, and 5 at 10 *min*, weighing 2600 *g*. At birth, she required oxygen support via an ambu-bag and was subsequently transferred to the NICU, where she was placed on bubble CPAP due to apnea on day 1 of life. She was discharged from the NICU 3 days later. Umbilical cord blood tests at delivery, as well as on days 3 and 5, showed no abnormalities, and no evidence of neonatal alloimmune

thrombocytopenia was noted. The patient was discharged on day 4 with a platelet count rising from 50000/mm^3 preoperatively to 193000/mm^3 postoperatively, and a hemoglobin level of 9.6 *g/dL*.

At the postpartum visit, the patient reported no gingival bleeding or petechiae on her abdomen or extremities. Her blood tests showed normal platelets levels of 165000/mm^3 and a normal hemoglobin level of 11.3 *g/dL*. Subsequent follow-up did not indicate thrombocytopenia in either the mother or the baby.

Discussion

Generally, the primary function of platelets is to facilitate blood clotting. A decrease in platelet levels increases the risk of bleeding and bruising, and such bleeding may be difficult to control (23). Immune thrombocytopenic purpura is an autoimmune condition in which the body produces antibodies that target its own platelets, leading to a reduction in platelet count (23). There are many known and some unknown risk factors associated with the development of ITP. During pregnancy, ITP poses significant risks for the mother and can complicate childbirth. As an autoimmune condition, these antibodies can occasionally cross the placenta and attack the fetal platelets (24). Generally, most cases of ITPs in pregnancy do not require treatment. ITP is suspected when platelet levels drop below 100,000/mm^3 and more specifically if they fall below 80,000/mm^3. Platelet levels can guide treatment decisions, with normal ranges typically between 150,000/mm^3 to 400,000/mm^3. Treatment is usually indicated if platelet levels drop below 20,000/mm^3 in pregnancy or if the patient is symptomatic (25). Treatment is also recommended when platelet levels fall below 50,000/mm^3 around delivery. Locoregional anesthesia is usually considered safe when platelet levels are above 70,000/mm^3 (25). Symptoms of thrombocytopenia range from petechiae, purpura, mucosal bleeding, and the difficulty to stop bleeding following an injury.

The mainstay treatments of ITP in pregnancy are prednisolone and IVIG. Prednisolone is indicated when platelet levels drop below 50,000/mm^3 while IVIG is used when the platelet levels drop below 20,000/mm^3 (25). Prednisolone acts by stopping the immune system from destroying the body's own platelets (26). In contrast, intravenous immunoglobulins function by inhibiting the antibodies from attacking the body's own platelets (26). A multidisciplinary team approach in the management of ITP is essential to ensure safe maternal and neonatal outcomes.

Conclusion

Immune thrombocytopenic purpura is a rare but significant cause of thrombocytopenia during pregnancy. Although it most commonly presents in the first trimester, it can occur at any time during gestation. Women with ITP are at a higher risk of severe postpartum hemorrhage, making it essential for them to deliver in specialized units equipped to handle such complications. The mainstays of treatment for ITP include IVIG and low-dose corticosteroids. Moreover, newborns should be screened for neonatal immune thrombocytopenia. Accurate diagnosis of ITP is crucial, as it facilitates the exclusion of other potential causes of thrombocytopenia and is essential for effective management.

Conflict of Interest

Authors declare no conflict of interest.

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