CASE REPORT

Case of twin pregnancy complicated by idiopathic thrombocytopenic purpura treated with intravenous immunoglobulin: Review of the literature

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Abstract

Idiopathic thrombocytopenic purpura (ITP) is an acquired thrombocytopenia without other clear cause of thrombocytopenia. It is not common in a singleton pregnancy and less common in twin pregnancy. We report a 33-year-old ITP pluripara whose first pregnancy was uneventful. She carried twin pregnancy, complicated by recurrent very low platelets, and gave birth to preterm twins. This patient received multiple courses of intravenous immunoglobulin (IVIG) and showed a significant platelet count improvement with IVIG therapy.

Key words: Idiopathic thrombocytopenic purpura, intravenous immunoglobulin, twin gestation

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Introduction

Idiopathic thrombocytopenic purpura (ITP) is an acquired thrombocytopenia without other clear cause of the thrombocytopenia. It may result from antiplatelet antibodies which can accelerate clearance and destruction of opsonized platelets by the reticuloendothelial system. In addition, antiplatelet antibodies also target antigens on megakaryocytes so that platelet production is suppressed.[1]

ITP is not common in pregnancy, and less common in twin pregnancy. In general, patients with ITP experience, a severe reduction of platelet count during pregnancy,[2] which is more severe in women with twin pregnancies.[3] Herein, we present a pluripara with ITP who carried twin pregnancy complicated by recurrent very low platelets. Her pregnancy ended in preterm delivery. Her preceding first pregnancy was uneventful.

Case Report

A 33-year-old woman with twin pregnancy, gravida 3 para 1 was found a low platelet count of 16 × 10^9/L at 12 weeks and 1 day of gestation during her first antenatal care visit. She denied any history of hematemesis or epistaxis. She was admitted.

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At 23-year-old, she experienced easy bruising with a low platelet count of 13 × 10^9/L. After the exclusion of all other causes of thrombocytopenia, including a normal bone marrow examination, a diagnosis of ITP was made. She was treated with prednisone for 1 month, and platelet count was improved to 80 × 10^9/L. During pregnancy with her first baby 6 years ago, the platelet was kept at the level of 60 × 10^9/L. Such level of platelet was maintained until the first trimester of this pregnancy.

On this admission, the complete blood count test showed a low platelet count of 16 × 10^9/L. Laboratory examinations were otherwise unremarkable. The patient had no complaint of bleeding or bruising, and physical examination revealed no signs of bleeding. She received intravenous immunoglobulin (IVIG) 0.4 g/kg/day for five consecutive days. The platelet count on day 3 of the 5-day IVIG treatment was raised to 60 × 10^9/L. At 15 weeks and 2 days of gestation, another IVIG therapy was administered. She received complete 5-day injections of IVIG every 2–3 weeks until delivery at 32 weeks and 6 days of gestation. The details are shown in Table 1. At 29 weeks and 2 days of gestation, because of regular uterine contractions and decreasing cervical length, the oxytocin receptor antagonist atosiban was administered. At 32 weeks of gestation, she experienced frequent uterine contractions. She was given prednisone (25 mg bid) to raise platelet count because preterm delivery was anticipated. At 32 weeks and 6 days of gestation, preterm labor was inevitable with a 2-cm dilation of cervical os. Cesarean section was performed because of the second twin in a transverse lie. The birth weight of the first twin was 2015 g (at the 52nd percentile for birth weight), and Apgar score was 10. The second twin weighed 2160 g (at the 65th percentile for birth weight) and her Apgar score was 9. Both twins shared a common placenta, weighing 650 g. The platelet counts of both newborns were normal.

Table 1: Details about intravenous immunoglobulin therapy

Gestational age (weeks)	Platelet count before IVIG (×10^9/L)	Platelet count day 5 of IVIG (×10^9/L)
12+1	16	60
15+2	15	70
18	6	36
20+2	8	40
23+4	1	31
26+4	10	28
29+2	10	29
32	7	74

IVIG=Intravenous immunoglobulin

Discussion

Diagnosis of idiopathic thrombocytopenic purpura in pregnancy

The incidence of ITP varies from 1 in 1000 to 2 in 1000 pregnancies.[4] Compared to an ITP diagnosis during pregnancy, a diagnosis of ITP before pregnancy may indicate a higher risk for obstetric complication, such as fetal loss or stillbirth, premature delivery.[5] As in the nonpregnant patients, the diagnosis of ITP in pregnant women is a clinical one.[6] Since there are no diagnostic tests to confirm ITP, the diagnosis of ITP in pregnancy is made by exclusion of secondary causes of thrombocytopenia, such as gestational thrombocytopenia, preeclampsia and hemolysis, elevated liver enzymes, and low platelets syndrome. Antibody testing for ITP utilizing the monoclonal antibody-specific immobilization of platelet antigens assay in pregnant women is unnecessary for lack of diagnostic specificity.[7,8] In a large study,[9] autoantibodies were identified in <7% of thrombocytopenic pregnant women. Moreover, the prevalence of autoantibodies between thrombocytopenic and nonthrombocytopenic pregnant women was not statistically significant.[9] Furthermore, maternal circulating antiplatelet antibodies did not correlate with neonatal thrombocytopenia.[6] Similarly, as in nonpregnant individuals, bone marrow examination is not recommended for diagnosis of ITP.[6,10]

Kasai *et al.* found that gestational thrombocytopenia with platelet counts of <10 × 10^9/L is common in twin pregnancies,[11] which suggests that twin pregnancy complicated by ITP will experience much lower platelet counts than singleton pregnancy with ITP. In the present paper, our patient presented with severe thrombocytopenia as early as in the first trimester of her twin pregnancy whereas her first childbirth was uneventful.

Differential diagnosis

Gestational thrombocytopenia is the most common cause of thrombocytopenia during pregnancy (approximately 75% of cases). ITP may be difficult to differentiate from it. However, gestational thrombocytopenia is generally associated with mild thrombocytopenia, usually >70 × 10^9/L, whereas severe thrombocytopenia is common in pregnancy complicated by ITP. Gestational thrombocytopenia usually takes place during the second or third trimester of pregnancy while ITP is often first recognized in the first trimester. Adverse events for the mother and newborn are rare in patients with gestational thrombocytopenia. In most cases, pregnancy might result in worsening of thrombocytopenia in ITP patients.[12] This may result from the effects of the hormonal milieu of pregnancy on the reticuloendothelial

system, which is similar to those reported in autoimmune hemolytic anemia.[13]

Management of idiopathic thrombocytopenic purpura in pregnancy

The management of ITP in pregnant women is similar to that in nonpregnant women. Experts on the American Society of Hematology (ASH) panel recommended treatment when a platelet count is below 10×10^9/L at any time during pregnancy, below 30×10^9/L in the second or third trimester, or when the patients present with bleeding.[7] In the British Committee for Standards in Haematology (BCSH) guidelines, it was recommended that treatment should be considered when the platelet count is below 20×10^9/L at any time during pregnancy.[8] In this patient, we initiated treatment when the platelet count was below 20×10^9/L.

Either corticosteroids or IVIG can be used as a first-line treatment during pregnancy.[10] Both are safe with regard to teratogenicity. In China, corticosteroid treatment is preferred for the cost is very expensive in IVIG use. When corticosteroids are chosen, their maternal side effects including the exacerbation of gestational diabetes mellitus (GDM) and induction of hypertension should be considered. ASH prefers longer courses of corticosteroids to shorter courses of corticosteroids. Longer courses of corticosteroids begin with prednisone 1 mg/kg/day orally for 21 days and then tapered off while shorter courses of corticosteroids consist of dexamethasone 40 mg/day orally for 4 days.[10] IVIG can be used with or without corticosteroids. It would raise platelet count rapidly. However, there are some patients who fail to respond to IVIG. ASH recommends an initial dose of 1 g/kg when IVIG is required. When the patients fail to respond to this dosage of IVIG, two choices can be considered: Higher doses (i.e., 2 g/kg)[14] of IVIG or corticosteroids. The dosage may be repeated when the platelet count falls below 20×10^9/L.

After the failure of first-line treatments, a thrombopoietin receptor agonist can be chosen. However, more studies are needed to research its safety for fetuses.[15]

The management of ITP in women with twin pregnancy is the same as in those with singleton pregnancy. However, the difference between the two groups should be noted. Twin pregnancy is associated with a higher risk of developing hypertension and GDM than singleton pregnancy[16,17] while the use of corticosteroids during pregnancy also increases the risk of hypertension and GDM. Therefore, taking into account that twin pregnancy is at higher risk of hypertension and GDM than singleton pregnancy when using corticosteroids, IVIG was chosen as the first-line treatment for our patient (0.4 g/kg/day for 5 consecutive days). We intended to administer corticosteroids before anticipated delivery to reduce their maternal side effects with administration of short-term corticosteroids. As shown Table 1, our patient required repeat treatment at 2–3-week intervals, and the response was weaker after two repeat IVIG treatment. The time interval of IVIG treatment for our patient was shorter than the time reported by Ali *et al.*[18] At 32 weeks of gestation, our patient experienced regular uterine contractions and decreasing cervical length. She was treated with atosiban, an inhibitor of the hormone oxytocin. Taking into account the possibility of preterm labor, our patient was prescribed prednisone (50 mg/day) along with IVIG to rapidly raise the platelet count. An excellent platelet response was found. As shown in Table 1, the platelet count on the day 5 of IVIG and prednisone rose to 74×10^9/L. In our experience, we found that the singleton pregnant patients complicated by ITP, who had a good platelet response to IVIG were prone to respond to prednisone therapy. For patients with platelet counts between 20 and 50×10^9/L who receive no therapy during pregnancy, short-term corticosteroids (10–20 mg/day) 1–2 weeks before anticipated delivery, or IVIG to prepare for delivery is recommended.[19]

Delivery

Both ASH and BCSH guidelines conclude that the maternal platelet count is not associated with neonatal thrombocytopenia. Therefore, for pregnant women with ITP, the mode of delivery should be decided on obstetrical criteria.[10] BCSH guidelines recommend that a maternal platelet count of 50×10^9/L is appropriate for vaginal delivery and platelet counts $>80 \times 10^9$/L are safe for spinal and/or epidural anesthesia and cesarean section if coagulation is otherwise normal.[8] When emergent deliveries happen to those ITP patients whose platelet counts are below adequate level, platelet transfusion is considered. Platelet transfusion in conjunction with IVIG is preferred to platelet transfusion alone because platelet transfusion alone results in inadequate posttransfusion increments or an initial rise in platelet count followed by returning to the baseline platelet count at subsequent 8-h or 12-h posttransfusion. Anesthesiologists in our center suggest a threshold of platelet counts $>75 \times 10^9$/L for spinal and/or epidural anesthesia, and we think this level is safe for cesarean section. At 32 weeks and 6 days of gestation, inevitable preterm labor happened to our patient. Because of the second twin in a transverse lie, she gave birth by cesarean section to two newborns with normal platelet counts. The patient had general anesthesia instead of spinal and epidural anesthesia because of her low platelet count of 74×10^9/L. The surfactant was administrated to the preterm twins.

Conclusion

The patients with twin pregnancy complicated by ITP are at risk of severe thrombocytopenia during pregnancy.

They should be monitored by multidisciplinary groups, including obstetricians, hematologists, neonatologists, and anesthesiologists, once pregnancy is confirmed and be administered optimal therapy when necessary.

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Conflicts of interest

There are no conflicts of interest.

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