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Research Letter

Management of severe immune thrombocytopenic purpura in a pregnant woman with inevitable preterm forceps breech delivery

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During pregnancy, maternal thrombocytopenia, platelet count below 100×10^9/L, is often associated with gestational thrombocytopenia, preeclampsia, systemic lupus erythematosus, immune thrombocytopenic purpura (ITP), drug-induced thrombocytopenia, antiphospholipid antibody syndrome, disseminated intravascualr coagulopathy, viral infection, vitamin B12 or folic acid shortage, and hypersplenism. ITP is caused by autoantibodies targeting platelet glycoprotein IIb/IIIa, Ib/IX, Ia/II, IV, and V. Antiplatelet antibodies may induce platelet aggregation and precipitate destruction of antibody-coated platelets by reticuloendothelial uptake. ITP is diagnosed by exclusion, meaning that it is diagnosed once other causes of thrombocytopenia are ruled out. Herein, the successful management of a case of severe ITP in a pregnant woman with inevitable preterm vaginal breech delivery is presented.

A 28-year-old Gravida 1 woman who had chronic ITP and was receiving regular follow-up at hematological clinics visited our delivery room at 31 gestational weeks because of preterm labor with a 2.5-cm dilation of cervical os, rupture of the amniotic membrane, and breech presentation. Her dosage of prednisolone had been increased from 20 mg/d to 30 mg/d at 29 gestational weeks because of a low platelet count of 17×10^9/L. On this admission, laboratory examinations revealed a platelet count of 30×10^9/L, a hemoglobin level of 11 g%, normal coagulation tests (prothrombin time and activated partial thromboplastin time), and no evidence of infection. Because she was going into active labor, she was given two alternative doses of dexamethasone (12 mg, 12 hours apart) to enhance fetal lung maturity and to treat maternal ITP. A total of 15 g of intravenous immunoglobulin (IVIG) (TBSF; CSL limited, Australia) was slowly administered (3 g each), the last infusion administered 6 hours before delivery. One adult dose of platelets was transfused 30 minutes before delivery. Fourteen hours after admission, a 1,610 g healthy boy was delivered by first intravenously administering nitroglycerine (NTG) for uterine/cervical relaxation and then delivering the fetal head with the use of Piper forceps. Apgar scores of the newborn were 6 and 7 at 1 and 5 minutes, respectively. The platelet count of the newborn was 174×10^9/L. Oxytocin, methylergonovine, transamine, and misoprostol (0.8 mg, rectal insertion) were given to prevent postpartum hemorrhage (PPH). The patient lost about 400 cc of blood and withstood the whole procedure very well. Unexpectedly, 90 minutes after delivery she lost an additional 300 cc of blood in the recovery room. Because the patient was not found to have retained placenta and genital tract laceration during delivery, she was given four units of vasopressin diluted to 100 cc and administered by injection into the uterine cervix, and she was also intravenously administered 1.2 mg of recombinant activated factor VII (Novo 7; Novo Nordisk, Denmark). This brought her uterine bleeding under control. Abdominal sonography revealed some blood clots, about $8 \times 3 \times 2$ cm, in the uterine cavity. She was prescribed oral misoprostol (0.2 mg/d) for 3 days and discharged in stable condition on postpartum Day 3. Her clinical course is summarized in Table 1. To date, the infant, currently 8 months old, has developed normally.

ITP is managed the same regardless of whether the patient is pregnant or not. Prednisolone is often used as an initial therapy with platelet counts ranging between 30×10^9/L and 50×10^9/L, depending on symptoms [1]. It is critical to avoid unnecessary treatment of asymptomatic patients with mild-to-moderate thrombocytopenia. Splenectomy, which can achieve a 65% complete remission rate by decreasing destruction of antibody-coated platelets and reducing antiplatelet antibody production, is always reserved for patients who have serious manifestations of ITP unresponsive to steroid therapy [2]. The effect of IVIG occurs quickly and elicits a higher response rate than steroid, making it a good alternative therapy for patients resistant to steroids. A platelet count higher than 50×10^9/L is considered safe for vaginal or cesarean delivery [3].

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Table 1
Summary of the clinical course

	Day −14	Labor, Day −1	Delivery, Day 0	PP Day 1	PP, Day 6	PP, Day 14
Platelet count	17×10^9/L	30×10^9/L	25×10^9/L	93×10^9/L	106×10^9/L	37×10^9/L
Transfusion			Platelets, 1 unit, before delivery			
Prednisolone	15 mg b.i.d.	15 mg b.i.d.	15 mg	15 mg b.i.d.	10 mg b.i.d.	10 mg b.i.d.
Dexamethasone		12 mg	12 mg (2 hr before delivery)			
IVIG		9 g	6 g (finished 6 hr before delivery)			
Delivery room			NTG; Piper forceps			
			Blood loss 400 cc			
			Uterotonic, transamine			
Recovery room			1.5 hr later, uterine bleeding 300 cc			
			vasopressin four units, novo 7 (1.2 mg)			

b.i.d. = twice a day; IVIG = intravenous immunoglobulin; NTG = nitroglycerine; PP = postpartum.

The main treatment goal for ITP is to provide a safe platelet count to prevent major hemorrhage when patients are bleeding or at risk of bleeding, rather than returning the platelet count to normal [1]. Patients are potentially at risk of prolonged bleeding after minor trauma when the platelet count is less than 50×10^9/L [4]. Spontaneous bleeding may occur at platelet counts between 20×10^9/L and 30×10^9/L. Life-threatening bleeding, including intracranial bleeding, has been reported at platelet counts below 10×10^9/L. Corticosteroids are effective in 75% of patients with ITP [4]. Platelet counts usually begin to rise 3–7 days after the initiation of prednisolone administration, reaching a maximal response in 2–3 weeks [5]. Eighty-five percent of those initially treated with high-dose dexamethasone has been reported to achieve a platelet count of 20×10^9/L by the third day and more than 50×10^9/L at 1 week [6]. Fifty percent of these responders can maintain a platelet count of 50×10^9/L or more for 2–5 years without additional treatment. Rituximab, which is an anti-CD20 antibody, has been reported to be effective in refractory ITP [4] and seems safe for use during the third trimester (Class C, Food and Drug Administration), although it may temporarily inhibit neonatal B-cell development.

Pregnant women are at inevitable risk of bleeding during delivery when episiotomy or cesarean section is performed or when the placenta is separated from the uterus. Therefore, the risk of PPH is increased when ITP is under poor control (platelet count lower than 50×10^9/L) at delivery. IVIG may be effective in raising the platelet count in 12–48 hours and is useful when there is active bleeding or before emergency surgical procedures [4,7]. Its effect may last for 2–3 weeks, depending on the dose of IVIG and severity of ITP. The recommended dose of IVIG in the treatment of patients with ITP is 1 g/kg/d for 1–2 days [8]. In view of the high cost of IVIG and its potential side effects (severe headache, renal failure, nephritis, and thrombosis) [4,9], a slow infusion rate and a small dose, without compromising its effect, should be considered. Although this patient had a low platelet count (25×10^9/L), platelet count saved enough for vaginal breech delivery was achieved with a low dose of IVIG (15 g) combined with platelets transfusion. The transfused platelets, binding to antiplatelet antibodies, are rapidly cleared by reticuloendothelial system, and thus should be administered immediately before delivery [4]. Entrapment of fetal head, although rare, is probably the most feared complication during vaginal breech delivery. Most of those cases occur in preterm fetuses less than 32 weeks of gestation. When the platelet count is lower than 50×10^9/L, regional (epidural) anesthesia is contraindicated [5]. NTG has been used to provide adequate uterine/cervical relaxation for preventing entrapment of fetal head during vaginal breech delivery. Because NTG has a very short half-life (about 2 minutes), it does not increase postpartum uterine bleeding. When NTG is administered and Piper forceps are used in a timely manner, there is less uterine bleeding during vaginal breech delivery than cesarean section. Cesarean section should be reserved for obstetric indications in patients with ITP.

The fetal platelet count is unpredictable and does not correlate with maternal platelet count, the levels of antiplatelet antibodies, or maternal response to therapy. Four to five percent of newborns have a platelet count less than 20×10^9/L and less than 1% will have severe intracranial hemorrhage [8]. Most infants exposed to maternal ITP reach their platelet count nadir on the second day of life, occasionally on Days 3–5. The complication rate of cordocentesis (particularly of pregnancy loss and hematoma) is 1–2%, possibly elevated in thrombocytopenic fetuses. In pregnant women with ITP, the risk of cordocentesis exceeds the benefit of determining the fetal platelet count, negating its clinical usefulness. In addition, IVIG can cross placenta and may improve fetal platelet count by decreasing platelet destruction [8], thus, making instrumental delivery safer and possibly reducing the risk of neonatal intracranial hemorrhage.

The use of vasopressin in the obstetric field is less mentioned [10]. When prostaglandin F2 alpha is not available, a small dose of vasopressin, which is injected into uterine cervix, may be considered as an alternative means of reducing postpartum uterine hemorrhage as it causes vasoconstriction and smooth muscle contraction. Its half-life is about 10–20 minutes. Intracervical injection is easily performed and can deliver a high concentration of vasopressin at the low segment of the uterus. Adverse effects of vasopressin, such as bradycardia or cardiac arrest, can be minimized by limiting a total dose to no more than four units, a low concentration (0.2 units/mL or less), and avoidance of inadvertent intravascular injection [11]. Recombinant activated factor VII, with a suggested dose of 0.09 mg/kg, is being used more often to successfully

manage life-threatening PPH because of coagulopathy or uterine atony [12]. According to the result in this case study, a small dose (1.2 mg) may effectively prevent deterioration of PPH when IVIG and platelet transfusion have been performed. Whether a small dose of recombinant activated factor VII can be used as a prophylactic method in patients at high risk of massive PPH deserves further investigation.

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