Pregnancy with Immune Thrombocytopenic Purpura and Neonatal Alloimmune Thrombocytopenia – Case Report
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Abstract: Immune thrombocytopenic purpura (ITP) is a diagnosis of exclusion. It is an autoimmune disorder caused by development of IgG autoantibodies, directed against number of platelet glycoproteins. A 28 years, primigravida, booked, admitted at St Stephens Hospital at 36 weeks of gestation with intrahepatic cholestasis, false labour pains and symptomatic severe thrombocytopenia with platelet count of 10,000/mm³. She was treated with oral steroids and platelet transfusion after admission. Patient was induced at 37+2 weeks. She delivered a healthy baby girl of weight 2.88kg vaginally. Baby showed neonatal alloimmune thrombocytopenia at day 4, which was treated with intravenous immunoglobulins (IVIg). Both mother and baby were discharged with good increment in the platelet count. The aim is to clarify; when thrombocytopenia in pregnancy is clinically important, to provide guidance regarding diagnosis, management options and information about potential risks to the mother and the fetus.

Keywords: Idiopathic thrombocytopenic purpura, pregnancy, Neonatal alloimmune thrombocytopenia.

INTRODUCTION
The normal range for peripheral blood platelet count in non-pregnant individuals is generally reported as 150-400x10⁹/L. Thrombocytopenia (platelet count <150x10⁹/L) occurs in 7.6% of women and are associated with no pathology. From practical point of view, any pregnant women with platelet count <100x10⁹/L in pregnancy should undergo further clinical and laboratory assessment [1].

Immune thrombocytopenic purpura (ITP) is an autoimmune disorder characterized by persistent thrombocytopenia due to autoantibody binding to platelet antigen(s) causing their premature destruction by the reticuloendothelial system, and in particular the spleen. Immune thrombocytopenia (ITP) occurs in 0.14% of pregnancies [2]. The great concern of ITP during pregnancy is the risk of thrombocytopenia in the newborn infant. We present here a case of ITP in pregnancy with neonatal alloimmune thrombocytopenia for its rarity, unique presentation who posed a therapeutic challenge with good maternal and fetal outcome.

CASE REPORT
A 28 years old lady, primigravida, known case of ITP came to ANC OPD in first trimester for regular antenatal visits. She had already been diagnosed with ITP in 2011 but was not taking any treatment. She had history of easy bruising on fall or injury during childhood. In 2011, bone marrow examination was done which was normal; blood peripheral smear showed normal white blood cell and red blood cell count and ITP was made as diagnosis of exclusion. There was no history of menorrhagia, gum bleeding or epistaxis or bleeding from any other site. Her blood pressure, urine albumin was checked at every antenatal visit which was normal. Apart from routine antenatal investigations her ANA, Anti dsDNA, lupus anticoagulant, antiphospholipid antibody were done, which were negative. Her platelet count was done monthly in first and second trimester and then 2 weekly after 28 weeks, which was always above 30,000/mm³. There was no history of bleeding from any site or petechiae, ecchymosis during antenatal visits so she was not started on steroids. At 34 weeks of gestation she was diagnosed with intrahepatic cholestasis of pregnancy (IHCP) and started on ursodeoxycholic acid. At 36 weeks gestation she was admitted in view of false labour pains and petechiae on both the legs. There was history of hematuria and hematochezia. Her platelet count was 10,000/mm³ on admission she was given platelet transfusion and started on tab prednisolone 40mg once a day. She was given total 8 platelet transfusions because of presence of hematuria on and off. She was planned for induction at 37 weeks in view...
of IHCP. So for immediate increase in platelet count she was given single donor platelet to reach a target of 80,000/mm³. At 37+2 weeks, after reaching platelet count of 90,000/mm³ labour was induced and she delivered a baby girl of 2.88kg vaginally. There was no postpartum haemorrhage or any other postnatal complications. Baby was examined by paediatrician; there was no petechie or cephalhæmatoma. Daily platelet count was done which showed decrement and development of neonatal alloimmune thrombocytopenia. At platelet count 46000/mm³ on day 4 baby was given IVIg at 1mg/kg over 4 hours (total 2 doses in 2days) which showed improvement. Intracranial bleed was ruled out by transfontanalle ultrasound. Mother and baby were discharged with good increment in platelet count.

**DISCUSSION**

Thrombocytopenia (TCP) is observed to affect only 1% of obstetric population at term [3]. Some patients are known to have medical illnesses that cause TCP, while in others, pregnancy is the first encounter of TCP. At term, TCP is mostly due to gestational thrombocytopenia (75%), hypertensive disorders of pregnancy (21%), disorders with autoimmune background as ITP and systemic lupus erythematosus (SLE) (4%), while other causes are rare and account only for <1% of cases [4]. ITP is diagnosed using standard criteria: (1) thrombocytopenia >6 months (2) a normal bone marrow examination (3) a normal white and red blood cell count (4) exclusion of other causes of thrombocytopenia[5]. The decision to treat pregnant woman with ITP is based on assessment of the risk of significant haemorrhage. The count usually falls as pregnancy progresses, the greatest rate of decline occur in the third trimester [6]. Therefore, careful planning is required to ensure a 'safe' platelet count at the time of delivery. Frequency of monitoring depends on the individual case, taking into account the absolute platelet count, rate of change and proximity of delivery. With levels above 50×10⁹/L remote from term, no treatment is started but close observation is due. In cases with counts 20-50×10⁹/L, no treatment is indicated unless complicated with bleeding or approaching delivery. Treatment is also indicated if the count is <10-20×10⁹/L in first trimester or <20-30×10⁹/L in other trimesters, even in asymptomatic patients. In the last few weeks of pregnancy, initiation or modification of treatment should be done to ensure a platelet count in the 50-70×10⁹/L range as labour and delivery might ensue suddenly. If caesarean delivery or regional anaesthesia is entertained, higher counts of 80-100×10⁹/L are targeted. Route of delivery should be determined according to standard obstetric considerations where most recent reports did not find increased neonatal bleeding risks associated with normal vaginal delivery[7, 8]. In general, 30-50% of ITP cases might need treatment during pregnancy [9].

Corticosteroids are considered as first line treatment for ITP due to their efficacy and low cost. The mechanisms of action of corticosteroids are due, at least in part, to the inhibition of phagocytosis of opsonised platelets, as well as impairment of autoantibody production. The typical therapeutic dose of prednisone is 1 mg/kg/day (based on the pre-pregnancy weight), which, after achieving a response, is gradually titrated to the lowest effective dose. However, the many adverse effects of corticosteroids are amplified during pregnancy, such as gestational diabetes, weight gain, acceleration of bone loss, hypertension and possibly placental abruption and premature labour. Furthermore, use of corticosteroids in the first trimester has been associated with congenital anomalies. Appreciation of such toxicities might suggest that in the patient in whom therapy is not indicated should not be started, if required, initiated at a low dose. Alternatively, intravenous immunoglobulin (IVIg) can be the first line therapy for pregnancy-associated ITP, especially when a long duration of therapy may not be required. Compared to corticosteroids, IVIg is less likely to induce toxicities such as hypertension. However, responses to IVIg tend to be transient, and multiple courses of therapy may be required at significant cost and patient inconvenience. Splenectomy may be considered as second line treatment for patients who fail to adequately respond to corticosteroids or IVIg[10]. Platelet transfusion is not part of management of ITP but it has been seen to be helpful near term when target platelet count has to be maintained for delivery[11].

ITP is associated with neonatal alloimmune thrombocytopenia (NAIT) due to passage of maternal antigens into the fetal circulation. This might not manifest at birth but platelet count continues to decrease in affected neonates, reaching nadir 2-5 days after delivery. This can reach <50×10⁹/L in 10-20% of cases and <20×10⁹/L in 5% of newborns in mothers with severe ITP [12]. Bleeding can affect 25-50% of newborns with severe TCP due to ITP, but severe bleeding especially intracranial haemorrhage affects only 1-2% [13]. Cord blood obtained should be analysed to determine the cord blood platelet count. If the cord sample suggests neonatal thrombocytopenia, a neonatal venous sample should be performed to confirm this. If the platelet count is less than 50×10⁹/L at delivery, a transcranial ultrasound should be performed. If thrombocytopenia is present, the neonate should be observed for signs of haemorrhage and alternate day platelet counts checked. Treatment of the neonate is rarely required. If haemorrhage is evident or the neonatal platelet count is less than 20×10⁹/L, treatment should be commenced. Intravenous immunoglobulin is the treatment of choice commencing with a 1 g/kg infusion, repeated if necessary. In the presence of life threatening haemorrhage platelet support should be given in addition to intravenous immunoglobulin. Following intravenous immunoglobulin the
thrombocytopenia may recur at approximately 4–6 weeks [14]. Further treatment may be required dependent upon the platelet count and clinical picture until the maternal antibody is cleared.

CONCLUSION

ITP is an uncommon, but important cause of thrombocytopenia in pregnancy. Though ITP is associated with a significant incidence of neonatal thrombocytopenia, it is generally not associated with major morbidity if properly managed. IVIg and low-dose corticosteroids comprise the mainstays of treatment in ITP, but prolonged corticosteroid therapy is associated with significant toxicity in the pregnant patient and should be avoided. At the time of delivery, target platelet count need to be maintained to avoid bleeding complications. Platelet transfusion can be used as mode of treatment near delivery. Despite the development of severe thrombocytopenia in approximately 5-10% of the offspring of patients with ITP, the incidence of neonatal intracranial haemorrhage in these individuals is extremely low. Moreover, delivery by caesarean section has not been shown to decrease the risk of neonatal intracranial haemorrhage compared to vaginal delivery, and thus the mode of delivery in pregnant patients with ITP should be solely dictated by maternal factors. ITP is associated with significant maternal and neonatal complications which can be avoided if properly managed.

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