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Laparoscopic Splenectomy for Resistant Immune Thrombocytopenia in Pregnancy- A Case Report and Review of Literature

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Abstract

Background: Thrombocytopenias in pregnancy are the second most common hematological disorder in pregnancy after anemia. About 7-10 percent of women experience this during pregnancy and most are due to gestational thrombocytopenia. About 3-4% are due to autoimmune process and is normally a diagnosis of exclusion. The management of this condition is mainly medical with splenectomy reserved only for very resistant cases. There is very limited literature on safety of laparoscopic splenectomy during pregnancy. We present such a case and a review of all cases of laparoscopic splenectomy in the literature.

Case Report: A primigravid woman presented with resistant Immune thrombocytopenia during early pregnancy. She had very little response to all the medical treatments that are offered in pregnancy. She then had an uncomplicated laparoscopic splenectomy with good response during pregnancy. There was good maternal and neonatal outcome.

Conclusion: Laparoscopic splenectomy can be safely considered for resistant cases of splenectomy during pregnancy.

Key Words: Immune Thrombocytopenia; Pregnancy; Laparoscopy; Splenectomy; Safety

Background

Immune Thrombocytopenia (ITP) is an autoimmune condition that is caused by immune mediated destruction of platelets. Pathophysiology of ITP is thought to predominantly involve IgG Antibodies binding to surface antigens Glycoprotein (GP) II b-III a or GPI b-IX. Platelets with such auto antibodies bound to the surface will be cleared from circulation by the reticuloendothelial system with resultant thrombocytopenia and increased risk of bleeding. Recent evidence shows that there is suboptimal production of platelets also due to increased apoptosis of megakaryocytes [2]. It is predominantly a disease of young adults, with a prevalence of 1/10,000. Hence it is not an uncommon entity in pregnancy and accounts for approximately 3% of all cases of thrombocytopenia in pregnancy [3]. ITP is a diagnosis of exclusion and in pregnancy preeclampsia, HELLP, infectious diseases, gestational thrombocytopenia must be considered in the differential. The majority of ITP cases identified during pregnancy are asymptomatic, but some can be associated with hemorrhagic complications that can be potentially hazardous for the mother and the fetus, as the antiplatelet IgG antibodies can cross the placenta and lead to passive neonatal ITP. There is no correlation between maternal and neonatal platelet count.

The treatment of ITP aims at restoring the platelet count to 30,000-50,000 x 109 /liter. First line treatment options include corticosteroids, intravenous immunoglobulin (IVIG) and intravenous anti-Rh (anti-D) infusions. Many of the second and third line cytotoxic and immunosuppressive therapies are not recommended in pregnancy. One surgical second line management option in pregnancy for resistant ITP is splenectomy, but this is rarely required and often not considered due to concerns of surgical risk to mother and baby. The safety of laparoscopic splenectomy is not reported in the literature.

We report a case of resistant ITP in pregnancy successfully and safely treated with laparoscopic splenectomy and compare this with available data on similar cases from the literature.

Case report

A 28-year-old G1P0 presented to our Multidisciplinary Clinic for Women with Bleeding Disorders in Pregnancy at 18 weeks gestation following the diagnosis of isolated thrombocytopenia. Her routine prenatal labs in a community hospital identified a platelet count of 8000 X 10^9/liter at 14 weeks gestational age. She was then admitted to hospital where clinical examination was remarkable solely for scattered diffuse petechiae and oral wet purpura. A full work up for thrombocytopenia was performed and no secondary causes of thrombocytopenia were identified.

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Therefore, the diagnosis of ITP was made. IVIG at a dose of one gram per kilogram was administered for two consecutive days. There was minimal response to the IVIG, the zenith platelet count response was 26,000 X 10^9/litre. It was at this point that she was referred to our clinic for assistance with management. Oral prednisone was commenced at one milligram per kilogram and IVIG was repeated to two further doses one month after the initial doses. The patient continued to have diffuse petechiae and small oral blood blisters. There was minimal response to either of these treatments and the patient was admitted to the hospital for consideration of additional therapy including a surgical consult for splenectomy and bone marrow biopsy. The bone marrow biopsy was consistent with ITP and no other abnormalities were identified. Additional studies were negative including the direct antiglobulin test, paroxysmal nocturnal hemoglobinuria flow cytometry, viral serology, *Helicobacter pylori* serology, antiphospholipid antibody tests and autoimmune serology. She was of blood group B positive. Whilst in the hospital, she was also treated with high dose anti-D (50 micrograms per kilogram) for

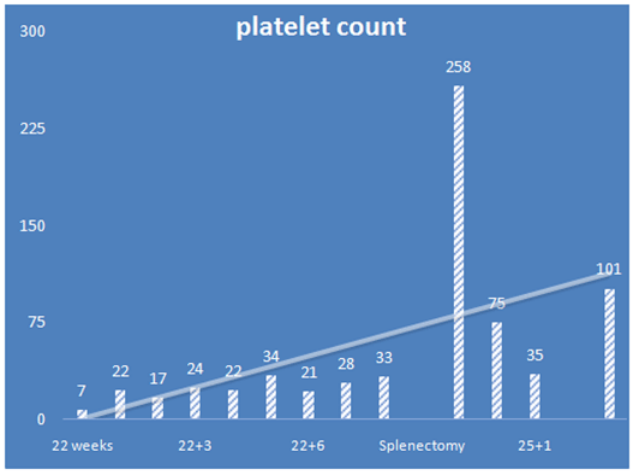

Figure 1: Platelet count according to patient gestational age in weeks and therapeutic trials

two consecutive days with no response once again. Anti-D was well tolerated; there was no evidence of maternal hemolysis nor fetal anemia on middle cerebral artery doppler ultrasound assessment. The patient refused additional immunosuppressive therapy including rituximab. Hence, the decision was made to proceed with a laparoscopic splenectomy at 22 weeks gestational age after appropriate immunizations. She received 2 adult pools of platelets prior to the procedure and underwent an uncomplicated laparoscopic splenectomy. The patient made an uneventful and rapid recovery. Immediately post operatively, she showed a good platelet count response (zenith 258,000 X 10^9/ liter but the platelets fell to 35,000 10^9/liter) two weeks' post-splenectomy at which point she was restarted on prednisone at 30mg daily with good response (Figure 1).

An attempt at tapering the prednisone dose was done which resulted in a platelet count drop to of 8000 X 10^9/liter. She received one more dose of IVIG and the prednisone was increased to 30mg/ day and this maintained a platelet count above 100,000 X 10^9/liter. The pregnancy progressed well and she had a preterm pre-labor rupture of membranes at 35 weeks and progressed to have a normal spontaneous vaginal delivery after five hours of a live male infant weighing 2775 grams. The infant's platelets at birth were 152,000 X 10^9/liter and there was no further decline in his platelet count. The postpartum and the neonatal course for mother and baby were uneventful and both were discharged on day 2 postpartum. She went into sustained remission postpartum and has since had a subsequent pregnancy with no evidence of relapse or neonatal thrombocytopenia.

Table 1:- All cases of antenatal laparoscopic splenectomy reported in the literature from 2000 to 2016. No adverse events occurred in any of the neonates born to mothers who had a splenectomy [8,9,10,11,12,13].

Case	Year	Authors	First line treatment	Gestation at splenectomy
1	2001	Anglin et al	Steroid	22 weeks
2	2001	K Iwase et al	-	23 weeks
3	2005	Griffiths et al	Steroid+IVIg +anti-D globulin	20 weeks
4	2007	Felbinger et al	Steroid	20 weeks
5	2014	Koji Kubota et al	Steroid + IVIG	24 weeks
6	2015	Bernal-Macías et al	Steroid + IVIG	13 weeks
7	Current		Steroid + IVIG + Anti D	22 weeks

Discussion

Thrombocytopenia is one of the most common hematological disorders in pregnancy, second only to anemia. There is a physiological fall in platelet count during pregnancy due to various reasons like hemodilution, increased platelet clearance by enhanced macrophage activation, and increased platelet aggregation driven by increased levels of thromboxane A2. Thrombocytopenia may be diagnosed for the first time in pregnancy and the distinction between gestational thrombocytopenia and ITP can be challenging as it relies purely on phenomenologic criteria [4]. The current expert-guided recommendation is to start treatment for ITP in pregnancy when the platelet count is less than 30,000 to 50,000 x 10^9/ liter, or sooner when there is evidence of clinical bleeding or when pregnancy approaches term due to risk aversion regarding neuraxial anesthesia and postpartum hemorrhage. The first line treatment for ITP in pregnancy is oral prednisone and IVIG both of which are considered safe in pregnancy. Large doses of intravenous anti-D have been used for treatment outside pregnancy in Rh positive non-splenectomised patients as it results in preferential splenic phagocytosis of the antibody coated red blood cells rather than platelets [18]. The use of anti-D in pregnancy is limited to small

studies but the response rate is similar to that of IVIG [5]. Even though medications like azathioprine have been used successfully in non-pregnant populations, its success in pregnancy has yet to be determined and its use is limited by delayed onset of action in the order of months Also, rituximab, a chimeric monoclonal antibody targeting CD20 B-cell surface antigen has been shown to be of benefit in the treatment of ITP. A recent meta-analysis of rituximab use in ITP suggested it has a place early in the tailored strategy of treatment of ITP, especially before splenectomy [17].The safety data for rituximab is largely unknown and the data is extrapolated from women who required therapy for lymphoma in pregnancy. The thrombopoietin receptor agonists which are effective therapy for resistant and refractory ITP is contraindicated in pregnancy.

Splenectomy during pregnancy was once considered a high-risk procedure with high mortality rate. During early pregnancy, it is associated with increased risk of fetal loss and premature labor and during later stages, splenectomy may be technically challenging due to uterine enlargement. The first case of splenectomy via laparotomy in pregnancy was reported in 1996 by Steimer on a primigravid woman who presented at 28 weeks of gestation with life-threatening pulmonary hemorrhage and severe thrombocytopenia [16,7]. Since then several cases of open splenectomy have been reported both during the antepartum period and during cesarean section [9,10,11,12,13]. The safety of laparoscopic surgeries in pregnancy, mainly for ectopic pregnancies and adnexal masses, has been well established and also results in improved outcomes such as earlier return to activity and reduction in narcotic use. Given the state of surgical advances, efficacy and safety of laparoscopic techniques, splenectomy can be considered when required for management of resistant ITP in pregnancy [14,15].

Conclusion

In conclusion, our recent case and the six previously reported cases of laparoscopic splenectomy during pregnancy suggest that splenectomy can be safely considered in cases of resistant ITP in pregnancy in carefully selected cases. One can make an argument to watch and wait if the patient does not have any symptoms of bleeding. The bleeding phenotype in our patient led to the aggressive management. Splenectomy is a reasonable and safe option for patients who fail to respond to the traditional first line treatments and when there is no time for azathioprine action

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