Severe Thrombocytopenia in an Immune Thrombocytopenic Parturient Non-responder to Medical Line of Treatment: Anaesthetic Management for Splenectomy Combined with Caesarean Section

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Abstract We report anaesthesia management of a parturient with severe thrombocytopenia secondary to immune thrombocytopenic purpura (ITP). Her platelet count remained around $3 \times 10^9/l$ in spite of optimum medical therapy and hence was posted for splenectomy combined with caesarean section. Anaesthesia implications of severe thrombocytopenia comprises risk of central nervous system bleeding, perioperative haemorrhage causing placental hypoperfusion and foetal hypoxia, risk of trauma to compromised airway and risk of epidural haematoma. The purpose of this paper is to discuss the risk factors associated, different management strategies and also to review the literature in an attempt to ameliorate the anaesthesiologist in perioperative management of these cases.

Keywords Caesarean section · Splenectomy · Thrombocytopenia · Immune purpura · Idiopathic purpura · Non-responder · Anaesthesia

Introduction

Thrombocytopenia is encountered in 7–10% cases during pregnancy [1, 2]. Causes of thrombocytopenia during pregnancy are enumerated in Table 1.

Immune thrombocytopenic purpura (ITP) (previously called Idiopathic Thrombocytopenic Purpura) [3, 4] accounts for 3% cases of thrombocytopenia during pregnancy [5]. ITP is defined as an acquired immune-mediated

disorder characterised by isolated thrombocytopenia, defined as peripheral blood platelet count less than $100 \times 10^9/l$, and the absence of any obvious initiating and/or underlying cause of the thrombocytopenia [3, 4]. There are antiplatelet antibodies which bind to platelet antigens and cause accelerated platelet destruction in reticuloendothelial system (RES). Females in reproductive age group are most commonly affected who may consequently present with ITP during pregnancy [1, 5]. An ITP patient has a 5% risk of fatal haemorrhage throughout the life [6]. Likewise during pregnancy both mother and foetus are at risk of life threatening bleeding complications. The peripartum period can be further complicated if ITP during pregnancy is non-responder to medical treatment. These non-responder cases may necessitate splenectomy; either during pregnancy or along with caesarean section; to restore platelet count [4].

Case

Twenty-six years old, 32 weeks fourth gravida female presented with bleeding per vaginum, blood in urine, oral mucosal bleed and petechial patches since 7 days to a nursing home. She was a diagnosed case of ITP but was not compliant with advised treatment. There she received injection methylprednisolone 1 g intravenously (IV), injection dexamethasone 8 mg 8 hourly IV and immunoglobulins 20 g IV for 5 days. Even then her platelet count remained below $5 \times 10^9/l$ and hence was referred to our hospital for further management.

She was a gravida four—para one with previous full term normal delivery 5 years back. She gave history of appendicectomy under general anaesthesia uneventfully before 6 years. She also gave history of two abortions 4 and

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3 years back respectively. During second abortion, she had excessive per vaginal bleeding and petechiae, for which she was investigated and diagnosed to have ITP. She was started on tablet prednisolone. However she stopped it on her own after abortion as she had no symptoms. No details of it were available with patient.

On examination, she weighed 49 kg, had mild pallor, petechiae and her BP was 130/80 mmHg. There was no hepatosplenomegaly. Cardiovascular and respiratory examination revealed no abnormality. Mallampati class was one with acceptable airway parameters. Investigations showed haemoglobin 9.7 g%, WBC count $17,500/\text{mm}^3$ and platelet count $3 \times 10^9/\text{l}$. Renal and liver function tests, serum electrolytes, prothrombin time and partial thromboplastin time were within normal limits. HIV and anti-nuclear antibody test was negative. There was no evidence of either retroplacental haemorrhage or intracranial haemorrhage in foetus on ultrasonography.

On admission to our hospital; injection methylprednisolone 1 g IV and immunoglobulin 20 g IV were continued and dose of injection dexamethasone was increased to 40 mg IV per day. She received this for two more days. Thus she received methylprednisolone, dexamethasone and immunoglobulins for 7 days. However no improvement in her platelet counts or her bleeding symptoms were noticed. She was diagnosed to be a non-responder to medical line of treatment. Thus necessity for splenectomy was identified to restore her platelet count. However as it was 32 weeks of pregnancy, splenectomy was not possible unless combined with caesarean section. Therefore, to minimise morbidity associated with severe thrombocytopenia to both mother and foetus, splenectomy was planned along with caesarean section as an effective treatment modality.

Table 1 Causes of thrombocytopenia during pregnancy

(1) Gestational thrombocytopenia
(2) Disorders with increased platelet destruction:
Immune thrombocytopenia
Pregnancy induced hypertension
HELLP syndrome
Thrombotic thrombocytopenic purpura
Haemolytic uraemic syndrome
Systemic lupus erythematosus
Infection associated (HIV, malaria)
Drug induced
Disseminated intravascular coagulation
(3) Disorders with reduced platelet production:
Congenital thrombocytopenia
Aplastic anaemia
Leukaemia
Myelodysplasia
Drug induced

Patient received 20 g immunoglobulin IV and 8 units of random donor platelet transfusion prior to induction of anaesthesia to maintain platelet count above $20 \times 10^9/\text{l}$ so as to minimise the risk of intracerebral hemorrhage.

Patient was placed in supine position with wedge under right hip and premedicated with IV ranitidine 50 mg, metaclopromide 10 mg, glycopyrrolate 0.2 mg. Following preoxygenation for 5 min, anaesthesia was induced with thiopentone 250 mg IV. Suxamethonium 2 mg kg^{-1} was used to facilitate passage of No 6.5 cuffed endotracheal tube down the trachea, aided with Sellick's manoeuvre. Muscle relaxation was achieved with vecuronium and intermittent positive pressure ventilation was established. Anaesthesia was maintained with sevoflurane 0.4–0.8% in (50:50) oxygen and nitrous oxide. Injection fentanyl 100 microgram was given after baby delivery to provide analgesia. Patient was monitored with pulseoximeter, electrocardiogram, noninvasive blood pressure, end tidal CO_2 monitor and urine output.

In surgical steps, ligation of splenic artery preceded lower segment caesarean section. Completion of caesarean section was followed by splenectomy. During intraoperative period she was given four units of random donor platelets to ensure surgical haemostasis. No haemorrhagic complication was observed intraoperatively. At the end, neuromuscular blockade was reversed with neostigmine 2.5 mg and glycopyrrolate 0.4 mg IV and extubated uneventfully. Her platelet count after ligation of splenic artery was $29 \times 10^9/\text{l}$ and immediate postoperative count was $33 \times 10^9/\text{l}$. On first postoperative day her platelet count was $48 \times 10^9/\text{l}$. Postoperative course was uneventful with Hb 9.4 mg/dl and platelet count always above $30 \times 10^9/\text{l}$ till she was discharged on eighth postoperative day.

A male child weighing 2 kg was delivered who did not require any active resuscitation and was shifted to neonatal intensive care unit for observation. At birth, baby's colour was pink and activity was moderate. Baby had tachypnoea up to 60 per minute and tachycardia up to 165 per minute, which settled by 12 h of life and required no special treatment. Baby's platelet count at birth was $120 \times 10^9/\text{l}$ which decreased to $80 \times 10^9/\text{l}$ on second day and $68 \times 10^9/\text{l}$ on third day of his life (neonatal autoimmune thrombocytopenia). He received IV immunoglobulin 2 g on the same day after which his platelet count increased to $120 \times 10^9/\text{l}$ on fourth day and remained more than $110 \times 10^9/\text{l}$ till his discharge from hospital on ninth day.

Discussion

ITP is diagnosed by exclusion because there are no clinical or laboratory parameters which can accurately diagnose ITP [3,

4, 7]. Presentation of parturient with ITP depends on platelet count [8]. Patients with platelets higher than $50 \times 10^9/l$ are usually asymptomatic. Minor symptoms like easy bruising or purpura may occur at $30\text{--}50 \times 10^9/l$ counts. Moderate symptoms like spontaneous bruising; prolonged bleeding after trauma may occur at $10\text{--}30 \times 10^9/l$ counts. Severe bleeding in the form of mucosal bleed in genitourinary or gastrointestinal tract, epistaxis may occur below $10 \times 10^9/l$ counts.

Management of these patients is based on guidelines given by American Society of Haematology (ASH) [6] which are recently reviewed and observed to be effective [4, 9]. The indications to treat a parturient with thrombocytopenia are based on risk of haemorrhage and summarized in Table 2 [3, 4, 6, 10].

IV immunoglobulins (IVIg) is the most accepted first line treatment for platelet counts below $10 \times 10^9/l$ in third trimester or $10\text{--}30 \times 10^9/l$ who are bleeding [4, 6, 10]. IVIg supposedly slows down platelet destruction by blocking RES. It is safe during pregnancy but expensive. Corticosteroids and glucocorticoids are also recommended; which reduces antiplatelet antibody production. However; steroids enhances possibility of pregnancy induced hypertension and gestational diabetes and may cause excessive weight gain, osteoporosis and psychosis [3, 4, 11]. Immunosuppressant drugs like cyclophosphamide, rituximab, danazol and vinca alkaloids prescribed in non-pregnant ITP patients are better avoided during pregnancy because of risk of teratogenicity [3, 4]. Although azathioprine is safe during pregnancy, the response is slow and no published reports about its successful use in pregnancy for ITP [4].

ITP Patients who fail to respond to standard medical line of treatment are termed as non-responder and are defined as a platelet count $<30 \times 10^9$ or a less than two fold increase in platelet count from baseline or the presence of bleeding [4]. For these patients, splenectomy is considered appropriate treatment modality [1, 4, 6, 9, 10]. During pregnancy, splenectomy should ideally be performed in second trimester as it is associated with premature labour in first trimester and is technically difficult in third trimester [1, 3, 4, 6, 10, 11]. Whenever indicated in third trimester, splenectomy is performed along with caesarean section to enhance exposure. Laparoscopic splenectomy has also been safely performed during pregnancy [3, 4, 12].

It has been proposed that women with previously diagnosed ITP may experience exacerbations during pregnancy [3]. That may be the case in our patient, therefore, in spite of optimum medical therapy, her platelet count remained 3×10^9 and her bleeding symptoms remained persistent. Hence necessity of splenectomy was identified. However as it was 32 weeks of pregnancy, splenectomy was not possible unless combined with caesarean section. The possibility of prematurity of neonate was explained to

Table 2 Indications for treatment of ITP in pregnancy

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- Platelet count above $30 \times 10^9/l$ are considered safe for normal vaginal delivery
 - Counts above $50 \times 10^9/l$ are considered safe for caesarean section
 - Counts above $75 \times 10^9/l$ are considered safe for central neuroaxial anaesthesia
 - Platelet count $30\text{--}50 \times 10^9/l$ in first and second trimester: do not require specific treatment
 - Medical treatment is required if count $<10 \times 10^9/l$ or counts of $10\text{--}30 \times 10^9/l$ in second or third trimester or bleeding
 - IVIg is the most accepted initial medical line of treatment whenever indicated
 - Patients non-responder to medical line of management with counts below $10 \times 10^9/l$ and who are bleeding: splenectomy
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patient and her husband. Other factors like baby's weight on ultrasonography (approximately 2,100 g), on going steroid therapy which might have helped foetal lung maturity and good neonatal care back up at our hospital were also discussed. Considering her very low platelet counts which were not responding to medical therapy, they consented for splenectomy combined with caesarean section at 32 weeks.

Major risk in parturient with ITP is likelihood of bleeding complications that can arise with surgery. However platelet counts above $30 \times 10^9/l$ are considered sufficient to prevent these haemorrhagic complications. A patient whose count is below $10 \times 10^9/l$ with mucous membrane bleeding should be prophylactically transfused with platelets to optimise perioperative platelet count [3]. Four to eight units of random donor platelet or a single unit of platelet aphaeresis (single donor) is generally acceptable for prevention or control of bleeding in a thrombocytopenic patient [13]. However single donor platelets carry the advantage of low risk of alloimmunisation and bacterial contamination. Platelet transfusions are unnecessary if counts are above $30 \times 10^9/l$ and no bleeding symptoms. IVIg 1 g/kg can also be used along with platelet transfusion for rapid response [3].

Anaesthesia implications of severe thrombocytopenia comprises risk of central nervous system bleeding, perioperative haemorrhage causing placental hypoperfusion and foetal hypoxia, risk of trauma to compromised airway and risk of epidural haematoma. Anaesthesia technique for splenectomy (during pregnancy or at caesarean section) is selected considering period of gestation, coagulation profile, history of bleeding and associated obstetric and medical history.

There are reports of use of uncomplicated central neuroaxial blockade (CNB) in parturient above $50 \times 10^9/l$ platelets in literature [14–17]. Whenever indicated; fine

needle single prick spinal anaesthesia can be chosen over epidural anaesthesia. However epidural for labour analgesia may be utilised after considering platelet count, risk of bleeding and benefits of analgesia. In our case we avoided CNB in view of (1) risk of epidural haematoma due to platelet count below $50 \times 10^9/l$ and (2) limitation to use CNB in splenectomy as very high level of blocks are needed which may cause hypotension with resultant placental hypoperfusion. We preferred a balanced general anaesthesia with due consideration to difficult intubation, risk of pulmonary aspiration and supine hypotension. In view of thrombocytopenia, a smaller endotracheal tube and gentle airway manipulations after optimum intubating conditions are recommended to reduce chances of airway injury. Sellik's manoeuvre helps to prevent regurgitation of gastric contents and pulmonary aspiration. Nasal intubation and intramuscular injections must be avoided. We recommend a long peripheral venous line [e.g.: Cavafix® (B. Braun)] introduced preoperatively in antecubital vein which will provide a large bore; long term IV access and reduce frequency of venous punctures.

There is no correlation between severity of maternal thrombocytopenia and risk of neonatal thrombocytopenia [3]. However neonates born to parturient with ITP must be closely monitored for platelet count and/or evidence of bleeding as they are prone to thrombocytopenia [4]. Their platelet count usually decreases during second to fifth day of life [3]. IVIg is the treatment of choice for neonatal thrombocytopenia [3].

Conclusion

In conclusion, severe thrombocytopenia in a parturient theoretically has greater risk of peripartum haemorrhage. ITP parturient non-responder to medical therapy may necessitate splenectomy during pregnancy or along with caesarean section. Anaesthesia plan must contemplate limitations of regional anaesthesia, prophylactic use of agents to raise platelet count, appropriate care to avoid airway trauma and avoidance of pulmonary aspiration and placental hypoperfusion. Moreover a multidisciplinary strategy should be prepared by haematologist, obstetrician, general surgeon, anaesthesiologist, and neonatologist.

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