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Case Report

Anesthetic Challenges in Pregnancy with Wilson's Disease Associated with Massive Splenomegaly Complicated with Intramyometrial Carboprost: A Case Report

Jyoti P Deshpande, Merlin Elizabeth Jacob*

Department of Anaesthesiology and Critical Care, Smt Kashibai Navale Medical College and General Hospital Narhe-Pune, MUHS University, Nashik, India.

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ABSTRACT

Wilson's disease is a rare autosomal recessive condition, that affects the liver and brain mainly. Pregnancy in these patients is of high risk due to involvement of liver and high incidence of abortion, preeclampsia, HELLP syndrome. We report a case of a 24year old G2A1 (35+2 weeks) diagnosed with wilson's disease 6 years ago, currently on tab zinc. She presented with thrombocytopenia, anemia, extrahepatic portal vein occlusion with splenomegaly and mild ascites. She was taken up for elective section at 35+2 weeks, under general anesthesia. With intramyometrial injection of carboprost, there was sudden desaturation and bronchospasm. However, we managed the case successfully with safe outcome of both the mother and child. There are only very few case reports of Wilson's disease in pregnancy undergoing C-section under general anesthesia in the presence of hepatic dysfunction.

Wilson's disease (WD), also known as hepatolenticular degeneration is a rare autosomal recessive disorder with an incidence of 1:50,0000 to 1:1,00,000 [1]. It is due to the mutation of ATP7B gene, resulting in decreased synthesis of ceruloplasmin, a copper transporter protein [2]. This causes accumulation of copper in various body tissues, mainly the liver, brain and cornea. Osteomuscular involvement may present as dystonia and muscle rigidity [3]. Excess copper is certainly teratogenic and is associated with intrauterine growth restriction in the fetus as well as neurological complications. There may be higher risk of hypertension during pregnancy, HELLP (hemolytic anemia, elevated liver enzymes and low platelet count) and also placental abruption in these cases [4].

Cases of WD in pregnancy undergoing elective section under general anesthesia are seldom reported. The anesthetic management in the presence of hepatic dysfunction, splenomegaly with thrombocytopenia was a challenging one.

Case Report

24-year-old, G2A1 35+2weeks with gross splenomegaly and WD was posted for elective section. After being diagnosed in 2016, she was on tab penicillamine 250mg BD for 3 years and then stopped them on her own due to unavailability in her town. After being off medications for 1.5years, she was started on tab zinc acetate 50 mg BD and tab propranolol 10mg BD. She also has a history of variceal banding for grade IV varices, twice in 2016. She has received blood transfusions multiple times since diagnosis.

During her recent admission, following USG abdomen to estimate disease severity, it was found that the patient had caudate lobe hypertrophy, extrahepatic portal vein thrombus, gross splenomegaly(28cms) with prominent splenic vein, mild ascites and non-obstructive renal calculi of the right kidney. Investigations revealed,

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*Corresponding author.
E-mail address: merlinelizabethjacob@gmail.com

anemia with thrombocytopenia, near normal liver function tests, normal renal and other parameters. Serum ceruloplasmin and serum copper levels were also normal. Preoperative auscultation of chest was clear. Bilateral pedal edema was present. All other examinations were normal.

The day before surgery, 1 unit packed cell volume (PCV) and 1 single donor platelet (SDP) was transfused to the patient. Post transfusion, Hb was 10.9gm% and platelet increased from 23,000/cumm to 50,000/cumm. Apart from this, 2 PCV, 4 fresh frozen plasma (FFP) and 4 random donor platelets (RDP) were kept reserved.

On the day of surgery NBM status, intake of morning dose of beta blocker and anti- aspiration prophylaxis were confirmed. High risk consent explaining the possibility of postoperative ICU stay and chances of haemorrhage was also taken.

Plan of anesthesia in this patient was general anesthesia with orotracheal intubation using 7.0mm ID cuffed tube and maintenance using 50% O2: air with the inhalational agent sevoflurane.

Once the patient was in the OT, all standard monitors according to ASA guidelines (SpO2, NIBP, ECG, EtCO2) were attached and 4 RDP's were transfused prior to induction. The patient was induced with inj propofol 100mg IV and inj atracurium 40mg IV and maintained with 50% O2: air and sevoflurane. Once the baby was delivered, inj oxytocin 20IU according to institutional protocol, inj fentanyl 100mg and inj midazolam 1mg IV were given and sevoflurane concentration was reduced. Blood sugar levels were monitored and was within normal limit.

Intraoperatively, in view of intermittent uterine atony and hematuria, the gynecologist insisted on giving intamyometrial injection of carboprost, since the recent liver and renal parameters were within normal limits. In about 10 mins following intramyometrial injection, the patient developed desaturation and bronchospasm associated with copius oral secretion. As this was immediately identified, we administered nebulization through orotracheal tube with salbutamol (an alpha2 adrenergic agonist) and also inj lasix 20mg IV, inj hydrocortisone 200mg IV and inj dexamethasone 8mg IV were given. Secretions were suctioned out thoroughly. Blood loss was only about 400ml despite the intermittent uterine atony. Crystalloids upto 1000ml and inj paracetamol 1gm IV since her liver function was not deranged was administered. Following these measures, the SpO2 gradually began to improve and bronchospasm was relieved. Urine output was now clear and no hematuria was present. Intraoperative urine output was 700ml. We avoided transversus abdominis plane block in view of hematuria, thrombocytopenia and gross splenomegaly.

The patient was extubated once fully awake and obeying commands. She was shifted to the ICU for clinical after care and also to assess biochemical levels. Her baby was shifted to the NICU in view of subcostal retractions and was on oxygen supplementation for half a day. Day 1 labs of the baby were within normal limits. Tab propranolol 10mg BD and tab zinc 50mg BD were restarted postoperatively. On post-operative day (POD)1, her platelet count decreased to 34,000/cumm and the next day it rose to 36,000/cumm. However, patient was vitally stable. Both, baby and mother were shifted from the ICU on POD 2. They were discharged on POD5, absolutely healthy and fine.

Discussion

This case is a deviation from the normal progress of such cases. Pregnancy in WD is considered high risk and is associated with preeclampsia, thrombocytopenia and deranged coagulation. It is also associated with increased incidence of abortions [5].

The main stay of treatment in WD is reducing dietary copper intake, antagonizing its absorption with zinc or chelation of copper with penicillamine, trientine or ammonium tetrathiomolybdate. Liver transplantation is advised when all medical measures fail [6-7]. Penicillamine, trientine and zinc are drugs approved by the US FDA in pregnancy. Trientine may result in chromosomal abnormality if taken during pregnancy. Brewer et al reported that the use of zinc in 26 pregnancies with WD resulted in 24 healthy pregnancies, one baby requiring surgery at 6months for a heart defect and another baby was born with microcephaly [7]. Our patient was taking zinc therapy during pregnancy period without any complications or congenital abnormalities.

Administration of RDP was preferred just prior to induction as its activity peaks in 10 mins of transfusion and is max at 1 hour. This helps platelet formation and therefore decreases the chances of uncontrolled bleeding during surgery. The duration of platelet function is 5-7days and the duration of activity of externally transfused platelet is only 2-3days. Hence, a fall in platelet count can be expected in the postoperative days. We preferred general anesthesia over central neuraxial blockade due to thrombocytopenia. Although general anesthesia has its share of disadvantages, it proved to be a better modality of anesthesia in this patient. Neuraxial blockade can be considered in the absence of coagulopathy [8-9]. Kousalya et al. reported a case of emergency caesarean section in WD patient with lower limb weakness which was managed under spinal anaesthesia successfully [6-7]. General anaesthesia usually causes hypotension and decreases hepatic blood flow. This can cause more damage to an already compromised organ. Liver is the major pathway for absorption, distribution, metabolism and excretion and with its involvement, the management under general anesthesia can be a challenge.

The opioid of choice was fentanyl as it is least affected by liver disease. Propofol was the induction agent, because the clearance of this drug is not significantly affected by liver disease. We avoided the use of succinylcholine because, these patients may have

reduced pseudocholinesterase levels and the metabolism of suxamethonium may be slowed, causing prolonged duration. They are also more sensitive to neuromuscular relaxants due to either reduced muscle function secondary to the disease, elevated blood copper levels interfering with neuromuscular transmission or the chronic use of d-penicillamine [10]. Keeping with that, we preferred atracurium over suxamethonium which is spontaneously degraded by Hoffmann elimination and is liver independant. Sevoflurane was chosen as the inhalational agent, since according to literature, sevoflurane has been reported to have the least associated complications in hepatic disease [11]. We did not hesitate in giving inj paracetamol intraoperatively as the liver enzymes were only mildly deranged. Short-term use at reduced doses can be given safely in patients with non-alcoholic liver disease [12].

Carboprost is ideally contraindicated in patients with asthma, cardiovascular, renal and hepatic involvement and it has to be used with caution in cases of anemia, jaundice, seizure disorders and should have been avoided. This could have been the culprit in our scenario. Bronchospasm may be attributed to injection of the uterotonic, carboprost. Garg et al; reported a case of a primigravida who developed life threatening cardiovascular ST segment changes following intramyometrial carboprost injection [13]. Wilson's disease in itself, the long term usage of penicillin and the intramyometrial injection of carboprost could have triggered bronchospasm in our case. However, uterus tone was attained following carboprost.

There have been reports of exacerbation of liver failure in patients with WD, who have discontinued d-penicillamine treatment [14]. This could have been the reason for her impending liver failure. However, due to appropriate management and a resultant satisfactory outcome, they were discharged on POD 5.

Conclusion

Pregnancy with WD calls for vigilance to early recognition of clinical manifestation and appropriate management to ensure the safety of both the mother and child. With multisystem involvement, anesthesia management should be tailored according to the patient's clinical profile, physical status, site and duration of surgery. A multi-disciplinary approach in the post-operative period is mandatory. This includes a neonatologist for baby's care; gastroenterologist, hematologist and intensivist apart from the treating gynecologist and anesthetist to care for the mother. We have aptly managed the caesarean section of WD with 35 weeks' pregnancy, where we faced complication due to the disease per se and carboprost administration. So we suggest that the right choices be made, rapid diagnosis and prompt treatment be done for the safe outcome of the mother and child.

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