Anesthetic management of a parturient with Methylene Tetrahydrofolate Reductase (MTHFR) mutations: A case report

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Abstract

Methionine synthase catalyzes methylation of homocysteine to methionine, while also demethylating 5-methyltetrahydrofolate to produce tetrahydrofolate. Mutations in the Methylene Tetrahydrofolate Reductase is a risk factor for recurrent abortion. As pregnancy is considered a full-stomach and airway edema associated with the high progesterone level imposes the anaesthetist for a difficult airway management. Sometimes the patients with this mutation are on anticoagulant therapy making a concern for neuraxial anaesthesia. We present a case of pregnancy induced hypertension with MTHFR mutation successfully managed with regional anaesthesia.

Keywords: Methionine synthase, Mutation, Neuraxial anaesthesia, Pregnancy Induced Hypertension.

INTRODUCTION

A call was received for emergency caesarean section for a patient with bad obstetric history (BOH) with Pregnancy Induced Hypertension (PIH) and bleeding per vaginum (PV). She was also a diagnosed case of MTHFR mutation. General anaesthesia is itself a challenge for a gravid patient with MTHFR mutation because of not only the concern of changes in airway associated with pregnancy but also because of adverse effects of nitrous oxide on homocystine metabolism. Such patients are also receiving anticoagulants during pregnancy which may make spinal anaesthesia contraindicated. Hyperhomocysteinemia and its correlation with vascular occlusive diseases and thrombosis has been extensively studied [1]. Hyperhomocysteinemia itself can be a cause for recurrent abortion. This case report emphasizes the anesthetic implications and management of a patient with hyperhomocysteinemia undergoing an emergent caesarean delivery.

CASE REPORT

A 33-year-old, G6P4L1 parturient at gestational age 32 weeks 2 days of gestation, 70 Kg, 155cm, non-vegetarian by diet with Mallampati grade 2 airway, was admitted to labour room with bleeding per vaginum and preterm labour. She was a diagnosed case of Hyperhomocysteinemia.

She had a previous Lower Segment Caesarean Section (LSCS) with BOH with gestational diabetes mellitus, Pregnancy induced hypertension (PIH), Intra-uterine growth retardation (IUGR), oligohydramnios with Rh negative pregnancy. Her first baby was born 10 years back with meningomyelocele and died during surgery, second and third baby also died because of multiple congenital anomalies and hypoplastic heart syndrome within less than 48 hours of birth. She had a spontaneous abortion at 2 months of gestational age following which she was advised genetic testing and was found to have MTHFR mutation type 677CT.

Her 5th conception was born by LSCS, done for gestational diabetes mellitus with PIH with IUGR with oligohydramnios with controlled homocystine levels. She had no history of any Transient Ischaemic Attacks (TIA) or syncope and her neurological examination was without any deficit. She was in continuous follow up during her 6th pregnancy and was taking metformin and vitamin folate 1 mg daily, iron tablets, aspirin 75 mg daily was given along with sildenafil 20 mg during pregnancy.
It was planned to do emergency LSCS for the patient and was shifted to operating room. On arrival in operation theatre her blood pressure was 156/94 mm Hg. Since she was haemodynamically stable and was not taking any drug other than aspirin, it was decided to perform a spinal anaesthesia for surgery. A 26 gauge Quincke spinal needle was used for sub arachnoid block and 10 mg (2 ml) of bupivacaine heavy 0.5 % along with 25 microgram of fentanyl was given in L3/L4 space. Surgery was uneventful with estimated blood loss of 750 ml. She received 2000 ml of ringer lactate. A live female baby was delivered with an Apgar score of 8 and 9 at 1 minute and 5 minutes respectively. 24 hrs after surgery she was started on clexane 40 mg subcutaneously. DVT suspicion was ruled out after using ultrasound. The patient was discharged home on postoperative day 5.

DISCUSSION

Homocysteine is a sulfur containing amino acid and homocysteinemia is defined as increase in serum levels of homocysteine. Homocysteine is methylated to methionine and this reaction is catalyzed by methionine synthase. This enzyme uses vitamin B12 as cofactor and methyltetrahydrofolate as methyl donor. Methylenetetrahydrofolate reductase deficiency causes formation of methyl tetrahydro folate. Genetic abnormalities in MTHFR gene causes impairment in the synthesis of MTHF and hence causes increase in homocysteine levels. Homocysteinemia can also be caused by deficiency of any of the required enzymes or cofactors involved in the pathway of methionine metabolism. People consuming strictly vegetarian diet and hence deficient in vitamin B12 and folic acid and hence are more prone for homocysteinemia.

Methylenetetrahydrofolate reductase deficiency is an autosomal recessive disorder with a spectrum of manifestations including neurologic symptoms, premature atherosclerosis, venous and arterial thrombosis, and lens dislocation. A total of 29 mutations in MTHFR are associated with severe deficiency, with a resulting activity level that is usually 0% to 30% of control activity. Most patients are heterozygous for multiple MTHFR substitutions; a small minority is homozygous for mutations at this locus. Among these mutations, the C677T polymorphism is the most important.

An elevated homocystein level is toxic for endothelial lining of blood vessel and increases risk for developing atherosclerosis, coronary artery disease, myocardial infarction, peripheral arterial disease and stroke. Homocysteine also acts as atherogenic and thrombophilic agent predisposing the patient for thrombus formation and thromboembolism. Hyperhomocysteinemia in a pregnant female causes neural tube defects in fetus. It also causes recurrent pregnancy losses, preeclampsia, and placenta abruption and IUGR.

Use of nitrous oxide causes irreversible inhibition of methionine synthase and hence can further increase homocysteine levels which predispose the patient to its procoagulant action and increase the chances of other adverse effect arising because of embolism of thrombus.

In our patient we wanted to avoid using nitrous oxide to our patient and since she was not taking any anti-coagulant we went ahead with the spinal anaesthesia for our patient.

CONCLUSION

To conclude, those parturients with MTHFR gene mutation that are not on anti-coagulant treatment can be safely managed by neuraxial anaesthetic technique.

Conflicts of interests

All authors have no conflict of interests.

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