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PERIOPERATIVE MANAGEMENT OF CAESAREAN SECTION IN A PARTURIENT WITH MITOCHONDRIAL MYOPATHY

Parul Upreti[1*], Ranju Singh[2], Rashi Sardana[3], Arjun Saili[4], Sangeet Tanwar[5]

[1*]Senior Resident, Department of Anaesthesiology & Critical Care Lady Hardinge Medical College & Associated Shrimati Sucheta Kriplani Hospital, New Delhi, India Parulupreti64@gmail.com 0000-0003-3668-5630
[2]Director Professor, Department of Anaesthesiology & Critical Care Lady Hardinge Medical College & Associated Shrimati Sucheta Kriplani Hospital, New Delhi, India ranjusingh1503@gmail.com 0000-0001-9058-2478
[3]Senior Resident , Department of Anaesthesiology & Critical Care Lady Hardinge Medical College & Associated Shrimati Sucheta Kriplani Hospital, New Delhi, India rashi.doc.18@gmail.com 0000-0002-5984-2603
[4]Senior Resident, Department of Anaesthesiology & Critical Care Lady Hardinge Medical College & Associated Shrimati Sucheta Kriplani Hospital, New Delhi, India Arjunsaili88@gmail.com 0000-0003-4145-0369
[5]Senior Resident, Department of Anaesthesiology & Critical Care Lady Hardinge Medical College & Associated Shrimati Sucheta Kriplani Hospital, New Delhi, India Sangeet.tanwar@gmail.com 0009-0000-2728-9375

ABSTRACT:
Mitochondrial myopathies, one type of mitochondrial disease, usually result in clinical disorders of the muscle and other tissues that require a high energy supply, resulting in clinical manifestations such as fatigue, muscle weakness and exercise intolerance which were present in our patient. The optimal anaesthetic technique for these patients is not known but we decided to administer SA. Besides ameliorating metabolic stress and pain which can be detrimental in these patients, it helped avoid general anaesthetics(most anaesthetic drugs have depressant effects on mitochondrial function), sedatives and muscle relaxants which have the potential to cause postoperative residual muscle blockade and thus respiratory compromise due to the increased sensitivity described in them anaesthetics.
Women with mitochondrial disease are likely to experience a variable clinical course before, during and after pregnancy. Multidisciplinary care (mitochondrial medicine, neurology) is indicated in these parturients. The anaesthesiologists should be aware of the disease, its possible varied presentation and the multiple anaesthetic implications.
Benefit of surgery should justify the anaesthetic risk.

KEYWORDS: Mitochondrial Myopathy, Parturiant with genetic mutation, Anesthetic concerns in Mitochondrial myopathy

INTRODUCTION

Mitochondrial myopathies comprise a heterogeneous group of neuromuscular disorders induced by dysfunction of the mitochondrial respiratory chain that disrupts energy production. The mitochondrial diseasesin general show a variety of inheritance patternsand may have variedmultisystem manifestations.The range of possible clinical presentations is very broad** and may include: deafness, diabetes, proximal myopathy, external ophthalmoplegia, visual loss, gastrointestinal dysmotility, cardiomyopathy, cardiac conduction defects, epilepsy and in rarer cases encephalopathy and stroke like episodes.Pregnancy with its increased respiratory and cardiovascular demands, may increase the risk of deterioration in symptoms and obstetric complications in women who already have impaired mitochondrial function.We report a case of a patient with mitochondrial myopathy presenting for emergency cesarean delivery and discuss the anaesthetic implications and perioperative management of this uncommon condition. Our case was atypical because she was a 5th gravida with previous normal pregnancies.

Case report

A 27 year old unbooked multigravida (G5P4L2)with 37 weeks pregnancy presented to gynaecology and obstetrics casualty in labour with complaints of fatigue and weakness in lower limbs.She had difficulty in climbing stairs and in changing her posture. There was no history of weakness in upper limbs, no sensory loss and no associated tingling or numbness. There was no history of breathlessness and bladder/bowel sensations were also intact. The patient gave history of similar complaint at 12 years of age for the first time, subsequently againat 14 years of age,both resolved after some treatment, the details of which are not known. In 2013, at 23 years of age, she had a recurrence of the similar symptoms of muscle weakness. She was admitted to AIIMS and investigated which revealed a raised level of CPK-NAC (1950,normal is 22–198 U/L),) and the muscle biopsy done revealedred ragged fibres with modified gomori trichrome suggestingmitochondrial myopathy.She took multivitamins and coenzyme Q10 for 9 months.In 2015, she again developed muscle weakness and took

treatment for 6 months. In the obstetric history, she has had 2 uneventful normal vaginal deliveries 4 and 7 years back and 2 stillbirths (GCA/hydrocephalus). There was no family history of similar complaints.Patient was not able to maintain lithotomy position and was planned for emergency caesarean delivery (CD) in view of non-progression of labour. On physical examination she was of average built (height 156cm, weight 60Kgs) with a blood pressure of 122/76 mmHg, heart rate of 82 bpm, respiratory rate of 20/min, with mild pedal edema.Airway examination revealed bucked teeth, 3 finger breadth mouth opening and MPG grade III. Musculoskeletal examination revealed a normal muscle tone, muscle power 3/5 in lower limbs & 5/5 in upper limbs and normal sensory perception in bilateral upper and lower limbs. Her laboratory investigations were within normal limits, except, haemoglobin which was 8.9 gm%.The electrocardiography showed sinus rhythm with right axis deviationWolff–Parkinson–White syndrome.In arterial blood gas analysis all parameters were within normal limits except serum lactate which was 3.6mmol/L.It was decided to administer spinal anaesthesia for the CD and the patient was wheeled into a pre-warmed theatre. Along with an intravenous cannula an arterial line was secured to facilitate blood samples for arterial blood gas, serum lactate and blood glucose levels intraoperatively. Spinal anaesthesia was administered at L3-L4 interspace with 2 ml 0.5% ropivacaine + 25 mcg fentanyl to achieve a T6 sensory block. Warm intravenous fluids and an electrical heating blanket was used to prevent hypothermia.A healthy baby girl (weight 2.6Kgs) was delivered. Surgical course was uneventful and patient was shifted to postoperative ward where she was carefully monitored for any signs of respiratory distress or progression in muscle weakness. She was safely discharged home after 3 days.

DISCUSSION

Mitochondrial diseases are genetically and phenotypically a heterogeneous group with a variable clinical course and an estimated incidence of 1 per 500 [1].The varied clinical presentations make diagnosis difficult. Mitochondrial myopathies, one type of mitochondrial disease, usually result in clinical disorders of the muscle and other tissues that require a high energy supply, resulting in clinical manifestations such as fatigue, muscle weakness and exercise intolerance [2] which were present in our patient.

Preoperatively these patients need to be evaluated in detail and assessed for decreased cardiac function, conduction disorders (pre excitation syndromes)and metabolic dysfunction. Assessment of degree of musculoskeletal and neurological impairment including respiratory and swallowing functions should be made. Measurement of glucose, electrolytes, liver enzymes, lactate and creatine kinase and a 12 lead ECG should be done. Our patient had right bundle branch block and raised creatine kinase and lactate levels. Anaesthesiologists may need to prepare drugs or even a temporary pacemaker to cope with possible bradycardia during surgery. Prolonged preoperative fasting should be avoided.

Intraoperatively these patients can develop hypothermia, thus it is important to monitor temperature and take measures for active & passive warming and to prevent perioperative shivering.Clonidine has been described as safe for postoperative shivering. Positioning is a concern as peripheral nerves are at risk of positional damage.Many patients with mitochondrial diseases cannot metabolize lactate, therefore lactated Ringer's solution should be avoided, with regular monitoring of lactate levels. An arterial catheter may be required to monitor arterial blood pressure and for samples for arterial blood gas, serum lactate and blood glucose levels, which we had put in our patient.Stringent perioperative glucose management is required to prevent hypo/hyperglycaemia: latter leading to lactic acidosis.

Postoperatively these patients can develop muscle weakness, respiratory depression and cardiac insufficiency and thus require close monitoring in high dependency units/intensive care unit.Immobilisation due to muscle weakness may require prophylaxis for thrombosis, prolonged periods of immobilization should be avoided.If postoperative ventilation is necessary, non-invasive ventilation is preferred and aggressive weaning should be instituted.In spontaneously breathing patients, cautious use of opioids is recommended since further impairment in regulation of breathing may lead to respiratory acidosis adding to underlying metabolic acidosis. Throughout the perioperative course, drug therapy of these patients should be closely monitored as there are a number of drug interactions that can occur in these patients. These include corticosteroids aggravate muscle weakness (steroidal myopathy), valproateblocks OXPHOS and histone-deacetylase, increases bleeding tendencies, phenytoin inhibits mitochondrial ATPase, respiratory chain complex inhibitedby carvedilol,biguanides,thiazolinediediones,risperidone andquetiapine. Medications which cause bradycardia like beta blockers and amiodarone must be used with extreme caution.

The optimal anaesthetic technique for these patients is not known but we decided to administer SA. Besides ameliorating metabolic stress and pain which can be detrimental in these patients, it helped avoid general anaesthetics(most anaesthetic drugs have depressant effects on mitochondrial function), sedatives and muscle relaxants which have the potential to cause postoperative residual muscle blockade and thus respiratory compromise due to the increased sensitivity described in them. Propofol has been used safely but prolonged (>48 hrs) administration should be avoided. Total intravenous anaesthesia with short acting drugs has been described to facilitate intubation without muscle relaxants.Although no direct evidence links mitochondrial disorders to malignant hyperthermia, it seemed prudent to avoid the administration of agents known to trigger MH, such as succinylcholine and volatile anaesthetics. Thus if required for CD, modified rapid sequence intubation should be done without succinylcholine. Depolarising muscle relaxants should be strictly avoided

because of the possibility of hyperkalemiccardiac arrest. Essentially neuromuscular monitoring is a must if any muscle relaxant is used, as prolonged action is a definitive possibility.

We administered ropivacaine as the local anaesthetic agent in our patient as literature suggests that bupivacaine may not be a suitable choice for patients with mitochondrial disorders [3,4]. Although it has been safely used, bupivacaine can suppress lipid-based respiration in the myocardial mitochondria through inhibiting acylcarnitine exchange and carnitine deficiency increases sensitivity to bupivacaine-induced asystole.Epidural analgesia should be offered to these parturients as it may prevent life threatening lactic acidosis during labour.

A parturient with mitochondrial disease presents a challenge for the anaesthesiologists because little is known about the relationship between mitochondrial disease and pregnancy and the evidence is limited to the few published case reports. They are at increased risk of complications such as preterm delivery and preeclampsia. Berkowitz et al. [5] reported a patient with mitochondrial myopathy who hadvaginal delivery by use of low-outlet forceps and developedpre-eclampsia but did well postpartum. Magnesium may compete with calcium in mitochondria, interfering with oxidative phosphorylation even at therapeutic levels, women with mitochondrial disease appear to be at risk of toxicity if given magnesium sulphate for preeclampsia. Blake et al.[6] described a vaginal delivery by the use of vacuumextractor. The women may be able to deliver vaginally or may require a CD for non-progress of labour, as happened in our patient. Similar to our case, Dreval etal. [7] reported a patient who had a CD because of non-progress of labor.Rosaeg et al. [8] and Soccio et al. [9]have also reported cases delivered bycesarean section under neuraxial anaesthesia.

Outcome of pregnancy in patients affected by mitochondrialmyopathy is generally uncomplicated [5,6,7], but sometimes patients can develop complications. Yanagawa et al. [10] reported the case of a 31-year-old woman who developed mitochondrialmyopathy, encephalopathy, lactic acidosis, andstroke-like episodes (MELAS) during pregnancy; and concluded that pregnancy can aggravatemitochondrial diseases.Kovilam et al. [11] also described another patient with MELAS and stated that pregnancy, a highenergy-requiring state, contributed additional stress to analready compromised system. Patient can develop complications even after an uneventful pregnancy and delivery. Dessole et al described a case with mitochondrialmyopathy who, after cesarean section, had severe postpartumhemorrhage and incipient DIC requiring emergencyhysterectomy. Postpartum collapse and death [2] has also been associated with pregnancy and myopathy.The diagnosis be considered even if the patient has had previous uneventful pregnancies, as seen in our patient.

Women with mitochondrial disease are likely to experience a variable clinical course before, during and after pregnancy. If already diagnosed, the patient should be referred to a tertiary obstetric centre. Multidisciplinary care (mitochondrial medicine, neurology) is indicated in these parturients. Links with fetal medicine are also important since offspring of affected women can be symptomatic early in life.The anaesthesiologists should be aware of the disease, its possible varied presentation and the multiple anaesthetic implications.

Benefit of surgery should justify the anaesthetic risk.

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