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Case Report

Anesthesia Management of a 5 Months Old Infant with Mitochondrial Myopathy and Multiple Congenital Anomalies for Muscle Biopsy, a Case Report and Literature Review

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Abstract

A 5 months old female infant posted for left thigh muscle biopsy was diagnosed to have mitochondrial myopathy with lactic acidosis (MMLA) with history of preterm delivery with 2months NICU admission, microcephaly, pontocerebellar hypoplasia, neonatal onset epileptic encephalopathy, micrognathia, primum atrial septal defect, generalized, hypotonia and history of apnea of prematurity We report a successful anesthesia management of this challenging infant using awake spinal anesthesia without sedation.

The challenge for anaesthesiologist in patients with mitochondrial myopathy is to maintain metabolic stability and prevent complications.

A vigilant perioperative planning and care led to uneventful perioperative course.

Keywords: *Mitochondrial Myopathy; Multiple Congenital Anomalies; Muscle Biopsy*

Mitochondria is the principle source of energy production within the cell where the enzymes responsible for Krebs cycle, fatty acid oxidation and more importantly oxidative phosphorylation acts on metabolic substrates to release energy in form of ATP and high energy phosphate bonds supplying energy for cells.

Nerves and muscles are more dependent in this mitochondrial energy and the mitochondrial dysfunction is being recognized to cause increasingly number of myopathies and neuropathies with epileptic encephalopathy, failure to thrive and hypotonia as a primary presenting signs and a quiet variable presentation of cardiomyopathy and cerebellar ataxia, actually any organ in the body can be affected.

Of course cardiac muscles, respiratory system and CNS are also the main target of anesthetic drugs and particular care, must be taken when exposing such a patients to this agents.

Exposing child with mitochondrial myopathy to anesthesia can lead to respiratory failure and severe cardiac depression and avoidance of stresses that may provoke increased energy requirements and leads to such complications is the key for successful anesthesia management of such patients.

Here we are presenting a detailed management of an infant with a mitochondrial myopathy with lactic acidosis and multiple congenital anomalies under awake spinal anesthesia without sedation.

Case Report

A 5 months old female infant weighing 3.9 kg known to have mitochondrial myopathy with lactic acidosis for muscle biopsy from left thigh to confirm the diagnosis.

She has a microcephaly, pontocerebellar hypoplasia, neonatal onset epileptic encephalopathy, hypotonia, complete cleft palate, micrognathia and a restrictive primum atrial septal defect of 4 mm with left to right shunt.

She was admitted for 2 months in the NICU because of prematurity and frequent partial epileptic seizures manifested by head jerking and right sided facial twitching which was resistant to anti-epileptic medications. Also she has history of frequent apnea of prematurity.

At time of Preoperative examination she has dysmorphic face, microcephaly, O2 nasal cannula (2L flow) and NGT.

She is A febrile vitally stable with heart rate of 105 bp 65/37, respiratory rate of 32 and spo2 of 96. Chest was clear and heart s1+s2+grade 2systolic murmur @left parasternal area.

Airway: microcephaly, micrognathia and complete cleft palate with small mouth.

Lab and biochemistry: Hb12.6, TLC 14000, lactate 2.9 mmol with anion gap 19, platelets 357, ptt 27, INR 0.97, k 5.4, Na 136 and normal KFT.

Echo**:** Restrictive primum atrial septal defect of 4 mm, left to right shunt, no pulmonary hypertension and good overall ventricular function.

MRI of brain: Microcephaly and cerebellopontine hypoplasia.

EEG: Frequent epileptic waves of left temporal lobe.
Drug treatment: include phenytoin, phenobarbitone, valproic acid and clonazepam to control seizures.

Anesthesia management

A through pre-anesthesia evaluation was done and informed consent was obtained from father, NPO for 6h from milk formula and we orders IVF of D5 and 0.45NS, 20 ml/hr to keep infant well hydrated.

Our plan was to do neuraxial anesthesia with GA as standby plan because of concern regarding difficult airway, respiratory, cardiac and mitochondrial. Depressive effect of GA agents and because of the lower dose of local anesthetic to be given we proceeds with spinal anesthesia rather than caudal or local anesthesia. OR temperature was increased to 24^0C before shifting infant and once in OR 24g cannula was inserted in left hand dorsum, a bolus of warmed 40 ml of 5% albumin was given with complete deaeration of IV line (to eliminate the risk of paradoxical air embolism) and standard monitors of NIABP, ECG, SPO2, and axillary temperature probe plus capnography (fixed in front of right nostril for respiratory rate monitoring). Infant was turned to right lateral position, sterilization of back with povidone iodine, complete draping of back, local anesthesia infiltration of L5-S1 interspace, 1.5 inch neonatal 22 spinal needle, free flow of CSF, injection of 0.4 ml of hyperbaric 0.5% bupivacaine and finally infant was carefully returned to supine horizontal position with complete loss of motor activity of both lower limbs within 3 minutes.

A soother inserted in here mouth and the surgery started with careful monitoring of heart rate, blood pressure, spO_2 and respiratory rate using capnography waves where she was stable for the whole time with lowest recorded pulse rate of 87, b.p of 61/35, respiratory rate 28, temperature 36.2.

Infant was kept warm using forced air warming (bair hugger) and completely covering here body with transparent plastic drapes. IVF was continued in the same rate as Preoperative of 20 ml D5 0.45 NS. At middle of surgery measurement of blood sugar of 6.2 mmol was obtained with glucometer.

Surgery duration of 40 minutes and by the end of surgery infiltration of skin incision with 3 ml of 0.1% bupivacaine and 100 mg rectal paracetamol suppositories was given, the infant was shifted to PACU and kept there for 2h then discharged to PICU for overnight observation with no reports of any hemodynamic instability or desaturation or apneas.

Discussion and Conclusion

Mitochondrial production of ATP is the major source of energy production to maintain normal cellular physiology and the failure of ATP production to meet metabolic demands inevitably leads to lactic acidosis.

Surgery for children with mitochondrial disease usually involves general anesthesia and widely different anesthesia techniques have been successfully used for this patients but there is a reports of serious complications occurring during and following anesthesia exposure.

As a result a general opinion exists among anesthetist that these patients are at increased risk from stress of surgery and anesthesia. From anesthesia point of view the primary complications of mitochondrial myopathy includes respiratory failure, severe cardiac depression, dysphagia which can be caused by most of general anesthesia agents.

Advanced Disease Beyond TME

The perioperative period is a time during which a patient may be exposed to period of stress which can lead to inadequate aerobic ATP production by mitochondria to meet demands and this will leads to anaerobic metabolism and lactic acidosis. This stress includes prolonged fasting, hypovolemia, dehydration hypotension, PONV, hypothermia, hyperthermia, pain, acidosis, prolonged tourniquet and hypoglycemia. Avoidance of lactate containing IV fluid and use of glucose containing IV fluid is paramount for this patients.

It's not clear what hematocrit level is adequate for this patients but it's wise to keep them close to normal because they are less able to compensate for decreased oxygen delivery.

For our patients we try to avoid all the above mentioned factors whereas as example warm OR environment was achieved, we kept infant well hydrated, we monitor blood sugar during surgery, we avoids GA agents and we avoid Ringer lactate and a glucose containing IV fluid was given.

Unfortunately it should be noted that every general anesthetic studied has been shown to depress mitochondrial function with most notable of these are volatile agents and propofol.

In our case we avoid general anesthesia for this concern and of course because of suspected Difficult airway in this infant.

Generally speaking, Regional anesthesia is well tolerated by patients with mitochondrial myopathy but again LA agents is a mitochondrial depressant specially bupivacaine but fortunately most neural blockade requires doses of local anesthetic that are well below doses causing mitochondrial depression. If a muscle biopsy is being performed for diagnosis of mitochondrial myopathy, the muscle itself must not be exposed to LA which may lead to false defect in mitochondrial function.

In our patient we use spinal anesthesia rather than caudal or local anesthesia because of our believe of the lower total dose required for spinal anesthesia and to avoid direct drug injection to muscle during local infiltration.

For general anesthesia it's difficult to use inhalational agents in favour of intravenous anesthetic agents and vice versa.

The inhalational agent depress respiration and cause direct muscle relaxation and negatively interact with mitochondrial myopathy.

There is a reports of malignant hyperthermia like reactions following inhalational agents exposure in patient with mitochondrial myopathy but a real association between mitochondrial myopathy and malignant hyperthermia has not been established.

All intravenous anesthetic agents is a mitochondrial depressant but Propofol deserve special concern because its now, the most commonly used IV agent.

Propofol is well known to be a strong inhibitor of mitochondrial function and as a result a concern that patients with mitochondrial myopathy may have increased risk of Propofol infusion syndrome following Propofol exposure which is thought to result from mitochondrial dysfunction. At present the use of propofol infusion may not be considered of choice in patients with mitochondrial myopathy but it may be used as a single bolus for induction.

Sensitivity and resistance to nondepolarizing Neuromuscular blocking agents have been reported in children with Mitochondrial myopathies. To ensure appropriate dosing, the drugs should be Titrated judiciously while neuromuscular blockade is monitored.

As the motor neurons may be affected Succinylcholine may induce a severe hyperkalemic response and best to be avoided.

At the present we don't have the perfect anesthetic for patients with mitochondrial myopathy and when possible consideration should be given to the use of Local anesthetics in small amount for regional anesthesia.

In our case we avoided GA and we gives spinal anesthesia using total dose of 2 mg bupivacaine.

When GA is necessary probably each general anesthetic agent in use has its place. As seen previously it's not possible to eliminate one group as less safe than other and evidences would suggest that any technique might be used. It should be remembered that mitochondrial myopathy presents a wide variety of molecular defects and thus a wide range of different diseases with similar phenotypes and it's likely that some types of defects are more sensitive to inhibition by anesthetics than others [1-8].

In summary, most importantly is that all children's with mitochondrial myopathy must be monitored closely when administering any type of anesthetics, All medications should be titrated slowly and great care should be exercised to that the effect of anesthesia agents have largely dissipated before allowing patient to leave OR environment. Our patient was kept for 2hs in PACU and over-night in PICU.

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