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CASE REPORT ANESTHESIA & CONCURRENT DISEASE

Neuraxial anesthesia for extended endoscopic urological procedure in a patient with MELAS syndrome: a case report

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Abstract

We present a case of a 36-years-old male patient with MELAS syndrome (Mitochondrial myopathy, Encephalopathy, Lactic acidosis, and Stroke-like episodes) underwent ureteroscopy, lithotripsy and indwelling double J stent exchange under neuraxial anesthesia. MELAS is a progressive mitochondrial myopathy that results in defects in respiratory enzyme complexes I and IV, which lead to defects in aerobic metabolism, thus endangering high-energy-dependent organs. MELAS causes a wide range of physiologic changes that present a variety of challenges to the anesthetists. In this case, we managed our patient safely with spinal/epidural anesthesia without any major complications.

Abbreviations: MELAS - Mitochondrial myopathy, Encephalopathy, Lactic acidosis, and Stroke; MM - Mitochondrial myopathies; ATP - Adenosine triphosphate; ESWL - Extracorporeal shock wave lithotripsy; CPAP - Continuous positive airway pressure

Key words: MELAS; Acidosis, Lactic / genetics; Anesthetic management; Mitochondrial myopathies; Neuraxial anesthesia: Genetics.

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1. Introduction

Mitochondrial myopathies (MMs) represent a wide range of defects in the mitochondria. MELAS syndrome is a type of mitochondrial disease that is systemic in nature; it comprises *M*itochondrial myopathy, *E*ncephalopathy, *L*actic acidosis, and *S*troke-like episodes. The syndrome hinders mitochondrial ability to conduct oxidative phosphorylation. [1] The exact mechanism is not totally understood, but it has been speculated that the syndrome mainly affects respiratory enzyme complexes I and IV, which are essential in converting substrates from glycolysis, fatty acid oxidation, and tricarboxylic acid cycle to adenosine triphosphate (ATP). [2]

MELAS has many implications in anesthesia. Fasting before surgery, the type of medications used, and the type of surgery can all increase the metabolic burden, which leads to relapse in tissues dependent on large amounts of oxygen, such as the heart, the skeletal muscles, and the central nervous system. [3] MMs have been previously linked to malignant hyperthermia. Given the relatively few published experiences on this vulnerable population, we present this article about our experience in conducting neuraxial anesthesia for an extended endoscopic urologic procedure in a patient with MELAS syndrome and evaluate the outcomes in terms of safety and efficacy. Both general and regional anesthesia have been reported in this group of patients successfully, but we chose regional anesthesia to minimize depressive effects associated with many medications used in general anesthesia.

2. Case report

A 36-year-old male with MELAS syndrome was admitted to our hospital; a tertiary hospital in Amman, Jordan, as a case of several left renal stones for ureteroscopy, lithotripsy and indwelling double J stent exchange. The patient had a left ureter indwelling double J stent inserted four months back, and underwent multiple extracorporeal shock wave lithotripsy (ESWL) sessions. At the age of 30, the patient started to complain of parieto-temporal headaches and had multiple episodes of seizures. MRI diffusion weighted sequence showed lesions involving bilateral temporal lobes and subcortical white mater. Upon investigating lactic acid level was 5.96 mmol/L (normal; 0.5 to 2.2 mmol/L). Confirmatory genetic testing was done and showed typical A3243G point mutation in the tRNA (RiboNucleic Acid) for leucine. Patient's related medical conditions at presentation included hearing loss, visual impairment and severe muscle wasting. The patient was on wheelchair and dependent on continuous positive airway pressure (CPAP) for the last 5 y.

His surgical history included appendectomy at the age of fifteen years; which was done under general anesthesia, and stem cells implant as a potential therapy to MELAS, and double J stent insertion four months back under spinal anesthesia.

On examination, the patient was on a wheelchair, weighing 45 Kg with 152 cm height, and was using all his accessory muscles for breathing. Spastic dystonia was noted in all four limbs. Muscle power upon examination was noted to be 3 in upper limbs, 2 in lower limbs. While speaking, he could not finish sentences. He had a blood pressure of 103/57 mmHg, a pulse rate of 90 bpm, and a respiratory rate of 24 breaths/min. He was ASA-III.

The patient's medications included Co-enzyme Q10 100 mg, vitamin B3, Candesartan 4 mg daily and Bisoprolol 1.5 mg twice daily. Laboratory work-up included serum complete blood count, kidney function test, blood glucose level, ammonia level, serum electrolytes and coagulation studies. Hemoglobin level was 10.6 g/dL, platelet count was 95,000/μL, and all other lab values were within normal levels. On echocardiography, left ventricular ejection fraction was estimated to be 50%. The patient was diagnosed earlier by the cardiologist with cardiomyopathy. Arterial blood gases taken on room air before procedure showed hypoxemia with respiratory acidosis compensated by metabolic alkalosis (pH 7.401, $PaCO_2$ 57 mmHg, PO_2 57.7, HCO_3 34.6 mEq/L, BE 9.8 mmol/L).

He was assessed five days prior to surgery in the perioperative clinic. Anesthesia options, risks and perioperative care were all discussed with the patient and his family. Patient's consent was obtained for spinal/epidural anesthesia without sedation. The surgeon expected time for surgery to be two hours. The possibilities of conversion to general anesthesia, and the need of intensive care admission with mechanical ventilation postoperatively were all discussed and agreed by all parties.

In the operating room, routine monitors including standard ECG electrodes, arterial oxygen saturation, temperature probe and capnography were attached to the patient. Nasal cannula with a flow of 3 L/min oxygen was attached. Forced air warming blanket (Bear Hugger) was applied. An intravenous access was secured with an 18G cannula. For blood pressure monitoring, left radial intra-arterial catheter was inserted under local anesthesia. Baseline readings were: heart rate 84 bpm, respiratory rate 19 breaths/m, blood pressure 132/70 mmHg and temperature 36.8 °C. Gentamicin 80 mg was given intravenously to the patient after taking baseline readings. The patient then was placed in left lateral position, sterilization was done carefully, local anesthesia infiltration at level of L3/L4 was done using lidocaine 2%, and 22G Quincke spinal needle was then inserted. Upon encountering cerebrospinal fluid (CSF) backflow, 1 mL hyperbaric bupivacaine plus 25 μg fentanyl were injected. This was followed by level L4/L5 epidural anesthesia using 18G Touhy Portex® needle with loss-of-resistance technique. Epidural space was found at 5 cm, catheter was fixed at 9 cm on skin. After catheter placement, injection of 3 mL of a mixture of bupivacaine 0.1% and fentanyl 4 μg/mL was pushed. This was followed by continuous infusion of the same mixture at a rate of 3 mL/h. Vital signs readings following implementation of neuraxial anesthesia were: heart rate 71 bpm, respiratory rate 22 bpm, blood pressure 115/59 mmHg and temperature 36.9 °C.

Block was checked to be satisfactory with Bromage score of 2 and sensory level of T11 was achieved. The operation lasted for three and a half hours. Patient was comfortable and communicative all through and did not need CPAP intra-operatively. All vital signs remained stable throughout, without the need to use ephedrine or any other supporting medications. Warmed normal saline was given to a total of 750 mL.

Post-operatively the patient was transferred to the recovery room. Full routine monitors were attached for two hours. High flow nasal cannula was attached at a flow of 20 L/min, and epidural infusion was continued till the next day morning at a rate of 3 mL/hr. The patient was transferred to the ward with same pre-operative muscle power, he was alert, oriented, pain-free and without marked breathing distress. The patient did not need CPAP all through day 0. Arterial blood gases in the recovery room were: pH 7.361, $PaCO_2$ 52.9 mmHg, PO_2 76.9, HCO_3 29.3 mmol/L, and BE 3.9 mmol/L. Epidural catheter was removed after 24 h. The patient was

discharged the following day without any adverse change in his physical examination, vital signs or laboratory work-up. Patient was followed up two weeks postoperatively, and was found fine.

3. Discussion

Mitochondria use oxygen to convert substances into energy, producing almost 90% of the energy needed for the body. MELAS syndrome is the most common subtype of mitochondrial encephalopathies. The onset of illness is often in early adulthood. The first symptoms are usually neurological, ranging from episodic headaches to seizure-like activities. These episodes can produce stroke-like symptoms such as temporary vision loss, difficulty in speaking, or difficulty in understanding speech. Eventually, MELAS leads to progressive brain damage.

The metabolic derangements in MELAS syndrome include decreased ATP production, insufficient lipid metabolism and formation of damaging free radicals. [4] Anesthesia burden can cause further reduction in energy supplies, which might exacerbate preoperative symptoms. [5]

In our case, the patient had a history of stroke-like activity manifested by seizures, followed by hearing loss and visual impairment. He was CPAP-dependent at night-time. The diagnosis of MELAS was confirmed at the age of 30 y. He underwent stem cells implant trial 7 months back, but had minimal improvement, mainly in supporting his head. The patient was aware of his condition with vast knowledge.

During his visit to the pre-operative clinic, we discussed the type of anesthesia. The patient was aware of majority of the complications associated with each type of anesthesia, thanks to the internet facility, and had chosen to undergo neuraxial anesthesia. Upon reviewing the limited number of available reports on MELAS anesthesia, we described to the patient the possibility of systemic relapses following stressful conditions and our anesthetic plan to minimize the risk of these relapses.

Under stressful conditions, MELAS patients are at increased risk to develop lactic acidemia; especially after prolonged fasting. Hypoglycemia, postoperative nausea and vomiting, hypothermia and hypovolemia should be avoided because they increase the metabolic burden. [6] The choice of fluids in MELAS patients remains controversial. Although hypoglycemia should be avoided, glucose-containing fluids may not be optimal due to risk of seizures. [7]

According to Malignant Hyperthermia Association of the United States (MHAUS) recommendations, avoidance of volatile anesthetics is not necessary because of a lack of evidence to link MMs to increased susceptibility to malignant hyperthermia. [8] Avoidance of succinylcholine has been suggested following one case report in 1985, in which life-threatening hyperkalemia occurred in a patient with mitochondrial dysfunction after its administration; however, no definitive genetic link was shown between malignant hyperthermia and mitochondrial diseases such as MELAS. [9]

In a retrospective review of 64 patients with mitochondrial disease (of which 6 cases were MELAS), a variety of anesthetic techniques were reviewed with no significant risk of unanticipated hospital admission, cardiac arrest, hyperthermia or prolonged post-anesthesia stay. Increased risk of lactic acidosis and other metabolic derangements are the main concerns after exposure. [10] Multiple case reports have also documented successful administration of both general and regional anesthesia in MELAS patients, including total intravenous anesthesia, spinal anesthesia, combined general endotracheal anesthesia with epidural anesthesia, epidural anesthesia for postoperative pain, and epidural catheter placement for labor analgesia. [11, 12]

Postoperative monitoring must evaluate possible metabolic disturbances and postoperative respiratory failure. Adequate analgesia is warranted to prevent stress and hence acidosis. Other considerations include adequate control of nausea and vomiting and postoperative shivering. If metabolic derangements are severe, these patients should be monitored in the intensive care unit because potential life-threatening events might follow.

4. Conclusion

With optimum precautions, risk of complications of all types of anesthesia can be decreased in MELAS cases. The most important note of practice will be to decrease metabolic stress through avoidance of lactate containing fluids, hypoglycemia, hypothermia, prolonged fasting, postoperative nausea / vomiting, and shivering. Early intervention in case of respiratory deterioration is vital. Neuraxial anesthesia is suggested to be a safe and efficient mode of anesthesia for extended endoscopic urological procedures in these patients.

5. Institutional Review Board Statement

Ethical review and approval were waived as this study is a case report.

6. Informed consent statement

Patient consented on mode of anesthesia and use of this case for educational purposes.

7. Conflicts of Interest

The authors declare no conflict of interest.

8. Author Contributions

All authors have contributed equally to this work. All authors read and agreed to the published version of the manuscript.

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