Case report

Anesthetic management of a patient with MERRF syndrome

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Summary
There are several specific considerations regarding anesthesia in patients with mitochondrial disease. We describe the successful administration of a combined general and epidural anesthesia with sevoflurane maintenance in a patient with myoclonic epilepsy with ragged red fibers (MERRF syndrome) scheduled for surgical treatment of bilateral clubfoot.

Keywords: MERRF syndrome; anesthesia; mitochondrial encephalomyopathy; sevoflurane

Introduction
Mitochondrial encephalomyopathies are a rare group of disorders, of multisystemic nature and variable clinical presentation. They are genetically heterogeneous with either mitochondrial or nuclear mutations affecting mitochondrial oxidative phosphorylation processes and energy production (1,2).

MERRF syndrome (myoclonic epilepsy with ragged red fibers) is a rare chronic neurodegenerative disease, included in the group of mitochondrial cytopathies, with a peak of incidence in the second and third decade of life. It is maternally inherited and affects enzyme complexes I and IV of the respiratory chain. There is no curative therapy and treatment is based on symptomatic management with respiratory chain cofactors and vitamins (1).

Case description
An 11-year-old girl weighing 35 kg and 148 cm in height, diagnosed with MERRF syndrome was scheduled for surgical treatment of bilateral clubfoot. A significant issue in the family’s medical history was her brother’s death from Leigh’s disease.

Clinically the patient had psychomotor delay, ataxia, hypoacusia and myoclonia secondary to a mixed polyneuropathy in addition to cerebellar and pyramidal tract compromise. She was currently medicated with coenzyme Q10, piracetam, L-carnitine and a vitaminine complex (E, B6, B2, C, and methionine). The use of general anesthesia with sevoflurane in this patient at the age of 8 years for a neuroradiological scan proved uneventful.

Clinical examination showed a well hydrated but asthenic patient. Her vital signs, as well as cardiac, pulmonary, abdominal and airway examinations, were normal. The complete blood count, urea, electrolytes, liver function tests and serum lactic acid were also within normal limits.
During the preoperative fast, a 500 ml solution containing 3% dextrose plus 1 mmol·kg⁻¹ sodium bicarbonate and 0.3 mmol·kg⁻¹ KCl was infused at 75 ml·h⁻¹, to maintain blood glucose and serum lactic acid within the normal range.

The patient was premedicated with midazolam 0.05 mg·kg⁻¹ intravenously. Routine monitoring included electrocardiography, oxygen saturation, capnography, blood pressure and esophageal temperature. General anesthesia was induced with propofol 2 mg·kg⁻¹ and fentanyl 2 μg·kg⁻¹. After deepening anesthesia with sevoflurane 6–8% and nitrous oxide 55% in oxygen, the trachea was intubated. An epidural catheter was then inserted through an 18-gauge Tuohy needle after at the L3/4 space with the patient in a left lateral position. Bupivacaine (10 ml, 0.35%) were administered without significant cardiovascular changes. Anesthesia was maintained with 1.5% sevoflurane and 55% nitrous oxide in oxygen, with the patient breathing spontaneously. To avoid hypoglycemia and to prevent an increase in lactic acid concentration, fluid balance was maintained with a 2.5% dextrose in 0.45% saline infusion. Anesthetic management and recovery presented no complications. Epidural analgesia was continued with a 0.125% bupivacaine 6 ml·h⁻¹ infusion for the first postoperative 24 h. The postoperative course was uneventful and the patient was discharged from hospital the following week.

**Discussion**

To our knowledge there are no reports regarding anesthetic management of MERRF syndrome in the English language journals. A review of the literature describing anesthetic management of patients with mitochondrial defects was most remarkable for the different approaches taken. Many agents and techniques have been used with success and responses to anesthetic agents vary widely from patient to patient.

Patients affected by mitochondrial cytopathies may require surgery for a muscle biopsy or for procedures unrelated to the disease. Independently of the specific diagnosis, clinical heterogeneity associated with mitochondrial diseases must be taken into account during the preoperative assessment of these patients (3). Anesthetic management should begin with careful investigation of the medical history and a complete physical examination to exclude possible associated comorbidity, as well as hypotonia, cardiac dysrhythmias, epileptic seizures, stroke-like episodes, gastrointestinal dysmotility, diabetes, and lactic-acidosis (1,4,5). Arterial blood gas analysis to determine baseline acid/base status is essential (4). Cardiac function and the conduction system must be evaluated (6). Renal and hepatic function should also be investigated, avoiding the risk of overt or subclinical involvement that predispose patients to prolonged drug effects, defective production of clotting factors as well as altered glucose, fat, protein and lactate metabolism (7,8).

Premedication with midazolam was considered as a great benefit in this patient, because deafness and dementia make communication and evaluation difficult with an increased potential for agitation during the perioperative period (9,10). Midazolam (3 mg) intravenously was titrated to a state of light sedation to avoid respiratory depression.

In the perioperative management, it is crucial to ensure normoglycemia, normothermia, normotension, normovolemia and optimal oxygenation; factors known to influence existing or latent lactic-acidosis (4,11). Because of increased risk of perioperative complications elective surgery should be delayed in case of increased lactate or glucose levels, high lactate-to-pyruvate ratio, infection or other reversible source of stress (5). As the liver may not completely metabolize an excess of endogenous lactate, lactate-containing fluids are better avoided. Lactic-acidosis maybe a continuous or intermittent phenomenon because of impaired oxidative phosphorylation of glucose and altered lactate metabolism. Prolonged fasting may exacerbate lactic-acidosis; in the presence of hepatic dysfunction, hypoglycemia secondary to impaired glucose homeostasis may further complicate fasting. Paradoxically excessive glycolytic oxidation of glucose in the face of disturbed oxidative phosphorylation may also increase lactate levels. Maintenance of normal serum glucose could be challenging but will help to prevent or minimize acidosis.

We tried to limit anesthetic drug doses to a minimum, necessary for airway instrumentation and surgery. The possibility of increased sensitivity to volatile and intravenous induction agents in these cases makes careful titration and monitoring essential (12–15).
Although individuals with mitochondrial cytopathies are considered at increased risk for malignant hyperthermia there are conflicting reports regarding this issue, with patients having been exposed to triggering drugs such as suxamethonium and volatile agents without sequelae (8,9,16). The use of sevoflurane in these patients is controversial, though other volatile agents have been used uneventfully in patients with mitochondrial diseases (4,15,17,18). Sevoflurane allowed a rapid smooth induction without the need for neuromuscular blocking drugs during airway instrumentation and surgery, while maintaining spontaneous ventilation. In addition, sevoflurane elimination does not follow renal and hepatic pathways, which could be compromised in this patient.

We did not use any neuromuscular blocking drugs in this patient. Because of a potentially increased sensitivity to neuromuscular relaxants, blockade should always be monitored or even avoided, especially in severe cases. There are several reports of extreme sensitivity to nondepolarizing muscle relaxants with prolonged recovery and inadequate reversal by anticholinesterases (9,19,20).

Regional techniques allow the avoidance of complications associated with muscle relaxants and general anesthetics (3,4,8). In this patient epidural anesthesia in combination with general anesthesia minimized the stress response to pain with effective analgesia that extended into the postoperative period (3,10). Another advantage was a reduction in parenteral opioid requirements decreasing potential for respiratory depression in the perioperative period.

In conclusion, we have described the successful administration of combined general and epidural anesthesia with sevoflurane in a patient with MERRF syndrome.

References

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