

# Anesthetic management in MNGIE Syndrome

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## Abstract

We describe the anesthesia management of a 15-year-old girl, diagnosed with mitochondrial neurogastrointestinal encephalomyopathy (MNGIE), who presented with gastrointestinal perforation. MNGIE is an autosomal recessive disease associated with multiple deletions and depletion of mitochondrial DNA in skeletal muscle. The disease is characterized clinically by ptosis, progressive external ophthalmoparesis, severe gastrointestinal dysmotility, peripheral neuropathy, and leukoencephalopathy. We report on the anaesthetic management of a paediatric patient with MNGIE, and briefly discuss the pathophysiology and anaesthetic implications of this disorder. We describe the successful administration of a general anesthesia without muscle relaxants, maintenance in a patient with MNGIE.

## INTRODUCTION

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is an autosomal recessive disease associated with multiple deletions and depletion of mitochondrial DNA in skeletal muscle (1,2). It has been identified that mutations in the gene encoding thymidine phosphorylase located on chromosome 22q 13.32-qter is the cause of MNGIE. The disease is characterized clinically by ptosis, progressive external ophthalmoparesis, severe gastrointestinal dysmotility, peripheral neuropathy, and leukoencephalopathy. (1,3,4). Many of these patients present for surgery, or undergo anaesthesia in the course of investigation of their illness (5). 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.

In this case report we aimed to discuss anesthesia management of MNGI syndrome in a gastrointestinal perforation cases.

## CASE REPORT

A 15 year-old girl, weighing 25 kg, with height of 125 cm, was diagnosed with MNGIE syndrome and scheduled for emergency surgical treatment of gastrointestinal perforation. A significant issue in the family's medical history was her brother's death from MNGIE's disease.

Preoperatively, the patient was awake, afebrile (37.1 C rectal), spontaneously breathing, with reduced muscle tone. Clinically she was cachectic and dehydrated. Her vital signs, as well as cardiopulmonary, and airway examinations were normal (blood pressure; 100/70 mmHg, heartbeat; 96 beats per minute, respiratory rate; 13 breaths min<sup>-1</sup>). Laboratory data showed leucocytosis (34,000/mm<sup>3</sup>), uremia (60mg.dl<sup>-1</sup>), hipocalcemia (7.75mg.dl<sup>-1</sup>) and hipoalbuminemia (2.4 g.dl<sup>-1</sup>).

During the preoperative fast, a 500 ml saline solution was given. Routine monitoring included electrocardiography, oxygen saturation, capnography, blood pressure and esophageal temperature (Datex - Engstrom AS/3 monitor, Helsinki, Finland).

General anesthesia was induced with propofol 2.5 mg.kg<sup>-1</sup> and remifentanil 1mcg.kg<sup>-1</sup>. After deepening anesthesia the trachea was intubated via 7 mm cuffed endotracheal tube without use any muscle relaxant agent. Anesthesia was maintained with sevoflurane % 3 in oxygen-air combination and remifentanil 0.25-1 µg.kg<sup>-1</sup> of infusion. Positive pressure ventilation was provided a pressure controlled ventilation mode (mean airway pressure=10-15 cmH<sub>2</sub>O, tidal volum= 8 mL kg<sup>-1</sup>). The respiratory frequency was adjusted to achieve an en-tidal carbon dioxide pressure of 35-45 mmHg. Neuromuscular blocking agent was not administered during the operation. During the haemodynamics changes were stable and heart rate and blood pressure remained in the normal range (heart rate

90–100 beats/min; systolic blood pressure 110–120 mmHg) Remifentanyl infusion was stopped 5 min prior to end of surgery. Sevoflurane was discontinued at last suture. After spontaneous ventilation, patient was extubated within 5 min and transferred to the postoperative care unit. Tramadol 25 mg was given intravenously for postoperative analgesia.

After 10 day of surgery the patients was discharged without any post-operative complications.

### DISCUSSION

Mitochondrial diseases cause dysfunctional aerobic metabolism including several clinical features. Clinically, MNGIE presents between the 1st and the 5th decades with ptosis, ophthalmoparesis or both; skeletal myopathy; peripheral neuropathy; gastrointestinal dysmotility, manifesting as diarrhea and pseudo-obstruction; and cachexia (1). 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 in these patients (5,6,7). In this case report we performed successful anesthetic management with propofol-remifentanyl induction and sevoflurane maintenance anesthesia without muscle relaxant in an intestinal perforation patient with MNGIE.

Remifentanyl has become increasingly popular in paediatric anaesthesia (8,9,10) and can be administered safely to children without prolonged opioid effects on ventilation and gives stable intraoperative haemodynamics (11,12). It can be used with propofol for non-muscle relaxant endotracheal intubation techniques (13). There is one case report of a probable seizure after remifentanyl administration in a child (14), but a recent review of the pharmacokinetics and pharmacodynamics of remifentanyl suggests that remifentanyl is a safe drug, even in children with encephalomyopathies (15). We did not observe any seizures like phenomena after propofol-remifentanyl induction. minutes after discontinuation of the remifentanyl infusion, the child was awake and spontaneously breathing. In addition we did not see any impaired regulation of breathing or respiratory depression in postoperative period.

The use of muscle relaxants in a patient with mitochondrial disease also presents some potential difficulties. There has been one case report of a child with mitochondrial disease who developed signs of malignant hyperthermia after administration of suxamethonium with induction of general

anesthesia, along with a case of myotonic rigidity (5). The possibility of sensitivity to nondepolarizing relaxants has also been suggested (16). However atracurium is also successfully used like these diseases in some cases (17). We did not use any neuromuscular blocking agents for preventing increased sensitivity of neuromuscular relaxants and the possibility of malignant hyperthermia due to these drugs. Tracheal intubation with combination of propofol and remifentanyl was performed easily in our case and it has caused minimal hemodynamic changes.

Low soluble and low pungent inhaler anesthetic agent sevoflurane is ideal for rapid and smooth inhalational induction (5) and it has little propensity to produce cardiac arrhythmias. In addition, elimination of sevoflurane does not follow renal and hepatic pathways (7). We think that sevoflurane will be best choice for anesthesia maintenance in our case.

The most important symptoms of mitochondrial diseases are spasticity, seizure disorders, respiratory weakness, central hypoventilation, conduction abnormalities, cardiomyopathy, renal and hepatic insufficiency, diabetes mellitus, lacticacidaemia and thrombocytopaenia (6). Our patient was cachectic, had reduced muscle tone and a minimal renal dysfunction.

There are several specific considerations with regards to anaesthesia in patients with mitochondrial disease. The overall aim should be to avoid further stresses to an already dysfunctional system of aerobic metabolism (18). Hence special attention should be given to optimizing oxygenation in the perioperative period and avoidance of metabolic stresses which may provoke or worsen lactic acidosis. These patients may also respond abnormally to anaesthetic agents, making careful dose titration and adequate monitoring essential (6).

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 this case makes careful titration and monitoring (6,7,18).

MNGIE is caused by loss-of-function mutations in the gene encoding thymidine phosphorylase (TP; endothelial cell growth factor 1)(18). Deficiency of TP leads to dramatically elevated levels of circulating thymidine and deoxyuridine. The alterations of pyrimidine nucleoside metabolism are hypothesized to cause imbalances of mitochondrial

nucleotide pools that, in turn, may cause somatic alterations of mtDNA (18). Mitochondrial encephalomyopathies are clinically and genetically heterogeneous because mitochondria are the products of 2 genomes: mitochondrial DNA (mtDNA) and nuclear DNA (nDNA). Among the mendelian-inherited mitochondrial diseases are defects of intergenomic communication, disorders due to nDNA mutations that cause depletion and multiple deletions of mtDNA (1).

Minimizing oxygen demand may be beneficial in avoiding exacerbations of acidosis. Our patient arterial blood gases analysis was normal physiologic range (pH: 7.380, pCO<sub>2</sub>: 35, pO<sub>2</sub>:104 base excess: -1).

Adequate analgesia is important both intra- and postoperatively. The absence of residual analgesic effect after remifentanyl-based anaesthesia makes adequate postoperative analgesia important (19). In our case, we used tramadol 1mg/kg iv and im to provide same aim,

In conclusion, in this case report we have described a successful anesthetic management with propofol-remifentanyl induction and sevoflurane maintenance anaesthesia without muscle relaxant in an intestinal perforation patient with MNGIE syndrome.

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