




CASE REPORTS

Regional anesthesia in two consecutive surgeries in a patient with mitochondrial neurogastrointestinal encephalomyopathy: a case report

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KEYWORDS

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Abstract Mitochondrial Neurogastrointestinal Encephalomyopathy (MNGIE) is a rare autosomal-recessive disorder which is due to mutations in TYMP. The case reported here is of an 18-year-old male with MNGIE syndrome who presented for two different operations on two different occasions under regional anesthesia. The patient presented with urinary incontinence and abdominal pain. A cystoscopy under spinal anesthesia was scheduled. At 3 months after discharge, gastric perforation was diagnosed and combined spinal-epidural anesthesia, surgical repair was planned. Surgical and perioperative periods were uneventful. Based on this experience, we believe that regional anesthesia can be considered safe for use in patients with MNGIE disease.

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Introduction

Mitochondrial neurogastrointestinal encephalomyopathy (MNGIE) is a rare autosomal-recessive disorder which is due to mutations in gene TYMP, for which the prevalence is unknown. This mutation causes loss of function of

Thymidine Phosphorylase (TP), nucleoside accumulation in plasma and tissues, and mitochondrial dysfunction. Mitochondria use thymidine to produce new molecules of Mitochondrial DNA (mtDNA), and excess thymidine results in mutations that damage the replication, maintenance, and repair of mtDNA. MNGIE patients usually present with gastrointestinal dysmotility, cachexia, ptosis, exophthalmos, peripheral neuropathy, and diffuse leukoencephalopathy. The onset of symptoms is usually between the first and fifth decades of life, and in 60% of patients, symptoms begin

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before 20 years of age. Diagnosis of MNGIE disease can be determined by detection of biallelic pathogenic variants in TYMP (formerly known as ECGF1), or decreased thymidine phosphorylase enzyme activity, or high plasma thymidine and deoxyuridine concentrations. MNGIE patients generally present with unexplained abdominal pain, weight loss, persistent diarrhea, hearing problems, atypical cachexia and loss of strength.¹ Therefore, anesthesia may be required for endoscopy, colonoscopy, diagnostic laparotomy and similar operations for MNGIE patients. Although there have been a few case reports of general anesthesia for MNGIE patients, to the best of our knowledge, there is no study or case report in the public domain regarding regional anesthesia in MNGIE. The case reported here is of an 18-year-old male with MNGIE syndrome who presented for two different operations on two different occasions under regional anesthesia. Informed consent for publication of this case report was obtained from the patient and his parents.

Case report

An 18-year-old male presented with urinary incontinence and abdominal pain on his first admission to our hospital and cystoscopy under spinal anesthesia was scheduled. The patient had been diagnosed as MNGIE six months before by genetic testing. The medical history included an uneventful general anesthesia for endoscopy–colonoscopy and appendectomy two years previously. Preoperative blood tests were normal except for hypoalbuminemia. Pulmonary function tests showed a restrictive pattern. In the preanesthetic evaluation, a thin body habitus (height: 170 cm, weight: 30 kg), reduced muscle mass and hepatomegaly were detected. On arrival in the operating room, standard monitoring, including non-invasive Blood Pressure (BP), three-lead electrocardiography and pulse oximetry were applied. Vital signs were recorded as pulse rate 92 per minute, BP 123/77 and oxygen saturation 99%. Spinal anesthesia was performed at the L3–L4 level using a 27G Quincke spinal anesthetic needle (Egemen, Egemen Gaziemir, Izmir, Turkey) in the sitting position after meticulous disinfection with 10% povidone iodine. Hyperbaric 0.5% bupivacaine (Buvasin 0.5% spinal heavy, VEM İlaç, Turkey) was used as the local anesthetic for spinal anesthesia at the dose of 5 mg to achieve sensory block at T10 level. At 30 seconds after the injection, the patient was positioned supine, then moved into the lithotomy position while the upper body was covered with pre-warmed cotton blankets. The operation was completed in 20 minutes uneventfully and the patient was transferred to the recovery room.

Three months after discharge the patient was admitted to the Emergency Department with severe abdominal pain and gastric perforation was diagnosed. His laboratory examination showed hypoalbuminemia of 2.8 g.dL⁻¹ and total protein of 5.2 g.dL⁻¹. Chest X-Ray showed mild pleural effusion. Electrocardiogram was normal. The preoperative fasting period was about 3 hours. Combined spinal-epidural anesthesia was planned for surgical repair of gastric perforation. On arrival in the operating room, standard monitoring including invasive blood pressure via 20G cannula in the left radial artery (BP), three-lead electrocardiography and

pulse oximetry was applied. Vital signs were pulse rate 122 per minute, intra-arterial blood pressure 89/57 and oxygen saturation 99%. The patient received no premedication. With the patient in the sitting position, the combined spinal epidural anesthesia was performed at the T9–T10 vertebral interspace using spinal epidural combined set (Combifix Standard, Egemen International, Izmir, Turkey). After epidural puncture was completed with an 18G Tuohy needle with the loss-of-resistance to air method, a 27G pencil point spinal needle was advanced through the Tuohy needle. Flow of clear cerebrospinal fluid was confirmed, and 10 mg of 0.5% hyperbaric bupivacaine was injected into the subarachnoid space. After injection, spinal needle was removed, and then epidural catheter was placed and fixed at 4 cm within the epidural space. The upper level of anesthesia was controlled below the T6 vertebra. Lidocaine 2% 100 mg was administered epidurally at 90 minutes after the surgery started because the patient complained of pain. A 0.5 µg.kg⁻¹ infusion of dexmedetomidine was intravenously administered during the surgery. Degree of sedation and anxiolysis was maintained between 0 to -2 using the Richmond Agitation-Sedation Scale (RASS). The patient remained hemodynamically stable throughout the surgery. The surgery lasted 110 minutes and was completed uneventfully. The patient was transferred to the intensive care unit for immediate follow-up, then to the general surgery ward the following day.

Discussion

Clinical symptoms in MNGIE patients include gastrointestinal (loss of appetite, weight loss, chronic diarrhea, abdominal pain, chronic distension, nausea, dysphagia), ocular (external ophthalmoplegia, ptosis, retinal pigmentary changes, glaucoma, optic nerve atrophy), auditory (deafness), central nervous system (mental changes, subcortical loss of cognitive functions, memory impairment), peripheral neuropathies (numbness and paresthesia), skeletal muscle (proximal myopathy), and others (endocarditis, spontaneous abdominal esophageal perforation, short stature, cardiomyopathy, psoriasis).¹

As in other mitochondrial diseases, there are various challenges in the anesthesia management of MNGIE patients such as respiratory failure, heart, conduction disorders, and dysphagia. Although it has been reported that there is no reason to avoid any particular anesthetic agent in patients with a mitochondrial disorder diagnosis, those patients with more severe clinical disease may be at greater risk after general anesthesia.²

Progressive gastrointestinal dysmotility caused by enteric myopathy occurs in most individuals. Although gastric and small bowel hypomotility are most common, any part of the gastrointestinal tract can be affected.¹ Gastric hypomotility may increase the risk of aspiration from delayed gastric emptying. General anesthesia may exacerbate gastric distention precipitating vomiting and aspiration. For this reason, as in the current case, regional anesthesia may prefer especially in patients undergoing emergency surgery without properly fasting. In the current case, combined spinal epidural anesthesia at T9–T10 vertebral interspace was preferred. Generally, although the option to place a

spinal anesthetic at T9–T10 level seems hazardous by some anesthesiologists, the safety of this technique has been reported by many clinical and radiological studies. Lee et al.³ reported that sitting head down position increased the posterior separation of the spinal cord and dural sheath at thoracic levels. van Zundert et al.⁴ stated that the use of a combined spinal epidural system could limit the length of needle advanced through the epidural needle, which might minimize the risk of contact with neural tissue. In the current case, no complications related to combined spinal epidural anesthesia were observed.

It has been reported that both parenteral and volatile anesthetics affect mitochondrial function. However, it is often said that these agents only depress mitochondria at doses higher than their clinical concentrations.² While ketamine, etomidate and barbiturates inhibit mitochondrial function by only one mechanism, propofol has been found to depress mitochondrial function by four different mechanisms. Although propofol has little negative effect when it is used as an induction agent and/or low bolus doses, increased susceptibility to propofol infusion syndrome has been reported in patients with mitochondrial disease. Volatile anesthetics may be more advantageous than intravenous anesthetics because they do not require metabolism for excretion unlike intravenous anesthetics which are dependent on energy requiring metabolism. Even so, to avoid the side-effects of volatile agents, patients with mitochondrial disease may require support during the perioperative period. Although there is no evidence that muscle relaxants and narcotic analgesics inhibit mitochondrial function, they must be used carefully in patients who may already have respiratory compromise.² Dexmedetomidine can relieve the neuronal damage that may be caused by mitochondrial membrane oxidative stress, decrease the damage to mitochondrial-related enzyme system activity and reduce the damage to the activities of mitochondrial respiratory chain enzyme complexes I, II, III, and IV.⁵ Therefore, dexmedetomidine may be an alternative to general anesthetics due to its positive effects on mitochondria and cognitive functions.

When local anesthetics have been used on patients with mitochondrial diseases, although it seems likely that there may be increased sensitivity to adverse effects from propofol, such evidence has not been clearly stated in the literature. In addition, bupivacaine and other local anesthetics may cause cardiac arrhythmias, especially when used at high doses. A mechanism underlying the cardiovascular toxicity of local anesthetics is inhibition of mitochondrial transport of fatty acid.²

Preoperative fasting can be detrimental to patients with mitochondrial disease. The patients should be fed with lactic acid-free liquids containing dextrose (such as 5% dextrose–0.9% saline) during the preoperative period to prevent lactic acidosis. Excessive glycolytic oxidation of glucose may increase lactate levels if normal glucose levels are not achieved. Prolonged fasting, hypoglycemia, postoperative nausea and vomiting, hypothermia (with resultant shivering), long tourniquet times, acidosis, and hypovolemia should be avoided.²

Mitochondrial myopathies are a heterogeneous group of diseases including MNGIE. Due to the low incidence and large differences in clinical tables, the literature on anesthesia is limited. To avoid possible complications of general anesthesia, regional anesthesia was preferred for both operations on this patient. Based on this experience, regional anesthesia can be considered safe for use in patients with MNGIE disease.

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Conflicts of interest

The authors declare no conflicts of interest.

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