Anesthetic Management in Ambulatory Setting for a Patient with MELAS Syndrome.

Primary Author: Dritan Prifti MD
Cleveland Clinic

Co-Authors: Hui Yang, MD;

Introduction:
MELAS (Mitochondrial myopathy, Encephalopathy, Lactic Acidosis, and Stroke-like episodes) Syndrome is caused by mutations in the genes in the mitochondrial DNA, which leads to impaired oxidative metabolism, thus having clinical manifestations predominantly in organs with high energy requirements such as brain, lungs, liver and kidneys.

General anesthesia has several potential hazards to patients with MELAS, especially in the ambulatory setting where inadequate preoperative optimization and unreadiness for postoperative outpatient discharge make the management very challenging.

Case Summary
41 yo F was scheduled for dacryocystorhinostomy in the ambulatory setting.

Patient presented with PMH significant for Mitochondrial DNA (mtDNA) mutations that can lead to MELAS Syndrome & Leber Hereditary Optic Neuropathy. Her symptoms were significant for bilateral sensorineural hearing loss, bilateral pigmentary retinopathy, vertigo, migraines and depression. Her surgical history was significant for C-section 1995, splenectomy 2/2 MVA resulting in splenic rupture 1979, thyroidectomy and radiation for papillary thyroid carcinoma 2012 and bilateral dacryocystorhinostomy 2012. She was allergic to Darvocet & Percocet and was on following oral medications: Synthroid, Levocarnitine, citalopram, magnezium and Coenzyme Q10. Patient was 160 cm tall with weight of 64.6 kg.

Patient was admitted the night before surgery for fluid and metabolic optimization and presented the morning of surgery with complains of nausea. She had been NPO for 12 hours and had been given IV fluids of LR @ 75 ml/hr overnight. Patient’s physical exam including airway exam exam was unremarkable. Her preoperative lab test, EKG and Echo were within normal limits.

Per Neurogenetics specialist’s recommendation, we started dextrose-containing fluid (D5%-0.2%NS) bolus followed by infusion @ 1.25-1.5 times the maintenance rate and ondansetron IV which resulted in resolution of nausea. Patient was taken to OR and general anesthesia was induced with midazolam, lidocaine, fentanyl and etomidate. Patient developed significant myoclonus following etomidate administration, which impeded mask ventilation. Succinylcholine was given, mask ventilation became adequate and endotracheal intubation was performed. Anesthesia was maintained with sevoflurane, decadron was given for PONV prophylaxis and intraop accucheck was 148. Patient emerged from surgery without complications and was taken to PACU were she developed severe nausea with stable vital signs. ABG showed pH= 7.34, BE-5, HCO3 20, Na 136,
K 3.5, Glucose= 297, LA= 2.7, Ica 0.97 and IMg 0.42. Patient was given insulin and fluid/electrolyte replacement. Her Neurogenetics specialist was contacted regarding the safe pharmacological options for antiemetic medication. Per recommendation, promethazine was given, and metoclopramide was cancelled. After nausea resolved in PACU, she was readmitted to the ward for observation. Special instructions regarding fluid and metabolic management were given to the floor team by staff anesthesiologist. Patient was able to tolerate regular diet later and discharged home the day after surgery.

Discussion:

The MELAS Syndrome was first described by Pavlakis et al. in 1984. This multisystem disorder is characterized clinically by stroke-like episodes; evidence of mitochondrial dysfunction in the form of lactic acidosis, ragged-red fibers, or both; and at least two of the following: focal or generalized seizures, dementia, recurrent headaches, or vomiting.

There is significant phenotypic variability in MELAS while some patients suffer from multiple strokes, seizures and limb weakness, others, such as our patient are less severely affected. This phenotypic variability is probably due to a feature of mitochondrial inheritance termed "heteroplasmy". Within each individual cell there are multiple mitochondria, each containing multiple genomes. During cell division, these mitochondria are distributed randomly among daughter cells, with various cells or tissues receiving a mixture of normal and mutant genomes (heteroplasmy). If a threshold level of mutant mitochondria is reached within a particular tissue, organ dysfunction and clinical disorders may occur.

Due to significant cardiovascular, neurological, skeletomuscular, hepatic and renal comorbidities that may present in these patient populations, severity of clinical symptoms and risk of surgery need to be carefully evaluated before scheduling patient for outpatient procedure.

Cardiovascular system including cardiomyopathy, WPW syndrome, and conduction disturbances are prevalent in MELAS patients. Therefore, preop EKG is essential, and Echocardiography tests should be taken if possible. Moreover, the usage of drugs that may cause significant depression should be avoided or used carefully in small amounts during the operation.

Since patients with MELAS Syndrome may present with gastrointestinal involvement (our patient was nauseous and had received zofran prior to entering operating room), it is important to take precautions against aspirations, including rapid sequence induction if general anesthesia is required. It is paramount to avoid lactate administration due to increased lactate production, most likely resulting from defects in the respiratory chain necessitating anaerobic metabolism of glucose. Since patient scheduled for surgery require to be NPO for a relatively prolonged period of time, it is particularly important for patient with MELAS to have adequate hydration and substrate therapy. It is recommended that 5 or 10% dextrose containing fluids given at 1.25–1.5 times the maintenance rate. A high dextrose delivery with D10% or D20% might be needed, especially if acidosis or metabolic derangements are not correcting with 5% dextrose containing fluids. When a higher dextrose delivery is given, insulin may also be needed. Insulin not only controls hyperglycemia, but also serves as a potent anabolic hormone promoting protein and lipid synthesis.
It is very important to maintain normothermia during surgery, because hypothermia depresses mitochondrial function and, moreover, causes further metabolic stress in order to regain normothermia after surgery.

Several common intravenous induction agents may produce mitochondrial dysfunction. Propofol impairs mitochondrial electron transport chain by inducing a rise in malonyl carnitine, which subsequently inhibits carnitine palmytil transferase I, a protein involved in the mitochondrial transport of long fatty acids. Propofol also inhibits complex II of the respiratory chain resulting in an increase of C5-acylcarnitine. These mitochondrial effects of propofol are believed to be responsible for the “propofol infusio...” syndrome described in pediatric intensive care unit patients receiving prolonged propofol infusions. Propofol infusion syndrome presents with similar clinicopathological characteristics as mitochondrial cytopathies, including lactic acidosis, myocardial dysfunction and renal failure. Propofol should therefore be avoided in patients with MELAS Syndrome especially if prolonged infusions are required for sedation or anesthetic maintenance.

Conclusion:

1- Due to significant cardiovascular, neurological, skeletomuscular, hepatic and renal comorbidities that may present in patients with MELAS syndrome, severity of clinical symptoms and risk of surgery need to be carefully evaluated before scheduling patient for outpatient procedure.

2- Patient with MELAS syndrome are sensitive to physiologic stressors such as anesthesia, dehydration, prolonged fasting/starvation, fever and surgery, which may lead to rapid systemic decompensation. Thus, special precautions should be taken during the perioperative anesthetic management of these patients.