Lesson S24: Preanesthetic Assessment of the Patient with Mitochondrial Disease

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REVIEW DATE: March, 2012

Read this article, reflect on the information presented, then go online and complete the lesson post-test and course evaluation before the termination date below. (CME credit is not valid past this date.) You must achieve a score of 80% or better to earn CME credit.

TIME TO COMPLETE ACTIVITY: 2 hours
RELEASE DATE: May 1, 2012
TERMINATION DATE: May 31, 2013

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Professional Gaps

Mitochondrial diseases are rare but have important significance for anesthetic care. Most anesthesiologists may be unaware of the potential complications associated with patients afflicted with the disease. A current review and update of the literature is important knowledge for clinical anesthesiologists.

Learning Objectives

At the end of this activity, the participant should be able to:

1. State the incidence of mitochondrial disorders.
2. Describe the clinical presentation of mitochondrial disorders.
3. Distinguish between mitochondrial disorders, malignant hypertension and neuroleptic malignant syndrome (NMS).
4. Plan an anesthetic for a patient with MELAS.
5. Anticipate complications of mitochondrial disorders and anesthesia.
6. Order appropriate tests and consultations.
7. Identify the pathophysiology of mitochondrial disorders.
8. Understand the need for a multidisciplinary approach to care in patients with mitochondrial disorders.
9. Describe the role of the mitochondria in energy production.
10. Be aware of the Mitomap database.

Case History

A 19-year-old male presented for extensive dental restoration. It was reported that, as a child, he underwent open reduction and internal fixation of a fractured arm and was slow to awaken. He failed to regain his preoperative state and a review of the anesthetic care showed a stable course apart from an increased temperature postoperatively and marked lactic acidosis. The agents used in the procedure at that time included propofol, succinylcholine, isoflurane, nitrous oxide and fentanyl. There
was no family history of any adverse effects of anesthesia or malignant hyperthermia. At the time of the surgery, he was not receiving any medications. Neurologic deterioration had been slow but progressive over the ensuing 10 years and his dental decay was attributed to constant drooling and difficulty in swallowing. Tissue biopsy indicated red ragged fibers. A diagnosis of mitochondrial encephalopathy and lactic acidosis syndrome (MELAS) was made.

Introduction

Mitochondrial disorders are diseases that are characterized by a defect in mitochondrial metabolism. The mitochondria are subcellular organelles with faint, threadlike granules that convert energy from food molecules into adenosine triphosphate (ATP) that is used as energy for cell functions. ATP is produced through the Kreb’s citric acid cycle, fatty acid oxidation and oxidative phosphorylation (OXPHOS). OXPHOS is the main source for the formation of ATP. The mitochondrion is also involved in iron metabolism, which has been identified as a causative factor in Friedreich ataxia, amino acid biosynthesis and apoptosis or programmed cell death. A subclass of these disorders, mitochondrial myopathies, may be caused by OXPHOS defects.

Epidemiology

Mitochondrial diseases are caused by acquired or inherited mutations within mitochondrial DNA (mtDNA). Acquired dysfunction is usually the result of infection, adverse effects of drugs, or environmental causes. Mitochondrial DNA inheritance differs from autosomal and sexually linked inheritance in several ways. Nuclear DNA has two copies per cell (except for gametes) with one copy being inherited from the father and the other from the mother. In contrast, mitochondrial DNA is inherited entirely from the mother. Moreover, each mitochondrial organelle typically contains multiple mtDNA copies. During cell division the mitochondrial DNA copies segregate randomly between the two new mitochondria and make additional copies. If only a few of the mtDNA copies inherited from the mother are defective, mitochondrial division may cause most of the defective copies to congregate in only one of the new mitochondria. Thus there may be a large variation in the degree of impairment of any individual with defective mtDNA ranging from mild mental disturbance to neurogastrointestinal encephalopathy requiring total organ transplantation. Mitochondrial disease becomes clinically apparent once the number of affected mitochondria reaches a certain level, a phenomenon called "threshold expression".

To date, more than 200 disease-causing point mutations to the mitochondrial genome have been reported in the Mitomap database (http://www.MITOMAP.org). Mitomap is a database for the human mitochondrial genome, and has grown rapidly in data content over the past several years as interest in the role of mtDNA variation in human origins, forensics, degenerative diseases, cancer and aging has increased dramatically. Mitomap has implemented a new relational database and an improved search engine and is compatible with a new automatic mtDNA sequence analyzer known as Mitomaster1.

Although the structure of mtDNA has been known for over 40 years ago, the consequences of impairment of the OXPHOS pathway in creating mutations of the mitochondrial genome have only been described more recently.\textsuperscript{2,3,4} Much has been learned over the past 2 decades about mitochondrial disorders but the relationship between the molecular pathology of mtDNA-related diseases and the specific phenotypes associated with different mutations remains incompletely understood. Of the 200 disease causing points in the mitochondrial genome, at least 30 have been associated with a syndrome
termed “MELAS” - mitochondrial encephalopathy, lactic acidosis and stroke like symptoms - first described almost 30 years ago.\textsuperscript{5}

It takes about 3,000 genes to make a mitochondrion.\textsuperscript{6-7} Mitochondrial DNA encodes just 37 of these genes; the remaining genes are encoded in the cell nucleus and the resultant proteins are transported to the mitochondria. Approximately 3% of the genes (100 of 3,000) that comprise a mitochondrion are involved in ATP production. More than 95% (2,900 of 3,000) are involved with functions specific to the differentiated cell in which it resides. These functions change as the body develops from embryo to adult, and tissues grow, mature, and age. Non-ATP-related functions are intimately involved with most of the major metabolic pathways used by a cell to build, break down, and recycle its molecular building blocks. RNA and DNA cannot be produced without mitochondria and the necessary building blocks of purines and pyrimidines. Mitochondria contain the rate-limiting enzymes for pyrimidine biosynthesis (dihydroorotate dehydrogenase) and heme synthesis (d-amino levulinic acid synthetase) which are essential to the production of hemoglobin. In the liver, mitochondria are specialized to detoxify ammonia in the urea cycle. Mitochondria are also required for cholesterol metabolism, for estrogen and testosterone synthesis, for neurotransmitter metabolism, and for free radical production and detoxification.

Enzymes within mitochondria oxidize fat, protein, and carbohydrates to generate ATP via the electron transport chain in a process known as oxidative phosphorylation. The mitochondrial complexes (I-V) that are part of this process are multimeric proteins embedded in the inner mitochondrial membrane. Mutations in any of these proteins produce many different clinical manifestations. Although the majority of these proteins are encoded by nuclear DNA, producing Mendelian autosomal inheritance, some are encoded by mitochondrial DNA and therefore maternal inheritance is seen.

The first step of the respiratory chain/OXPHOS process is the conversion of NADH to NAD and it is the most common site of mitochondrial aberrations. Its three major forms include a fatal infantile multisystem disorder, myopathies, and mitochondrial encephalopathy. The latter two forms have variable course and prognosis and, other than metabolic supplements and dietary modifications to slow down progression of the disease, multivisceral organ transplantation may be the only definitive treatment.

**Genocopies of Mitochondrial Disease**

Genocopies are diseases that result from the same mutation but differ in clinical appearance. Because mitochondria perform so many different functions at different sites, mutations result in abnormalities that are expressed as hundreds of different mitochondrial diseases. This large spectrum of abnormalities can make a differential diagnosis difficult especially in the early stages. Because of the complex interplay between genes and cells required for metabolic stability, it is a hallmark of mitochondrial diseases that identical mtDNA mutations may not produce identical diseases.

**Phenocopies of Mitochondrial Disease**

The converse of genocopies also exists. Different mutations in mtDNA and nuclear DNA (nDNA) can cause the same diseases, known genetically as phenocopies. An example is Leigh syndrome, which can be caused by about a dozen different gene defects. Denis Archibald Leigh, a British psychiatrist, originally identified this syndrome in 1951 in a neuropathological description of the brain of one
affected child.\textsuperscript{8} It is also known as subacute necrotizing encephalomyelopathy and is characterized by bilaterally symmetrical MRI abnormalities in the brain stem, cerebellum, and basal ganglia, and often accompanied by elevated lactic acid levels in the blood or cerebrospinal fluid. Leigh syndrome may be caused by the NARP mutation (neurogenic muscle weakness, ataxia, retinitis pigmentosa); the MERRF mutation (myoclonic epilepsy with ragged red fibers); complex I deficiency, cytochrome oxidase (COX) deficiency, pyruvate dehydrogenase (PDH) deficiency, and other unmapped DNA changes. However, not all children with these DNA abnormalities go on to develop Leigh syndrome.

Another form of this disease, called the X-linked Leigh's syndrome (OMIM 308930), is a mutation in the oxidative phosphorylation enzymes which are on both the mtDNA and the nuclear DNA. The X-linked Leigh's disease is a mutation of a gene encoding PDHA1, part of the pyruvate dehydrogenase complex, located on the X chromosome.

Aging and other factors

Mitochondrial diseases are even more complex in adults because detectable changes in mtDNA occur with age and, thus, the aging process itself may result from deteriorating mitochondrial function. There is a broad spectrum of metabolic, inherited and acquired disorders in adults in which abnormal mitochondrial function has been postulated or demonstrated. Growth retardation is common.

Incidence

The estimated incidence of mitochondrial myopathies is about 1:4,000 but because of the variable symptomatology, this number is most probably an underestimate.\textsuperscript{9} About 1 in 4,000 children in the United States will develop mitochondrial disease by the age of 10 years. Up to 4,000 children per year in the US are born with a type of mitochondrial disease. Although most cases develop in childhood, an increasing number are first diagnosed in teenagers and adults.

Classification

Mitochondrial disorders are divided roughly into ragged red fiber disorders and non-ragged red fiber disorders based on accumulations of abnormal mitochondria. Ragged red fibers are formed by clumps of diseased mitochondria that accumulate in the subsarcolemmal region of the muscle fiber and appear as "ragged red fibers" when muscle is stained with modified Gömöri trichrome.

Ragged-red fiber disorders include:

- Kearns-Sayre syndrome
- Mitochondrial Encephalopathy with Lactic Acidosis and Stroke-like episodes (MELAS)
- Myoclonic epilepsy with ragged red fibers (MERRF)
- Progressive external ophthalmoplegia (PEO)
- Pearson syndrome

Non ragged-red fiber disorders include:

- Leigh encephalopathy
- Neuropathy, Ataxia, Retinitis Pigmentosa (NARP)
### Table 1: Manifestations of mitochondrial disorders

<table>
<thead>
<tr>
<th>MITOCHONDRIAL DISORDER</th>
<th>AGE AT DIAGNOSIS</th>
<th>MANIFESTATIONS</th>
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| Kearns-Sayre Syndrome        | > 5 yrs and < 15 yrs           | progressive external ophthalmoplegia  
retinitis pigmentosa  
cardiac conduction defect  
dilated cardiomyopathy |
| MELAS                        | late childhood, early adulthood | neurological symptoms – stroke, seizures, headaches  
lactic acidosis  
cardiac conduction defect  
cardiomyopathy |
| MERRF                        | childhood, young adulthood     | seizures  
progressive mental retardation |
| PEO                          | adulthood                      | similar to Kearns-Sayre syndrome |
| Pearson Syndrome             | infancy, early childhood       | refractory sideroblastic anemia  
insulin dependent diabetes mellitus  
exocrine pancreatic dysfunction  
usually fatal |
| Leigh encephalopathy         | perinatal time, early infancy  | diffuse encephalopathy  
dysphagia  
hypotonia  
central respiratory insufficiency |
| NARP                         | young adulthood                | weakness  
ataxia  
retinopathy  
learning disability |

Other diseases associated with mitochondrial dysfunction include:

- Diabetes mellitus and deafness (DAD).
  - When this combination is seen at an early age, mitochondrial disease should be suspected.
- Leber's hereditary optic neuropathy (LHON).
  - Visual loss beginning in young adulthood, characterized by progressive loss of central vision due to degeneration of the optic nerves and retina.
- Wolff Parkinson White syndrome
- Multiple sclerosis type disease
- Myoneurogenic gastrointestinal encephalopathy (MNGIE)
  - Gastrointestinal pseudo-obstruction
  - Neuropathy
Conditions such as Friedreich's ataxia can affect the mitochondria, but are not associated with mitochondrial proteins. Deficiencies of each of the respiratory chain complexes can result in separate conditions such as Complex I (NADH-CoQ reductase) deficiency. Deficiencies of these complexes, both individually and in combination, have been associated with the ragged and non-ragged red fiber disorders.

**Clinical Presentation**

Because of the numerous mutations, symptoms of mitochondrial disorders vary with age.\(^{10,11}\) Progressive muscle weakness and exercise intolerance are the predominant symptoms. In the neonate, first indications of the disorder are difficulty in sucking and holding the head up. Patients can have weakness of the muscles controlling the eyes and eyelids as a prominent feature. For some, the initial clinical manifestation can be weakness of the muscles of the face and neck with subsequent difficulty in speech and in swallowing. The degree of exercise intolerance varies with each individual; some experience problems with walking; in others, jogging or more intense activities increase the severity of symptoms. Muscle pain and muscle injury can result in rhabdomyolysis and myoglobinuria causing renal insufficiency and failure.

Since deficiency in ATP production is the end result of these disorders, organs with high-energy demands such as the brain, the heart and the kidneys may be involved early. Headaches, hearing deficits, seizures and learning disabilities with mental retardation can be the cerebral manifestations of ATP insufficiency (stroke-like episodes in MELAS). Cardiac conduction abnormalities requiring pacemaker placement and cardiac muscle damage with cardiomyopathy are common concerns in the cardiovascular system.

Abnormalities in the respiratory system result in shortness of breath and pulmonary insufficiency requiring ventilator support. When the gastrointestinal system is affected, symptoms include unexplained vomiting and dysphagia. Defects in the endocrine system are typically expressed as diabetes and exocrine pancreatic insufficiency.

**Diagnosis**

Mitochondrial disorders involve multiple systems and are usually progressive. Along with a history and physical, a complete neurological examination and follow up is warranted. Laboratory testing should include basic and specialized testing such as lactate, pyruvate, creatinine phosphokinase (CPK), plasma amino acid levels and urine for organic acids. (Table 2)

Although abnormal test results may support the diagnosis of mitochondrial disorder, a single normal test result does not rule it out. The triad of lactic acidosis, seizures and stroke-like episodes is central to the diagnosis of MELAS, occurring in more than 90% of patients.\(^ {12} \) Lactic acidosis is determined from serum or cerebrospinal fluid. Stroke-like episodes underscore the non-ischemic nature of these events. Affected areas of the brain have an irregular distribution, consistent with a metabolic or small vessel etiology rather than disease associated with compromise to major vascular supply. Clinically,
patients may have episodes of partially reversible aphasia, hemianopsia, and cortical blindness. Mild sensorineural hearing loss and migraine are common features.

A frequent systemic manifestation is diabetes mellitus, described in the earliest reports of mitochondrial disease.\textsuperscript{5} There appears to be a firm association between MELAS, the m.3243A>G mutation, and non-insulin dependent diabetes. Although episodic in nature, MELAS is progressive leading to dementia and severe neurologic deficits.

Brain imaging, audiology testing, ophthalmologic exam and electroencephalogram may identify central nervous system involvement. Electrocardiogram and echocardiogram can detect cardiac disease.\textsuperscript{13}

Skin or skeletal muscle biopsies can provide valuable information but are not 100\% sensitive. Fresh muscle biopsy may provide better results but is expensive (up to $10,000 for a complete analysis) and only performed at a few centers in North America.

Karyotyping and genetic consultation may benefit evaluation of patients with developmental and learning disabilities.

Diagnosis requires a team approach and should include consultations with specialists such as pediatricians, geneticists, psychiatrists, cardiologists and neurologists.

**Malignant hyperthermia**

For the undiagnosed myopathic patient, a non-triggering technique should be employed. Based on a record review, the estimated risk of malignant hyperthermia or rhabdomyolysis in a population of children with suspected neuromuscular dystrophy is less than 1\%.\textsuperscript{14}

The only known myopathic disorders associated with malignant hyperthermia and requiring non-triggering anesthesia are:

1. Central Core disease
2. King-Denborough syndrome and
3. Evans myopathy

Two earlier reports of malignant hyperthermia in association with mitochondrial disorders have been recorded; but most recent anesthesia reviews suggest that non-triggering anesthetics are not essential for the management of these disorders.\textsuperscript{14,15} A wide range of anesthetics has been used including general anesthesia with volatile anesthetics, intravenous anesthesia, or regional block with local anesthetics. Although lactic acidosis and high temperatures may be characteristic of mitochondrial disorders and malignant hyperthermia, these two entities have separate pathologies. A similar finding exists with neuroleptic malignant syndrome (NMS), a life-threatening neurological disorder most often caused by an adverse reaction to neuroleptic or antipsychotic drugs. NMS typically consists of muscle rigidity, fever, autonomic instability, and cognitive changes such as delirium, and is associated with elevated plasma creatine phosphokinase. Symptoms may be similar to mitochondrial disease, especially if they are manifest first in the perioperative period, but pathologies are considered to be separate.
Treatment

Therapeutic options for patients with mitochondrial diseases remain limited. A recent trial of the role of dichloroacetate was terminated because of peripheral toxicity.\(^\text{16}\) There are no curative therapies at present. Management of symptoms focuses on cardiac, renal, growth and nutritional issues. Other treatments use antioxidants, respiratory chain substrates and co-factors in the form of vitamins.\(^\text{17}\) No consistent benefits have been observed. However, recent studies of a therapeutic role for L-arginine have been promising.\(^\text{10}\) Dysfunction in COX activity and its effect on nitric oxide levels may cause angiopathic and stroke-like episodes; and L-arginine may affect the uptake of glutamate and the release of GABA, increasing the production of ornithine.\(^\text{18}\) A prospective trial and individual case studies report L-arginine given orally over 2 years significantly improved endothelial function.\(^\text{19}\) Although many neurologists recommend a variety of nutritional supplements (vitamins and antioxidants), there is little data to support the effectiveness of this therapy with the exception of Coenzyme Q supplementation. Since many patients are placed on regimens such as carnitine infusion, total parenteral nutrition or high dextrose infusions, it is important to continue these infusions intraoperatively to avoid a metabolic crisis.

Anesthetic Considerations

Preoperative history, physical and all laboratory and special testing should be performed in a time frame that allows sufficient time for interventions that may be indicated prior to the procedure. Electrolyte correction, especially acid-base balance, may be necessary. Coagulation parameters should be optimized and blood sugar should be normalized. A recent presentation of 9 surgical cases with MELAS who developed episodes of hyponatremia and hyperkalemia of varying severity demonstrated that these patients are prone to major electrolyte disturbances.\(^\text{20}\) The authors concluded that, given the propensity to develop acid-base disturbances and lactacidemia, it is prudent to review and normalize electrolyte abnormalities and to adjust the anesthetic plan accordingly.

The perioperative period carries several challenges for the anesthesiologist. A specific neurologic finding may require special attention; close monitoring may be indicated for those with cardiac conduction abnormalities or cardiomyopathy. Fasting guidelines indicate a minimum of 6-8 hours of solid meal avoidance and a minimum of 2 hours for clear liquids. Patients with mitochondrial disorders are at higher risk for aspiration because of weakness in the bulbar muscle and gut dysmotility. With prolonged fasting and inadequate glucose balance, they may also be in danger of a metabolic crisis. Therefore, a well thought out plan for their intravenous management should be in place. Avoidance of lactated Ringer's solution is also recommended to prevent an additional lactate load.

A systematic review may be carried out as follows:

**Neurologic**

Vision, hearing and speech may be impaired. Cognitive dysfunction is common, including language and memory difficulties. The ability to give informed consent may be impaired. Peripheral neuropathies and myodegenerative disorders are common and pose significant anesthetic concerns.\(^\text{21-23}\)
**Cardiac Manifestations**

Cardiac muscle has high-energy requirements and thus cardiomyopathy is common especially in children where it may be the sole anomaly. Cardiomyopathies and congestive cardiac failure should be evaluated and treated. Conduction defects such as Wolff Parkinson White syndrome should be documented. Bundle branch blocks and infranodal conduction defects are not uncommon and appropriate cardiac consultation should be sought.

**Pulmonary Changes**

Intrinsic pulmonary disease is rare. Pulmonary artery hypertension has been reported and associated with serum and cerebrospinal fluid acidosis. Muscle biopsy in this case revealed cytochrome c oxidase-positive ragged red fibers, and molecular testing demonstrated the presence of the m.3243A>G mutation.

**Renal Abnormalities**

Renal disease occurs less commonly than cardiac or endocrine problems but may manifest as de Toni-Debre-Fanconi syndrome, nephrotic proteinuria or focal segmental glomerulosclerosis. Bartter-like syndrome, hypercalciuria and tubulointerstitial nephritis have also been reported.

**Gastrointestinal involvement**

Several features have been described associated with mitochondrial diseases including constipation, gastric discomfort, hepatic pathology, pancreatitis, gastroparesis, intestinal pseudo-obstruction and malabsorption.

**Dermatological changes**

Vitiligo, scaly and pruritic rashes with diffuse erythema and reticular pigmentation have all been described. Skin changes appear to be relatively minor but may interfere with intravenous placement.

**Intraoperative Management**

In addition to standard ASA monitoring, arterial cannulation should be instituted for continuous hemodynamic monitoring as well as for frequent sampling for blood gases, electrolytes, blood glucose and lactate monitoring. Normothermia should be the goal to prevent added stress and increase in metabolic demands.

Preventing aspiration with rapid sequence induction (RSI) and cricoid pressure may be considered in some patients depending on co-morbid conditions and degree of skeletal muscle weakness. Depending on hepatic and renal insufficiency, muscle relaxants should be used cautiously. Although there is paucity of data regarding succinylcholine and mitochondrial disorders, its association with malignant hyperthermia in two case reports and possible hyperkalemic response should be considered. In the aforementioned presentation of 9 surgical cases with MELAS, 20 general anesthetics were given to the 9 patients and 12 of those interventions were prior to making the
Diagnosis of MELAS. The patients appeared to tolerate all commonly used anesthetics and muscle relaxants, including succinylcholine. Although volatile anesthetics have been used in patients with mitochondrial disorders without complications, they have been shown to impair OXPHOS by inhibition of complex I. This, in turn, can impair CNS metabolism and cause cardiac dysfunction leading to a potential increase in sensitivity to these agents. Other investigators have demonstrated in animal models that isoflurane induces caspase activation and apoptosis, which are part of Alzheimer degeneration, through the mitochondrial-dependent apoptosis pathway. Isoflurane appeared to be more likely to have detrimental effects on the mitochondria than desflurane, in mice studies.

Many have advocated total intravenous anesthesia as a safer, non-triggering anesthetic technique. A recent case report described the management of a patient with mitochondrial encephalopathy undergoing laparoscopic cholecystotomy using continuous infusions of propofol and remifentanil with intermittent doses of rocuronium. Another account describes the management of an emergency patient with mitochondrial neurogastrointestinal encephalopathy maintained with intravenous propofol after an RSI with midazolam, fentanyl, propofol and rocuronium. The safety of propofol has been questioned because of the potential for its lipid component to affect fatty acid oxidation and because of a direct effect on the mitochondrial respiratory chain. Both of these effects may predispose patients to a propofol infusion-like syndrome characterized by lactic acidosis, bradycardia, rhabdomyolysis, cardiac and renal failure. Although it is more likely to occur with infusions of longer duration (> 48 hours), in susceptible patients, even short-term infusions can cause symptoms. Ketamine has not been implicated as a deleterious agent in mitochondrial disorders and its analgesic properties can be an adjunct to the overall anesthetic management.

Regional anesthesia may be an attractive alternative for patients with mitochondrial disorders but local anesthetics have been shown to impair OXPHOS and may lead to inefficient ATP synthesis. Clinically, regional anesthesia has been used successfully and reduces the requirement for opioids thereby lowering risk of respiratory depression with worsening acidosis. Also if a regional technique were used alone, volatile anesthetic sensitivity would be avoided.

Postoperatively, the goal is to minimize metabolic stress and prevent increases in metabolic demand. It is important to prevent shivering, provide adequate analgesia, maintain normoglycemia and normal respiration. Even with a diligent perioperative plan, patients with mitochondrial disorders may require close monitoring in an intensive care setting.

Management of the Case Presented

The patient had a high level of anxiety. After administration of antacid prophylaxis, he was given midazolam 1.5mg. An induction dose of propofol was given as well as fentanyl 100ug. Intubation was achieved with rocuronium and the anesthetic continued with desflurane in oxygen. The dental surgeon injected local anesthesia. At the conclusion of the 2-hour surgery, the patient was slow to awaken. His temperature rose to 39.5 degrees Centigrade in the recovery room and he was aggressively cooled. Blood gases indicated some metabolic acidosis and he was given sodium bicarbonate. Ventilation was continued for several hours. By the next morning he was awake and the endotracheal tube was removed. He was observed for the next 2 days in hospital and when the team was assured that he had returned to his baseline state, he was discharged.
Conclusion

Although uncommon, patients with mitochondrial disorders can pose many challenges for the anesthesiologist. There has not been a single anesthetic technique deemed to be the “safest”. The choice of anesthetic must be individualized to the patient’s needs. Limited data suggest that patients with MELAS tolerate commonly used anesthetic drugs well. Multidisciplinary consultation with experts in the field and sub-specialists can provide valuable assistance with co-morbid issues and allow for good prognosis even in complex patients with multi-organ disease.

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REFERENCES


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Post-test

1. The most predominant symptoms of patients with mitochondrial disorders are:
   a. Renal failure and mental retardation
   b. Congestive heart failure and conduction abnormalities
   c. Progressive muscle weakness and exercise intolerance
   d. Seizures and learning disabilities

2. In patients with mitochondrial disorders, which of the following should be obtained first?
   a. CSF studies
   b. Karyotyping
   c. Basic chemistries, glucose and serum lactate
   d. Renal ultrasound

3. Which of the following myopathies is associated with malignant hyperthermia?
   a. Kearns-Sayre syndrome
   b. Evans myopathy
   c. MELAS
   d. Pearson syndrome

4. In patients with mitochondrial disorders, anesthetic complications are least likely to include:
   a. Lactic acidosis
   b. Aspiration
   c. Metabolic crisis
   d. Stroke

5. Patients with MELAS who require anesthesia are best managed with:
   a. Regional techniques
   b. No “safe” anesthetic has been described
   c. Isoflurane in low doses
   d. Total intravenous anesthesia
6. **Mitochondrial diseases are caused by:**
   a. Acquired or inherited mutations
   b. Genetic inheritance
   c. Adverse drug effects
   d. All of the above

7. **Propofol infusion syndrome is characterized by all of the following except:**
   a. Lactic acidosis
   b. Tachycardia
   c. Rhabdomyolysis
   d. Cardiac failure

8. **Regarding therapy for a mitochondrial disorder:**
   a. Dichloroacetate is frequently administered.
   b. Focus is management of symptoms.
   c. Only antioxidants are proven to be beneficial.
   d. Data support the effectiveness of nutritional supplements.

9. **Regarding the use of muscle relaxants in patients with mitochondrial disorders:**
   a. The two entities have separate pathologies.
   b. Non-triggering anesthetics must be used for patient with mitochondrial disorders.
   c. Lactic acidosis is not characteristic of malignant hyperthermia.
   d. All of the above.

10. **Mitochondria functions include:**
    a. Detoxification of ammonia
    b. Cholesterol metabolism
    c. Estrogen synthesis
    d. All of the above