An Adult with Inherited Mitochondrial Encephalomyopathy: Report of A Case

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THE terms mitochondrial myopathy or inherited mitochondrial encephalomyopathy encompass a grouping of neurologic syndromes produced by genetic defects that disrupt mitochondrial energy production. Most have been described in detail only recently.¹² Many of these disorders are clinically apparent during infancy, but others first appear during the young or middle adult years and then eventually progress to incapacitation and premature death. It is uncertain whether these are truly rare disorders or whether they are relatively common but remain undiagnosed because they are insidious in onset and phenotypically pleiotropic. This report describes the anesthetic management of one such affected adult patient and discusses some of the anesthetic implications of inherited mitochondrial disease.

Case Report

A 41-yr-old man (height, 175 cm; weight, 84 kg), American Society of Anesthesiologists physical status III, with hiatal hernia and severe gastroesophageal reflux disease and choilothiasis was scheduled for Nissen fundoplication with partial cell vagotomy and cholecystectomy. He had been diagnosed by a neurologist several years earlier as having “NARP syndrome” because he exhibited the fundamental stigmata of that disorder: sensory Neuropathy, Ataxia, and Retinitis Pigmentosa. In addition, physical examination revealed mild mental retardation, progressive deafness, generalized limb weakness, and dysarthria. He had worked as a delivery man and drove a truck until his eyesight deteriorated significantly by age 28 years. Two years later, he had been given a general anesthetic consisting of thiopental, pancuronium, fentanyl, droperidol, and nitrous oxide in oxygen, apparently without complications, for open reduction and fixation of a hip that was fractured when he was struck by an automobile. He now lived alone but was visually assisted by a guide dog. Regular medications included omeprazole, alprazolam, amitriptyline, diazepam, coenzyme Q10, and ferrous sulfate. He was known to be allergic to iodinated contrast dye.

During this hospitalization, preoperative laboratory data were within the normal range. An epidural catheter for postoperative analgesia was offered but refused by the patient. Because of an anticipated difficult intubation (Mallampati class 3) and severe gastroesophageal reflux, his trachea was intubated using fiberoptic guidance with topical lidocaine anesthesia of the oropharynx and transmucosal block of the superior laryngeal nerves after the patient had been sedated with midazolam, fentanyl, and droperidol. He then underwent an uneventful general anesthetic with thiopental, fentanyl, rocuronium, and nitrous oxide 70% in oxygen. At the end of surgery, neuromuscular blockade was reversed easily within 5 min with neostigmine and glycopyrrolate. Exubated promptly on resumption of spontaneous ventilation and responsiveness to verbal commands, the patient was transported to the surgical intensive care unit for overnight monitoring and observation. He had no evidence of gastric aspiration or ventilatory insufficiency, and he was transferred to a regular surgical nursing unit on the first postoperative day.

Discussion

The molecular components of the five major enzyme–protein complexes needed for mitochondrial oxidative phosphorylation (ox/phos) are encoded in a complementary manner by the nuclear genome of the host cell and by a small circular genome found within the mitochondrion itself. Loss of mitochondrial bioenergetic capacity is a possible explanation for the ubiquitous and insidious deterioration of organ system functional reserve of normal aging and perhaps for much age-related disease.³⁴⁵ There are genetically transmitted mitochondrial disorders mediated by mutations of nuclear deoxyribonucleic acid that usually involve primary carnitine deficiencies and follow Mendelian (dominant–recessive) patterns of inheritance.⁶ Less well known are syndromes such as NARP that result from maternally transmitted mutations of mitochondrial DNA.
Fig. 1. There is a decrease in maximal oxidative phosphorylation (ox/phos) capacity (solid line) in visual, motor, muscle, and renal tissues throughout the adult years. However, in patients with inherited mitochondrial disorders (interrupted line), capacity may decrease below the minimum values needed for normal functioning (dotted lines) during early or middle adulthood. Redrawn from Wallace.7

(mtDNA). In those with NARP, a point mutation at base-pair position 8993 of mtDNA produces defects in adenine triphosphatase (ATPase). Reduced ATPase activity and lower rates of ATP production are found in mitochondrial isolates of lymphoblastoid cell lines obtained from NARP patients,8 and there are increased brain levels of phospho-creatine and inorganic phosphate in NARP patients compared with age- and sex-matched control subjects.9

Progressive decrease in cardiac, muscle, and nervous system functional reserve probably begins long before the appearance of overt signs or symptoms of NARP in young adulthood (fig. 1). The diversity of organ systems that are involved in this and other syndromes of inherited mitochondrial encephalomyopathy are a result of the markedly different metabolic demands of various tissues and of “heteroplasmy,” the uneven distribution of mutant mitochondrial genomes to different tissues during the early phases of embryogenesis.10 There are few case reports that describe the anesthetic treatment of adults with mitochondrial encephalomyopathy, and there are none of those with NARP syndrome. We chose a “nontriggering” anesthetic regimen for our patient because he had received this type of anesthesia uneventfully in the past and because we were not well versed in the likelihood of malignant hyperthermia (MH) in patients with NARP. However, susceptibility to MH and enhanced sensitivity to neuromuscular blockade, issues typically considered for patients with the more familiar muscular dystrophies and neurogenic myopathies, are probably not important for those with most forms of inherited mitochondrial encephalopathy and myopathy. Only the rare myopathies with “multicore” or “minicore” histology may be actually be associated with MH.11

Local anesthetics disrupt ox/phos in mitochondrial isolates, but clinical reports suggest that patients with mitochondrial disorders do well with regional anesthetics.13,14 Similarly, propofol and the potent inhalational agents interfere in vitro with mitochondrial energy production,15 although patients with inherited mitochondrial encephalomyopathies have been exposed to various general anesthetic regimens without and without neuromuscular blockade without apparent adverse consequences.16-18 It appears that these patients require preoperative assessment of functional organ system reserve rather than simple screening for the presence of disease. Other unique concerns include reduced anesthetic requirement and susceptibility to prolonged nervous system depression, intrinsic skeletal muscle hypotonia and decreased aerobic work capacity, and cardiomyopathy with increased risk of sudden death from conduction abnormalities.9,20 Overt encephalopathy may be present, and subclinical hepatic and renal involvement is always possible, predisposing the patient to prolonged drug effects and delayed recovery of neurologic function.

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Anaphylactic Shock Induced by an Antiseptic-coated Central Nervous Catheter

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ANAPHYLACTIC shock is a rare but life-threatening complication in clinical practice. A number of drugs used during perioperative management have been reported to cause anaphylactic shock. Recently a non-drug-related hypersensitivity reaction, latex allergy, has been increasing in incidence during anesthesia and surgery.1 We report a case of anaphylactic shock that occurred during the placement of an antiseptic-coated central venous catheter.

Case Report

A 47-yr-old woman with a history of uterine myoma was scheduled for hysterectomy. The patient had undergone the removal of uterine myoma at aged 30 yr, however, her medical history was free from allergic reactions. Her preoperative physical examination was significant only for well-controlled diabetes mellitus.

The patient was brought to the operating room after being premedicated with oral diazepam, 5 mg. Before induction of anesthesia, an epidural catheter was placed in the second lumbar interspace, and 2 ml of 1% meptivacaine was given as a test dose. Her preinduction blood pressure was 126/82 mmHg, with a heart rate of 82 beats/min in normal sinus rhythm. Anesthesia was induced with propofol (1.5 mg/kg), and tracheal intubation was facilitated with vecuronium (0.1 mg/kg). Anesthesia was maintained with sevoflurane in nitrous oxide and oxygen. After induction of anesthesia, an antiseptic-coated central venous catheter (ARROWgard Blue®; 14-gauge, Arrow International Inc., Reading, PA) was inserted from the right subclavian vein. During placement of the catheter, we recognized arterial hypotension (from 120/86 mmHg to 102/60 mmHg in 5 min) and reaching as low as 70/40 mmHg within 10 min, together with tachycardia (120 beats/min).

The hypotension was refractory, despite treatment with vasoactive agents (epinephrine; dopamine;norepinephrine), fluid replacement, or treatment with corticosteroid (methylprednisolone). We also noted a generalized, irregular, raised erythema. There was no evidence of bronchoconstriction. We made a diagnosis of hypersensitivity reaction on the basis of the clinical manifestations and postponed the surgical operation. Thirty minutes later, the blood pressure rose to 130/70 mmHg with the aid of dopamine (5 μg·kg⁻¹·min⁻¹) and became stable 40 min later without dopamine. The generalized erythema gradually subsided within 2 h. The central venous catheter


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