Myoclonic Epilepsy With Ragged Red Fibers

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Risk

- Prevalence: 1:400,000
- Maternal inheritance; less commonly a spontaneous mitochondrial gene mutation in those without family Hx

Perioperative Risks

- Lactic acidosis
- Cardiac/respiratory insufficiency/failure
- Delayed emergence

Worry About

- Respiratory failure following sedation.
- Consider aspiration risk.
- Lactic acidosis.
- Seizures.

Overview

- Mitochondrial myopathy most commonly characterized by cerebellar ataxia, myoclonus, epilepsy, lactic acidosis, hearing loss, peripheral neuropathy, and short stature.
- Excess lactic acid load leads to nausea, vomiting, abdominal pain, fatigue, and tachypnea.
- Most commonly maternal inheritance; less commonly results from a new mutation in a mitochondrial gene in those without a family Hx.
- Onset is in late adolescence through early adulthood.
- Muscle biopsy with hallmark appearance of ragged red fibers.
- DNA point mutation results in mutation of respiratory chain complexes I + IV.
- Inability to process lactate-containing fluids.
- Anesthetic sensitivity may manifest as decreased MAC of inhaled anesthetics, with increased respiratory insufficiency from sedatives and narcotics.

Etiology

- Most common mutation is the m.8344A>G mutation in the mitochondrial DNA gene, MT-TK, which encodes mitochondrial transfer (t)RNA lysine.
- Muscle biopsy shows ragged red fibers with deficient activity of COX, and presence of COX deficient vessels with SDH stain.

Usual Treatment

- Anticonvulsant (valproic acid, phenobarbital)
- Myoclonus therapy (clonazepam, tizanidine)
- Multivitamins (CoQ-10, CoQ-6, B-complex, L-carnitine)

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Sensorineural hearing loss Optic atrophy Pigmentary retinopathy	Hearing loss Vision loss	Decrease visual acuity	Hearing exam Ophtho exam
CV	Cardiomyopathy Conduction defects (WPW)	Symptoms of CHF Palpitations, dizziness, lightheadedness	Murmur, gallop, crackles	CXR, ECHO, ECG, exercise testing (VO_2 max)
RESP	Disorganized respiratory muscle effort	Hypoventilation, hypoxia, following sedative use	Rhonchi	CXR
GI	Swallowing impairment, GI dysmotility	Dysphagia, bloating, N/V		Barium swallow, Endoscopy, manometry
ENDO/METAB	Lactic acidosis DM	N/V Polyuria Polydipsia Polyphagia	Hyperventilation Orthostatic hypotension	Serum lactate, serum electrolytes, serum pyruvate, HbA_{1C}
CNS	Epilepsy, cerebellar ataxia, Dementia Intention tremor Degenerative changes in CNS, psychomotor regression	Developmental delay Vision loss Poor balance/coordination	Focal neurologic deficits Signs of seizure	Head CT/MRI, EEG
PNS	Peripheral neuropathy	Weakness Dysesthesias	Decreased strength, distal sensory loss, decreased DTR	Monofilament, tuning fork
MS	Myopathy myoclonus Spasticity	Weakness, involuntary twitching of extremities, stiffness, muscle spasms	Decreased strength, decreased ROM, muscle contractures	EMG, serum CK Ragged red fibers on SDH stain
OTHER	Short stature Lipomas (near the neck)			

Key References: Vilela H, Garcìa-Fernández J, Parodi E, et al.: Anesthetic management of a patient with MERRF syndrome, *Pediatr Anaesth* 15(1):77–79, 2005; Baum VC, O'Flaherty JE: MERRF syndrome. In Baum VC, O'Flaherty JE, editors: *Anesthesia for genetic, metabolic, & dysmorphic syndromes of childhood*, ed 3, Philadelphia, 2015, Wolters Kluwer, pp 283–284.

Perioperative Implications

Preoperative Preparation

- Assess cardiac involvement.
- Avoid prolonged fasting and dehydration because it worsens acidosis.
- Correct preop acidosis.
- When possible, start IV fluid (avoid lactate-containing fluids; bicarbonated Ringer is OK) at NPO time, allow for late (2 h prior) clear intake, and book as first case.
- H+P limitations (hearing loss, dementia).
- Assess medication list; anticonvulsants and myoclonus medications will affect sensitivity to certain anesthetics.
- Ensure most recent dose of anticonvulsant has been administered.
- Determine frequency, severity, and triggering factors of seizures.

Airway

- Aspiration risk

Monitoring

- Routine, assuming no severe cardiomyopathy or CHF.
- Consider BIS monitor prior to induction for possible increased anesthetic sensitivity.
- Longer procedures consider arterial line for intraop

Induction

- Avoid lactate-containing IVF (i.e., lactated Ringer).
- Avoid succinylcholine risk of uncharacterized myopathy/neuropathy leading to exaggerated hyperkalemia.
- Avoid etomidate as this has the highest incidence of CNS excitatory activity.

Maintenance

- Ensure normoglycemia, normothermia, normotension, normovolemia and optimal oxygenation (factors known to influence existing or latent lactic acidosis).
- Avoid propofol infusion as this leads to disruption of the electron transport chain worsening acidosis and reduced ATP production.
- Short-acting NMB if required (carefully titrated) but better to avoid if possible.
- Aggressive temp control; active warming techniques.
- Opioids carefully titrated with caution for increased risk of respiratory depression. Avoid meperidine secondary to strong association with myoclonus and seizure activity.
- Possible increased sensitivity to halogenated agents but can be used safely.
- Reduce spontaneous ventilation and natural airway, preventing muscle fatigue and respiratory failure.
- Severe lactic acidosis can be treated with dichloroacetate (15 mg/kg IV over 30 min) which stimulates pyruvate dehydrogenase which converts lactate to pyruvate.

Extubation

- Muscle weakness and anesthetic sensitivity may delay extubation.

Regional/Neuraxial

- Local anesthetics have potential to uncouple electron transport chain worsening lactic acidosis but have been used successfully.

Postoperative Period

- Close monitoring of respiratory function.
- Longer duration procedures: Consider obtaining lytes or ABG to assess for acidosis.

Anticipated Problems/Concerns

- Generally not associated with MH; however, critical ATP depletion may precipitate muscular contraction, mimicking MH.
- Although succinylcholine is not contraindicated (as in Duchenne or Becker MD), acidosis and neuropathy may predispose to hyperkalemia.