Anesthetic management for a child with QARS gene mutation

Department of Anesthesia & Critical Care, The University of Chicago Medicine
Tiffany Lin, MD, Andrew Wuenstel, MD, Igor Tkachenko, MD

Case presentation

HISTORY OF PRESENT ILLNESS

Patient is a 5-month-old 5 kg girl with heterozygous QARS gene mutation manifested by microcephaly, neonatal intractable epilepsy, and central hypotonia. She was admitted to PICU at 3 months of age for status epilepticus. During admission, she was found to have pharyngeal dysphagia, GERD with recurrent NBNB emesis, and aspiration. She also had biphasic stridor and bilateral rhonchi. She was scheduled for laparoscopic G-tube placement for long-term feeding solution, direct laryngoscopy and bronchoscopy for airway examination.

PAST MEDICAL HISTORY

- NSVD at term, weight 5 lb 6 oz (3%ile), length 18 in (3.3%ile), head circumference 29 cm (<0.01%ile)
- Perinatal complications: NICU stay x6 weeks for seizures that started at 6 hours of life
- Heterozygous QARS gene mutation
- Anemia: Hgb 8.3

MEDICATIONS

- Clobazam, felbamate, phenobarbital, valproic acid, lorazepam PRN, Famotidine, NJ tube feed

FAMILY AND SOCIAL HISTORY

- Mother 30yo, father 43yo, likely distant cousins
- Sister 3yo and healthy
- Paternal cousin with microcephaly and died at 2mo
  Paternal cousin with 2-yr history of epilepsy at age 10

PHYSICAL EXAMINATION

- Microcephaly, widely spaced eyes, micrognathia
- Central hypotonia, poor head control, poor eye tracking
- Biphasic stridor, bilateral rhonchi
- On 6 L HFNC for frequent apnea, desaturations, and seizures

Discussion

Aminoacyl t-RNA synthetase (ARS)

- Attach amino acids to their corresponding tRNA molecules during protein translation[1, 2]
- 37 ARS genes encoded in the human genome, 22 known to be mutated in human diseases: linked to mainly neurological pathologies (ex. neurodegeneration, hypomyelination, encephalopathy, seizures, peripheral neuropathies)[1, 2]

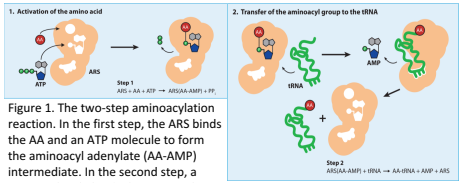

Figure 1. The two-step aminoacylation reaction. In the first step, the ARS binds the AA and an ATP molecule to form the aminoacyl adenylate (AA-AMP) intermediate. In the second step, a tRNA molecule binds the ARS via the anticodon binding domain and the AA is transferred to the tRNA. [1]

Glutaminyl-tRNA synthetase (QARS)

- Attaches glutamine to its corresponding tRNA molecule
- Enzymatic activity in both cytoplasm and mitochondria[1]
- Widely expressed in fetal human brain, required for dendritic and axonal terminal arborization during development, exhibits glutamine-dependent anti-apoptotic function[1, 2]
- QARS gene mutation: progressive microcephaly, diffuse cerebral and cerebellar atrophy, hypomyelination, early-onset epileptic encephalopathy, profound global developmental delay, severe hypotonia[2, 3]

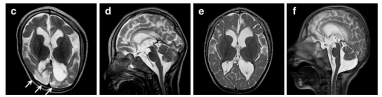

Figure 2. T2-weighted axial and sagittal images of 2 patients affected by QARS gene mutation. Diffuse cerebral atrophy with severe white matter volume loss, hypomyelination, hypoplastic corpus callosum, enlargement of the lateral ventricles, and cerebellar atrophy were observed in both individuals.[3]

QARS features	Anesthetic implications
Microcephaly, facial dysmorphism (micrognathia)	Potential difficult airway • Advanced intubation techniques may be required
Hypotonia	Increased aspiration risk • Pharyngeal dysphagia, decreased lower esophageal sphincter tone • Aspiration precaution: strict NPO, RSI with cricoid pressure Increased respiratory complications • Poor respiratory muscle tone → airway collapse, decreased FRC • Inability to clear secretions → increased risk of respiratory infections Increased risk of life-threatening hyperkalemia with succinylcholine administration • Avoid succinylcholine Increased risk of malignant hyperthermia (MH) • MH associated with many disorders characterized by congenital myopathy and hypotonia (ex. central core disease, King-Denborough syndrome)[4] • Avoid succinylcholine, volatile anesthetics
Mitochondrial involvement	Increased risk of propofol infusion syndrome • PRIS associated with younger age, severe critical illness of CNS/respiratory origin, subclinical mitochondrial disease[5] • QARS participates in protein translation in mitochondria • Avoid propofol infusion

Case resolution

In the operating room, patient underwent modified RSI with 0.75 mg midazolam, 15 mcg fentanyl, and 9 mg rocuronium. She was easily intubated with 3.0 microcuffed ETT by Miller 1 blade with Grade 2 view. Maintenance was achieved with 1 mcg/kg/hr dexmedetomidine and 0.1-0.15 mcg/kg/min remifentanil. 2.5 mg dexamethasone was given to minimize airway edema. After the surgery, neuromuscular blockade was reversed with 0.35 mg neostigmine and 0.07 mg glycopyrrolate and patient was extubated successfully. No anatomical airway abnormalities were found. Patient's stridor was attributed to poor muscle tone and airway collapse.

References

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