Anesthesia for a Patient with Aicardi Goutières Syndrome

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The Case

A 14-month-old, 7.6 kg female with Aicardi-Goutières Syndrome (AGS) presented for laparoscopic gastrostomy placement. Despite many associated anesthetic concerns, there has not been a published report of a patient with the syndrome undergoing anesthesia.

Our patient was born at term after an uneventful pregnancy. Her milestones were delayed, and at age 5 months she was admitted for workup. She had nystagmus, an exaggerated startle reflex, and irritability. MRI found diffuse parenchymal volume loss, diffuse confluent symmetric white matter signal abnormality, and scattered subcortical white matter areas compatible with calcifications. Her CSF had elevated neopterin and tetrahydrobiopterin. Genetic analysis revealed that she had two abnormal variants of RNaseH2B, establishing a diagnosis of AGS.

Aicardi Goutières Syndrome

AGS is a genetically heterogeneous autosomal recessive progressive inflammatory encephalopathy. When AGS manifests in the neonatal period, it can be mistaken for a TORCH syndrome. It can be distinguished by negative infectious titers and elevated CSF interferon-alpha (INF-α), neopterin and tetrahydrobiopterin.

Imaging findings	Neurological clinical findings	Autoimmune-like findings
Cerebral calcifications Leukodystrophy Cerebral atrophy	Acquired microcephaly Hypotonia Chronic irritability Aseptic hyperpyrexia Central blindness, nystagmus Feeding difficulties Seizures Exaggerated startle reflex Atypical sleep-wake cycles	Hepatosplenomgaly Thrombocytopenia Congenital glaucoma Hypothyroidism Hemolytic anemia Diabetes mellitus Cardiomyopathy Syndrome of inappropriate antidiuretic hormone Chilblain-like lesions

The pathogenesis of AGS is incompletely understood, but the involved genes seem to be involved in breaking down nucleic acids released by apoptosis. Possibly, inappropriately-processed DNA or RNA may be mistaken for viral material by the immune system and trigger an INF-α response. Often, there is an "active" phase with clinical regression with elevated CSF INF-α, followed by a more stable clinical course with normal INF-α.

	Intraoperative Concerns	In this Case
Neurologic	Unknown effect of anesthetics on altered nervous system. Antiepileptic drugs and their effect on medications.	Total intravenous anesthesia was used. Acetaminophen, ketorolac, and local anesthetic infiltration for analgesia. 0.4mg/kg rocuronium was used. No twitch response 30 minutes later. Neuromuscular blockade reversed with 4mg/kg sugammadex. Ketamine avoided given elevated risk of seizure with AGS. Succinylcholine avoided given risk of hyperkalemia with low muscle tone.
Cardiac	Pulmonary hyptertension secondary to obstructive sleep apnea (OSA)	
Pulmonary	Difficult airway OSA Aspiration Pneumonia Respiratory insufficiency	Our patient had microcephaly and micrognathia and possible sleep apnea, but was easily mask ventilated and intubated, although the latter may become more difficult when she is dentulous. She had a runny nose at presentation and a history of aspiration, but there was not airway hyperreactivity during the case. Extubated when fully awake at baseline vigor.
Gastrointestinal	Feeding difficulties GERD Refeeding syndrome Intraoperative hypoglycemia	Supported with D5-1/2LR intraoperatively. Monitored for refeeding syndrome postoperatively, not found to have clinical or laboratory abnormalities.
Renal	No frequent renal manifestations identified in AGS. Other autoimmune diseases associated with elevated INF-α have renal involvement.	
Immune	Concern in the AGS community that stress of surgery can trigger a flair.	Discussed anesthetic options with patient's parents. Used total intravenous anesthesia in part for its anecdotal lower association with postoperative flairs in the AGS community.
Musculoskeletal	Hypotonia Contractures	Careful positioning to avoid pressure
Integumentary	Chilblain-like lesions, inadequate padding may lead to decreased perfusion	Skin evaluation preoperatively identified no concerning lesions.
Endocrine	Diabetes mellitus Hypothyroidism Thermal dysregulation	Patient did not have these conditions when evaluated at 5 months. No concerning symptoms had developed in the interim. Body temperature closely monitored
Hematologic	Thrombocytopenia Hemolytic anemia	Normal platelet count and hemoglobin at 5 months No history of abnormal bruising or bleeding.

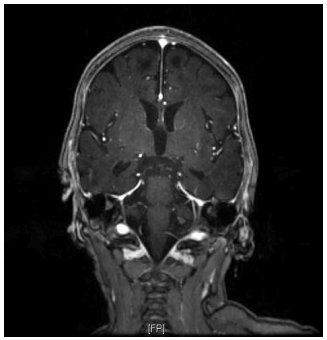
Conclusion and Lessons

Our patient was admitted postoperatively primarily for monitoring for refeeding syndrome. She quickly returned to her usual neurologic state and behavior. Her usual calming modalities, being held and parental presence, were used in the post-anesthesia care unit (PACU) in lieu of narcotics. Oxygen was weaned to room air in the PACU and her vital signs remained stable throughout admission. She was discharged home on postoperative day two.

Without any published cases of anesthesia for patients with AGS, concerning features were identified and lessons were learned about the response of patients with AGS to anesthesia.

- Avoiding long-acting opioid allowed for rapid restoration of baseline neurologic function.
- Neuromuscular blockade had a prolonged duration of action.
- Sugammadex was used without apparent complication.

This patient underwent general anesthesia safely, but more published cases and research are necessary to inform anesthetic plans for patients with AGS.



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