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A suspected case of anesthesia-induced rhabdomyolysis in a child undergoing strabismus surgery

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We report a case of acute rhabdomyolysis following general anesthesia for strabismus surgery in a previously healthy 11-year-old girl. The patient received a depolarizing muscle relaxant (succinylcholine) and halogenated volatile anesthetic agent (sevoflurane) during surgery. In rare cases, these classes of drugs can trigger malignant hyperthermia (MH) or anesthesia-induced rhabdomyolysis (AIR), which can cause significant morbidity and mortality if not recognized and treated promptly. Pathophysiology, early recognition, and special considerations in strabismus patients are discussed.

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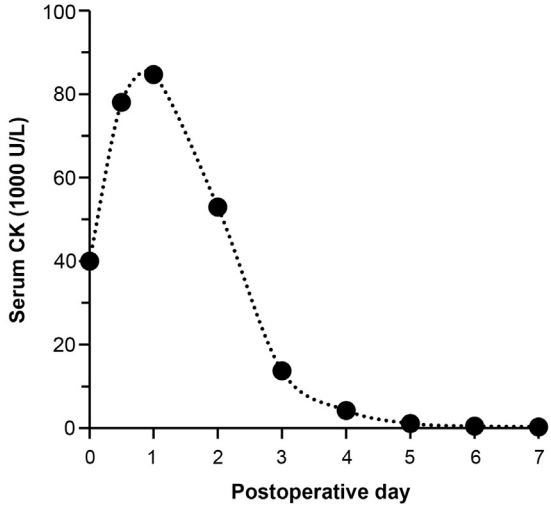

FIG 1. Perioperative serum creatine kinase (CK) levels in an 11-year-old girl undergoing strabismus surgery who experienced rhabdomyolysis after administration of sevoflurane and succinylcholine. She was managed postoperatively with above-maintenance intravenous fluids and sodium bicarbonate to alkalinize the urine.

Case Report

An 11-year-old girl presented at St. Joseph's Health Centre, Toronto, with a 1-year history of persistent horizontal diplopia, for which she had developed a habit of occluding one eye for symptomatic relief. Diplopia was constant on distance viewing and intermittent at near. She was otherwise in good health, with no medical, surgical, or family history of ocular or neurological diseases. On examination, visual acuity was 20/20 bilaterally, with an alternating comitant esotropia of 20^{Δ} at near and distance. Sensory testing with neutralizing prisms showed stereoacuity of 40 arcsec and bifoveal responses on 4^{Δ} base-out prism testing. Ductions were full, there was no ptosis, and pupillary examination was normal. Anterior segment and dilated fundus examinations were normal, and cycloplegic refraction was +1.25 D in each eye. Brain and orbital magnetic resonance imaging were unremarkable, and assessment by pediatric neurology revealed no evidence of a systemic neuromuscular disorder. Full refractive and prismatic correction was prescribed, but orthoptic measurements remained unchanged over a 4-month period. Bilateral medial rectus recession of 3.5 mm under general anesthesia was planned.

Sevoflurane, succinylcholine, and glycopyrrolate were used during induction of anesthesia for surgery. Within minutes of induction the patient became tachycardic (150–160 bpm), and the surgeons noted unusual resistance on forced duction testing in all directions, likening the resistance to "taffy-pulling." After approximately 10 minutes the heart rate lowered to 120 bpm and forced duction testing normalized to typical levels. The patient exhibited tachypnea (22-26 breaths/minute) and elevated end-tidal

Table 1. Comparison of malignant hyperthermia (MH) and anesthesia-induced rhabdomyolysis (AIR)

	MH	AIR
Definition	Skeletal muscle hypermetabolism following exposure to triggering agents in susceptible patients	Acute rhabdomyolysis with hyperkalemia following exposure to triggering agents
Triggering agents	Halogenated volatile anesthetics Succinylcholine	Halogenated volatile anesthetics Succinylcholine
Pathophysiology	Uncontrolled calcium release from sarcoplasmic reticulum; RYR1 mutation in >50% of cases[8]	Unknown; idiosyncratic reaction associated with Duchenne muscular dystrophy and other occult myopathies[5,10]
Incidence	Pediatric, 1:10,000 general anesthetics; lower in adults[6]	Unknown; likely under reported[10]
Mortality	Pediatric, 3%; higher in adults[6]	Unknown
Associated conditions	RYR-1 mutations Central core disease King Denborough syndrome Evans myopathy Multiminicore disease (some forms) Nemaline rod myopathy (some forms) Exertional heat stroke Exertional rhabdomyolysis (suggested association) Hypokalemic periodic paralysis Hyperkalemic periodic paralysis	Duchenne muscular dystrophy Becker dystrophy McArdle disease Carnitine palmitoyl transferase type 2 deficiency It is unclear whether there is an association with exertional rhabdomyolysis
Early signs[10]	Muscle rigidity Masseter spasm Tachycardia Hypercapnia Hyperkalemia	AIR is often occult early on Cardiac arrest/arrhythmia Hyperkalemia Elevated creatine kinase
Late signs[10]	Acidosis Hyperthermia Myoglobinuria Elevated creatine kinase Cardiac arrest/arrhythmia Disseminated intravascular coagulation	Acidosis Hyperthermia (rare) Hypercapnia Myoglobinuria Elevated creatine kinase Renal failure

RYR1, ryanodine receptor 1.

carbon dioxide levels (68–71 mm Hg), which were unchanged throughout surgery and were not associated with any abnormalities in temperature or blood pressure. At the end of surgery, the patient was transferred to recovery in a stable condition.

In the recovery room, the patient had tea-colored urine, which was dipstick positive for blood, suggestive of myoglobinuria. Blood testing revealed a markedly elevated creatine kinase (CK) at 39,870 U/L (reference range, 50–295 U/L). The patient was transferred to the Hospital for Sick Children, Toronto, for treatment of anesthesia-induced rhabdomyolysis (AIR). Over the next 12 hours, potassium and creatinine remained normal, but CK rose to 84,705 U/L (Figure 1), and the patient reported hip and back pain. She made a full recovery with supportive care, and was discharged home 1 week later. Genetic testing for malignant hyperthermia (MH) susceptibility was negative, and muscle biopsy for in vitro caffeine-halothane contracture testing was deferred until adulthood.

One year following surgery the patient was orthotropic, with a 5^{Δ} esophoria and normal stereoacuity.

Discussion

MH and AIR are perioperative syndromes requiring prompt recognition and treatment to prevent catastrophic outcomes. Both conditions arise from exposure to volatile halogenated anesthetic agents and/or succinylcholine in susceptible individuals with increased risk (at least for MH) when both agents are administered together.[1] Timely diagnosis of these conditions is challenging due to the nonspecific and often occult nature of early signs (see Table 1).

Our patient did not show any preoperative risk factors for MH or AIR. Tachycardia and muscle rigidity (limited to the extraocular muscles) were noted intraoperatively, but these signs were transient and potentially attributable to other factors. For example, transient tachycardia is an expected anticholinergic effect of glycopyrrolate, and succinylcholine can increase resistance to forced ductions for up to 20 minutes after administration.[2] Although tachypnea and hypercapnia are suggestive of metabolic acidosis, these were unchanged throughout surgery and did not require active treatment. Postoperatively, the tea-colored urine and urine dipstick result were recognized as probable myoglobinuria. This prompted investigation of blood CK levels confirming acute rhabdomyolysis. The lack of MH susceptibility risk factors, timing of onset, and clinical presentation suggested a diagnosis of AIR in this case.

Strabismus and ptosis tend to be over-represented in reported cases of MH.[3] Although this association between strabismus and MH is not proven, its potential consequences warrant clinical caution.[4] Occult myopathies should be considered in the differential diagnosis of unexplained strabismus as they may confer increased risk of susceptibility to MH and AIR.[5-7] If susceptibility to MH or AIR is suspected, preoperative consultation and testing with a regional MH service should be considered. For MH, in vitro contracture testing has a sensitivity of 97%-99% and genetic testing has a sensitivity of 50%-70%.[8,9] There are currently no means of predicting AIR risk beyond historical association with known susceptible conditions.[10] For strabismus surgery, we suggest that succinylcholine be avoided, because it not only risks triggering MH and AIR, but it also confounds forced duction testing.[2] Perioperative personnel should remain vigilant for early signs of AIR and MH (see Table 1), and if suspected, prompt treatment should be initiated according to guidelines available locally or at http://www.mhaus.org. In both conditions, key early responses are to stop exposure to triggering agents, recruit help, deliver 100% oxygen, administer dantrolene (if MH suspected), cool the patient (if >37°C), treat hyperkalemia, and prepare for resuscitation in the event of a cardiac arrest.

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Glaucoma and degenerative vitreoretinopathy in a girl with Nicolaides-Baraitser syndrome

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We report the case of a 12-year-old girl diagnosed with Nicolaides-Baraitser syndrome with novel ocular features. Diagnosis was based on clinical features, including developmental delay, sparse hair, and craniofacial features along with de novo mutation in *SMARCA2*. Eye findings included bilateral glaucoma, cataracts, and degenerative vitreoretinopathy. Given the absence of an associated recognizable disorder and the low prevalence of these ocular findings in the general population, we suggest that these ocular features may not be chance association.

Case Report

A 12-year-old girl with suspected collagen issues was referred to the Ocular Genetics service at Wills Eye Hospital to evaluate her high myopia, asymmetric cupping, concern for elevated eye pressures attributed to a difficult exam, and degenerative vitreous abnormalities in the setting of Nicolaides-Baraitser syndrome (NCBRS). She was previously diagnosed with NCBRS based on her clinical features and a de novo (parents tested negative) heterozygous c.2267C>T (p.T756I) mutation in *SMARCA2* detected by whole-exome sequencing. This variant was previously reported to be pathogenic in other individuals with NCBRS.[1] Other identified variants occurred in genes inconsistent with the proband's features and maternally or paternally inherited and associated with autosomal

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