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A CRYPTIC CAUSE OF CARDIAC ARREST

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☐ **Abstract—Background: RIPPLY2-associated spondylocostal dysostosis is a rare disorder that leads to segmentation defects of the vertebrae. These vertebral defects can result in severe instability of the cervical spine, leading to cardiac arrest after only minor whiplash injury. Case Report: We present the case of a healthy 7-year-old child who experienced an out-of-hospital cardiac arrest. He was reported to have profound respiratory distress and collapsed after going down a slide, without trauma. He was resuscitated in the field, and presented to the emergency department, where return of spontaneous circulation was achieved. Imaging of his cervical spine revealed multiple abnormalities. It was determined that a whiplash injury led to hypoxia and bradycardia due to the anatomic abnormalities of his cervical spine, resulting in cardiovascular collapse. He recovered fully and was later diagnosed with SCDO6, an autosomal recessive inherited disorder caused by a mutation in the RIPPLY2 gene. Why Should an Emergency Physician Be Aware of This?: Unfamiliarity of providers with this mechanism of cardiac arrest, and the rarity of the syndrome itself, make early recognition very difficult. Late diagnosis and lack of preventative measures, including immediate cervical spine stabilization, can lead to catastrophic outcomes. In patients with cardiac arrest of unclear etiology, early consideration of cervical spine immobilization and evaluation can be lifesaving.** © 2018 Elsevier Inc. All rights reserved.

☐ **Keywords—cardiac arrest; resuscitation; neurosurgery; gene mutation; CPR**

INTRODUCTION

More than 5000 children experience a non-traumatic out-of-hospital cardiac arrest (OHCA) in the United States each year (1). Most pediatric arrests are secondary to respiratory failure; however, the etiology may not always be immediately apparent (2). We present the case of a healthy 7-year-old male who experienced a sudden non-traumatic cardiac arrest.

CASE REPORT

A 7-year-old male with a medical history significant only for mild asthma was brought to the emergency department (ED) via Emergency Medical Services (EMS) after becoming unresponsive at a family party. According to witnesses, he slid to the bottom of a slide, suddenly experienced profound respiratory distress, and collapsed. Upon EMS arrival he was cyanotic and unresponsive, and bag-valve-mask ventilation and chest compressions were initiated. On arrival to the ED, return of spontaneous circulation was achieved, and he was tachycardic and bradypneic. Examination was significant for 3-mm, minimally but equally reactive pupils, and a Glasgow Coma Scale score of 3. Complete blood count was unremarkable. Arterial blood gas was significant for a mixed metabolic and respiratory acidosis with a lactate of 7.2 mmol/

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L. He was intubated due to poor neurologic status and bradypnea. Computed tomography scan of the head, chest, and abdomen were performed and unremarkable. He was admitted to our pediatric intensive care unit following transfer from the outside hospital, intubated, and sedated. A cervical spine collar was placed, despite a negative history of trauma.

Due to the unknown etiology of cardiac arrest, an extensive diagnostic evaluation was performed. His cardiac, infectious, neurologic, and toxicologic evaluations were within normal limits. Magnetic resonance imaging of the brain revealed no abnormalities; however, the cervical spine imaging revealed markedly abnormal anatomy (Figure 1). Multiple cervical spine vertebral anomalies were demonstrated, including incomplete atlanto-occipital assimilation with fusion of the anterior arch of C1 to the basion and posterior arch fused to the occiput, malformed C2 with hypoplastic dens, absent posterior elements of C2 and C3, hypoplastic C4 vertebra with anterior bullet-shaped appearance, hypoplastic C4 pedicles, posterior articular facets with spina bifida occulta, absent C6 left pedicle with articulation of C5 to C7 facets, and loss of vertebral height of C4–C7, with narrowing of the spinal canal at C4.

Additionally, the patient had evidence of whiplash injury with ligamentous disruption of the posterior longitudinal ligament and spinal cord injury demonstrated by a hyperintense T2 signal in the upper cervical cord, extending inferiorly to C3.

A two-stage repair was performed: an anterior approach of C3–C7 cervical discectomy and fusion, followed by a posterior approach for bilateral occiput, right C3, bilateral C5, bilateral C7 fusion, and C3–C5 laminectomy for decompression of the spinal cord (Figure 2). The patient was successfully extubated and discharged to an acute care rehabilitation facility for a requirement of non-invasive positive pressure ventilation and general rehabilitation needs. On discharge, the patient had weakness of his bilateral upper extremities, left more than right, left vocal cord paresis, and required continued nasogastric tube feeds for nutrition. At interval follow-up, the patient demonstrated complete recovery and had been discharged from rehabilitation.

Due to the multiple spinal abnormalities, a genetic evaluation was performed. The patient was not believed to be dysmorphic in appearance, and skeletal survey did not demonstrate additional abnormalities. Cardiac and renal evaluations were unremarkable. The family history was significant for the parents being second cousins of Salvadoran ancestry. Initial genetic concerns were consistent with vertebral malsegmentation defects, such as spondylocostal dysostosis (SCDO) or Klippel-Feil anomaly, though mucopolysaccharidosis (MPS) was considered in the differential diagnosis as well. Urine MPS screen, urine oligosaccharide screen, and enzyme testing for MPS IV and MPS VI were normal. Single nucleotide polymorphism microarray was normal. Whole-exome sequencing revealed homozygosity for a splice site mutation in the RIPPLY2 gene called IVS3-4T>G (c.240-4T>G).

DISCUSSION

The etiology of cardiac arrest is not always immediately apparent, which can be a challenge to front-line providers. Meert et al. recently found the primary etiology of OHCA among 295 children to be respiratory for 213 (72.2%) patients, cardiac for 37 (12.5%) patients, and other/unknown for 45 (15.3%) patients (3). Among this cohort of patients, those with unknown causes for their

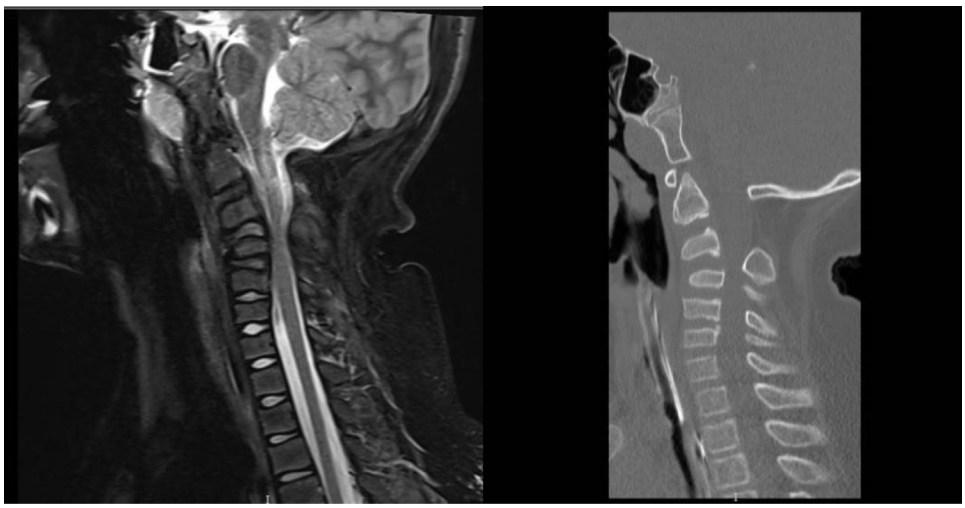

Figure 1. Preoperative sagittal magnetic resonance imaging and computed tomography images demonstrating spinal canal stenosis, bullet-shaped vertebral bodies, hypoplastic dens, malformed C2 and C3 posterior elements.

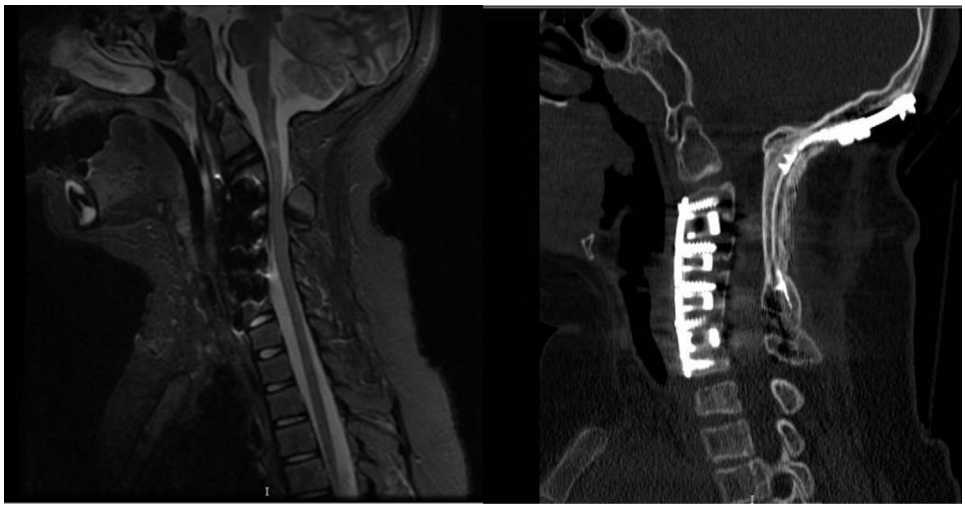

Figure 2. Postoperative stage 1 sagittal magnetic resonance imaging and 6 month postoperative computed tomography scan images. Bone fusion obtained from occiput to C7. Stage 1 anterior C3–C7 discectomy and fusion followed by stage 2 C3–C4 laminectomy and fusion of occiput to C7.

cardiac arrest had poorer 12-month survival, highlighting the importance of rapid diagnosis, such that definitive treatment for the underlying cause can be delivered (3). Our patient presented with an unknown cause of arrest, and even after initial diagnostic workup, the etiology was not immediately apparent. It was not until imaging of his cervical spine revealed multiple abnormalities did the diagnosis become evident.

RIPPLY2-associated spondylocostal dysostosis is a rare disorder that leads to segmentation defects of the vertebrae. RIPPLY2, known to be required for vertebral column formation during embryogenesis, and previously reported only twice in humans, interacts with TBX6 (SCDO5) and MESP2 (SCDO2), both of which have been shown to cause autosomal recessive SCDO (4,5). Previous RIPPLY2 compound heterozygous mutations, the same as those in our patient, were reported in two brothers with multiple vertebral segmentation defects phenotypically similar to the patient we present here (6). Additionally, a homozygous frameshift mutation in RIPPLY2 was reported in a 13-year-old with Klippel-Feil anomaly, Sprengel anomaly, pectus excavatum (superior)/pectus carinatum (inferior), unilateral renal agenesis, and situs totalis (4).

Our patient has a rare but significant diagnosis of SCDO and presented in cardiac arrest. The exact etiology of this event was not immediately clear, however, previous research provides insight into the likely mechanisms. The patient was noted to stop abruptly at the bottom of a slide, inducing a whiplash motion. Due to ligamentous laxity, he was particularly vulnerable to hyperflexion/extension, and the abnormalities of his cervical spine predisposed him to cervical injury. This mechanism of spinal cord injury has been described previously in infants subjected to shaking resulting in shaken baby syndrome, as reported by Ghatan and Ellenbogen (7). This cervical cord injury can result in brain stem injury leading to apnea, hypoxia, and cardiopulmonary arrest (8).

Cardiac arrest due to this type of cervical injury is secondary to disruption of cardiac sympathetic innervation, resulting in unopposed parasympathetic activity to the sino-atrial node. Increases in vagal activity without opposing sympathetic response can lead to profound bradycardia and cardiac arrest, a finding usually described in neurogenic shock due to high-impact traumatic injury (9). The presence of undetectable pulses on presentation in our patient is likely due to unopposed vagal activity secondary to the cervical spinal cord injury demonstrated on MRI.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

SCDO, and other syndromes with cervical vertebral anomalies, should be considered in patients with unexplained cardiac arrest. The absence of other associated anomalies, including cardiac and renal abnormalities, the rarity of the disorder, and a lack of familiarity among providers makes SCDO particularly challenging to diagnose. However, a failure to arrive at the right diagnosis places patients with SCDO at particular risk for recurrent events and death. While the specific genetic diagnosis is beyond the diagnostic evaluation during care in the ED, recognition that cervical cord abnormalities may lead to cardiac arrest is of the utmost importance. In this patient, the placement of a cervical collar, despite the lack of trauma during a witnessed event, likely protected him from further cord injury, recurrent arrest, and paralysis.

Thus, in patients with unexplained cardiac arrests, cervical spine immobilization and evaluation of possible cervical abnormalities should be considered early in care when more common causes of arrest have been excluded.

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