

## Sudden Cardiac Arrest in an Adolescent with X-Linked Ichthyosis

### INTRODUCTION

X-linked ichthyosis (XLI) is characterized by abnormal desquamation, presenting with dry and scaly skin.<sup>1</sup> It is caused by a deficiency of the steroid sulfatase enzyme, encoded by the steroid sulfatase (STS) (Xp22.3) gene. Steroid sulfatase cleaves sulfate groups from multiple steroid hormones, affecting their bioavailability.<sup>2</sup> With an incidence of 1 in 2500 to 1 in 6000 males, XLI is the second most common type of ichthyosis, following ichthyosis vulgaris.<sup>3</sup> These patients may have extracutaneous comorbidities, including cryptorchidism, corneal opacities, Dupuytren's contracture, cardiac arrhythmias, bleeding disorders, and neurodevelopmental and psychiatric conditions.<sup>4-6</sup> This case report describes an adolescent with an STS deletion identified after a sudden cardiac arrest.

### CASE REPORT

A 17-year-old male with no significant past medical history collapsed suddenly at a concert and experienced a 3-minute generalized tonic-clonic convulsion. He was transported to the emergency department of a nearby hospital in cardiac arrest and was resuscitated for 20 minutes. Cardiac defibrillation was performed 8 times due to ventricular fibrillation. After successful resuscitation, the patient was transferred to the adult intensive care unit, where he continued to have convulsions for 3 days. Echocardiography and coronary angiography revealed an ejection fraction of 25% and normal coronary arteries, respectively. After 3 days of follow-up, he was transferred to our institution's pediatric intensive care unit (PICU) with a Glasgow Coma Scale (GCS) score of 4.

Electrocardiography (ECG) showed a wandering atrial pacemaker, ST-segment elevation, and T-wave inversion. Echocardiography performed at our institution revealed a structurally and functionally normal heart (ejection fraction: 70%). Twenty-four-hour Holter monitoring revealed 2721 polymorphic ventricular extrasystoles (VES), which decreased in frequency with increased heart rate, 1 ventricular couplet, 13-beat 160/min ventricular tachycardia, and 131 ventricular bigeminies (Figure 1A). Cranial magnetic resonance imaging (MRI) showed findings consistent with hypoxic-ischemic encephalopathy, while electroencephalography showed no epileptic abnormalities. Although a cardiac MRI was planned, the family declined due to the risks associated with general anesthesia.

Pediatric genetics was consulted to investigate the etiology of the life-threatening arrhythmia (e.g., Brugada syndrome). Whole exome sequencing identified a 159.31 bp hemizygous deletion in the Xp22.31 region, including exons 2-11 of the STS gene. Remarkably, no significant skin findings had been noted before genetic testing (possibly due to leg hairiness and edema masking lesions). Reverse phenotyping following genetic analysis revealed mild dry, thickened, and scaly skin on the trunk and legs. The patient's mother reported that he had always had dry, peeling skin since birth. She also mentioned a maternal uncle with similar skin findings and a history of arrhythmias, although he declined to visit for a detailed evaluation.

The patient's natal and postnatal history was unremarkable. He had no history of seizures or chronic medication use. An implantable cardioverter-defibrillator was

### CASE REPORT

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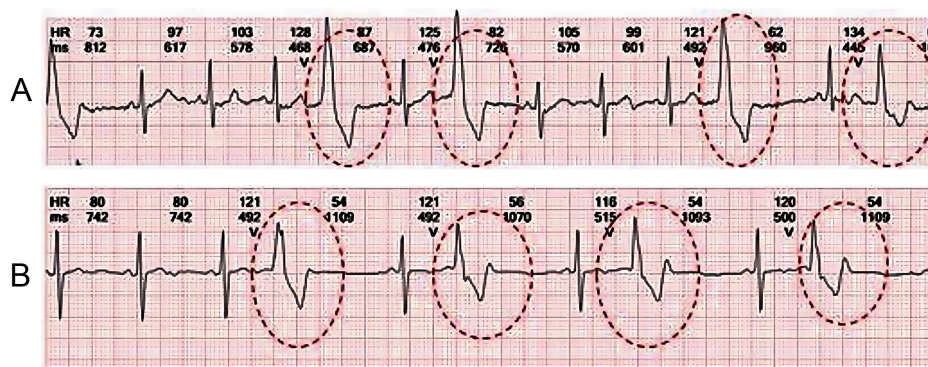
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**Figure 1. Examples of polymorphic ventricular bigeminy rhythms on Holter monitoring. (A) The holter record on the 55<sup>th</sup> day of aborted sudden cardiac arrest. (B) The holter record on the 135<sup>th</sup> day of aborted sudden cardiac arrest.**

placed for secondary prevention of sudden cardiac arrest, given the documented ventricular tachycardia and fibrillation. Concurrently, his neurological status was evaluated, and intrathecal mesenchymal stem cell therapy (4 sessions) was administered. The patient remained in the PICU for 55 days, including 30 days of intubation, and was discharged with a GCS score of 15. Follow-up Holter ECG, conducted 2 months after discharge, revealed VES, ventricular bigeminy, and trigeminy (Figure 1B).

## DISCUSSION

While population studies suggest an increased risk of arrhythmias in XLI patients,<sup>6</sup> the pathophysiology remains unclear, and no previous reports have associated STS mutations with cardiac arrest. In adult men with XLI, atrial fibrillation has been diagnosed in 60% of individuals with abnormal heart rhythms and tachycardia in 27%.<sup>4</sup> Dehydroepiandrosterone sulfate levels are elevated in XLI patients, on the other hand effects of STS deficiency on steroid hormones fail to explain the mechanism of arrhythmias, as murine models show no meaningful correlation between steroid hormone levels and cardiac arrhythmias.<sup>7</sup>

Triadin, a transmembrane protein in the cardiac sarcoplasmic reticulum, forms a quaternary complex with the ryanodine receptor Ca(2+) release channel.<sup>8</sup> Triadin knockout syndrome is a recessively inherited cardiac arrhythmia syndrome characterized by extensive T-wave inversion in precordial leads (V1-V4), consistent or transient QT prolongation, ventricular ectopy, exercise-induced cardiac arrest in early childhood, and possible muscle weakness. Murine models of STS deficiency have shown decreased triadin levels.<sup>7</sup> In a study of XLI patients undergoing exercise stress tests, 89% exhibited ventricular ectopy at an average onset heart rate of  $108 \pm 24$  bpm, with findings including premature ventricular contractions, bigeminy, couplets, and triplets.<sup>9</sup>

In XLI patients, it is essential to consider extracutaneous findings, including life-threatening cardiac arrhythmias. Clinical diagnosis alone is insufficient, and genetic testing is necessary for confirmation. Families should receive genetic counseling, and long-term follow-up should focus on arrhythmia management.

## CONCLUSION

Supraventricular arrhythmias have been reported in XLI; however, ventricular arrhythmias and sudden cardiac arrest have not been previously documented in adult males with STS deletions. Triadin levels, shown to decrease in murine models of XLI, have not been studied in humans. Among candidate molecules implicated in XLI, triadin's role in predisposing patients to ventricular arrhythmias warrants further functional studies.

Artificial intelligence-assisted technologies (such as Large Language Models, chatbots, or image creators) were not used in the production of the submitted work.

**Informed Consent:** Informed consent was obtained for the use of the patient's clinical information and medical imaging results in scientific contexts.

**Declaration of Interests:** The authors have no conflicts of interest to declare.

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