Previously unrecognized genetic mutation may underlie some cases of sudden infant death

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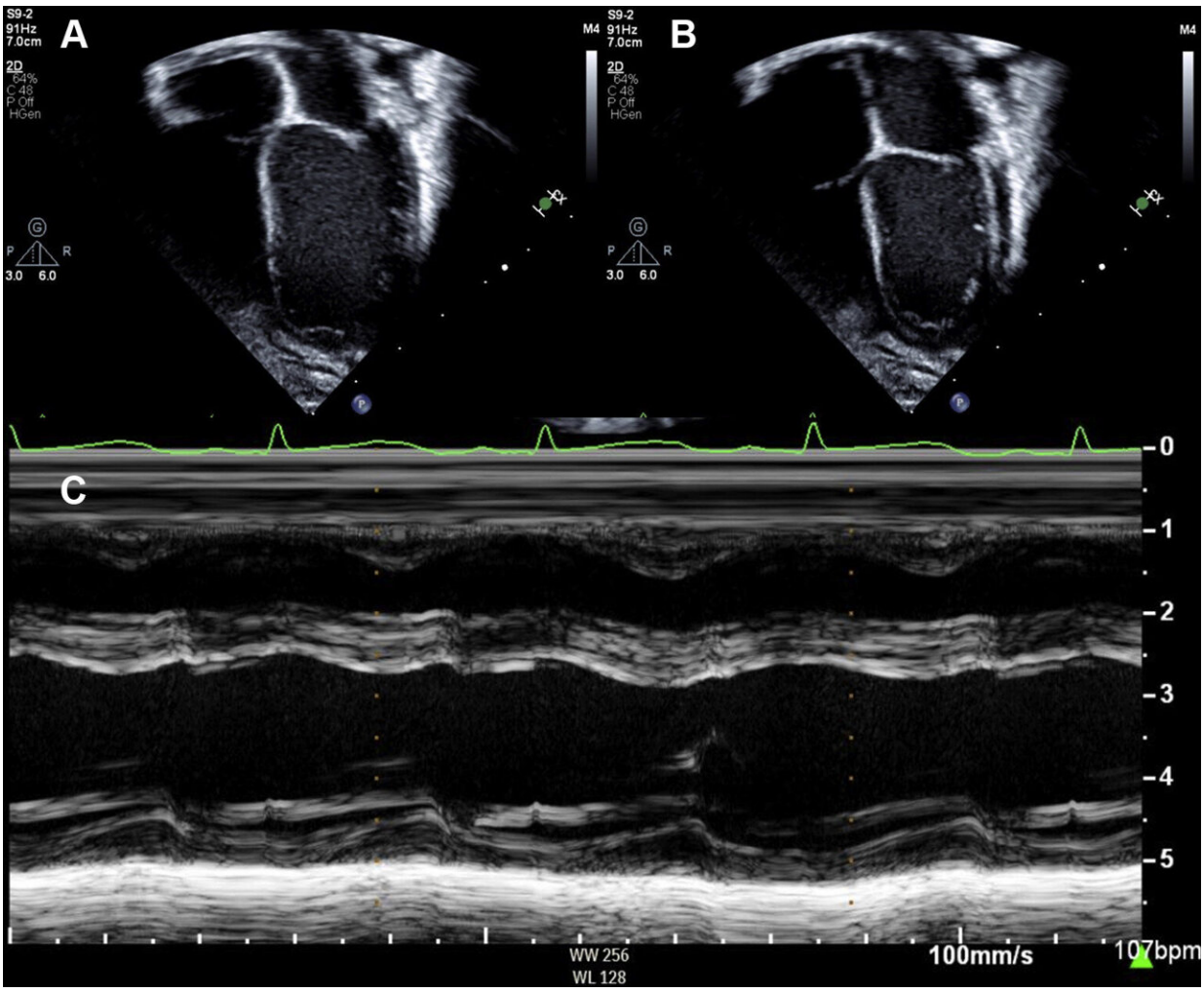

Apical 4-chamber at (A) end diastole and (B) end systole at initial presentation. M-mode from (C) parasternal short axis view at presentation. Ejection fraction

was 48.7% and shortening fraction 24.8%, which improved to 63.3% and 38.5%, respectively, at 1 month. There was normal valve morphology and function without evidence of ventricular hypertrophy, dilation, or noncompaction Credit: *Heart Rhythm Case Reports*

A previously healthy infant who suffered aborted sudden cardiac death was found to have a de novo genetic mutation in the SOS1 gene. Such mutations are typical of Noonan syndrome and suggests the syndrome may be a cause of unrecognized sudden death in infancy. The case is reported in *Heart Rhythm Case Reports*.

Noonan syndrome is a genetic disorder that affects normal development, causing skeletal, cardiac, and neurocognitive delays. The infant had none of the usual structural cardiac findings of Noonan syndrome, such as damaged heart valves or abnormally thick heart muscle tissue. However, they may appear later in development.

"Genetic testing in cases of unexplained aborted or sudden cardiac deaths, even in previously healthy children, can be valuable in establishing a diagnosis, determining the prognosis, and assessing risk to family members," said co-authors Christopher W. Follansbee, MD, and Lindsey Malloy-Walton, DO, of the Ward Family Heart Center, Children's Mercy Kansas City and University of Missouri School of Medicine Kansas City, Kansas City, MO, U.S..

A two-month-old female infant did not awaken as usual for her morning feeding; her mother found her limp, pale, and suffering from breathing difficulty. EMS arrived quickly and found the infant pulseless. Three shocks from a defibrillator were needed to restore sinus rhythm. On presentation to the ICU, the patient had incessant, rapid episodes of ectopic atrial tachycardia. This potentially serious arrhythmia is an

unusual finding in the neonatal postarrest period. Normal cardiac function was restored after medication and treatment. An echocardiogram revealed a structurally normal heart with normal valves, and there was no ventricular hypertrophy, dilation, or noncompaction noted. Other tests were normal.

The genetics team was consulted, and a standard family history was obtained. An older sibling had no known medical conditions. The child's paternal grandfather had died of a presumed heart attack in his 50s, but no autopsy had been performed. There was no family history of congenital heart disease, sudden death, development delay, or other conditions. A next-generation sequencing panel revealed the likely pathogenetic variant of the SOS1 gene associated with Noonan syndrome.

Noonan syndrome belongs to a family of related genetic syndromes known as RASopathies with overlapping phenotypic features, including skeletal, dermatologic, and neurocognitive findings. Cardiac phenotypes are also common. SOS1-mediated Noonan syndrome can have a mild phenotype, which may not be apparent until the child becomes older, when neurocognitive findings become more noticeable, as seems to be the case with this patient.

"To the extent of our knowledge, our case is the first reported ventricular fibrillation arrest associated with a RASopathy in the absence of the typical structural cardiac phenotypes of hypertrophic cardiomyopathy or pulmonary stenosis. In this patient's case it will allow for monitoring and early intervention on typical manifestations of Noonan syndrome as the patient grows," observed Dr. Follansbee and Dr. Malloy-Walton. "Continued research is essential to uncover underlying causes for unrecognized sudden deaths in infants."

More information: Christopher W. Follansbee et al, Ventricular

fibrillation due to a likely pathogenic SOS1 variant: An unrecognized etiology of infantile sudden death?, *HeartRhythm Case Reports* (2021). DOI: 10.1016/j.hrcr.2021.06.010