JACC: CASE REPORTS VOL. 3, NO. 12, 2021

CASE REPORT

INTERMEDIATE

CLINICAL CASE

Sudden Cardiac Arrest Secondary to Early Repolarization Syndrome

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ABSTRACT

A healthy 41-year-old man sustained cardiac arrest secondary to ventricular fibrillation. An extensive ischemic, structural, and genetic evaluation did not identify an attributable pathologic condition. Electrocardiograms were notable for early repolarization pattern. Here we review the diagnosis, prevalence, and prognostic significance of the early repolarization syndrome on sudden cardiac death. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:1422-1426) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 41-year-old man of South Asian descent presented after a witnessed cardiac arrest. He was found unresponsive in bed at night by his wife. She called Emergency Medical Services (EMS) and immediately began bystander cardiopulmonary resuscitation (CPR). When EMS arrived, the rhythm detected was ventricular fibrillation (VF). He underwent defibrillation in the field, and return of spontaneous circulation with normal sinus rhythm was achieved 33 minutes after the beginning of CPR. He was taken to the nearest hospital, where he was intubated and given vasopressors and an amiodarone infusion. He was subsequently transferred to the cardiac intensive care unit. On the day of his arrest, he was in his usual state of health without any prodrome. Earlier that afternoon, he was playing with his children in his backyard without symptoms.

His vital signs upon arrival were as follows: temperature 38.2°C, heart rate 92 beats/min, blood pressure 130/80 mm Hg on low-dose norepinephrine, and oxygen saturation 95% on minimal ventilatory settings. His cardiac examination result was notable for a jugular venous pressure of 7 cm, regular rate and rhythm, and normal S1 and S2. Chest computed tomography (CT) angiography did not illustrate a pulmonary embolism or other parenchymal abnormality. His laboratory results were notable for a lactate of 7.2 mmol/L, potassium of 4.1 mmol/L, troponin-I of

LEARNING OBJECTIVES

- To diagnose early repolarization in individuals presenting with cardiac arrest by detecting criteria on 12-lead ECG.
- To counsel patients with early repolarization by citing the epidemiology, prognostic significance, and pathophysiology of this condition.
- To manage ventricular arrhythmias in patients with early repolarization by selecting appropriate treatment options.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received May 5, 2021; revised manuscript received June 22, 2021, accepted July 7, 2021.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2021.07.006

1.9 ng/mL, and NT-proBNP of 474 pg/mL. Electrocardiogram (ECG) upon arrival showed sinus tachycardia, borderline right axis deviation, and a QTc of 422 ms but notably had early repolarization (ER) pattern in the inferior leads.

Routine postarrest care was provided, and he was given a targeted temperature management protocol.

MEDICAL HISTORY

The patient had a medical history of prediabetes and vitamin D deficiency; cholecalciferol was his only ambulatory medication therapy. There was no family history of sudden cardiac death (SCD). He did not have any history of tobacco, alcohol, or drug use.

DIFFERENTIAL DIAGNOSIS

Given the patient's demographics, ECG findings, and lack of significant cardiac history, the differential diagnosis included ischemic ventricular arrhythmia, undiagnosed structural heart disease, myocarditis, ER syndrome, or other primary arrhythmogenic disorder (e.g., Brugada, long QT syndrome).

INVESTIGATIONS

The initial ECG showed sinus tachycardia, borderline right axis deviation, and ER in the inferior leads (**Figures 1 and 2**). Lead III contained the maximum J-point elevation of 2.5 mm with associated QRS notching. ECG within hours of presentation also demonstrated QRS notching in the lateral precordial leads (**Figures 3 and 4**). A high precordial lead ECG did not demonstrate any Brugada patterns. Had the clinical suspicion for Brugada syndrome been higher, a more comprehensive investigation would have included provocative testing with sodium channel blockers (e.g., flecainide, procainamide, ajmaline, or pilsicainide) to potentially unmask Brugada patterns.

A transthoracic echocardiogram demonstrated normal biventricular size and function, with left ventricular ejection fraction of 65% and tricuspid annular plane systolic excursion of 2.0 cm. There were no regional wall motion or valvular abnormalities; specifically, the mitral valve and annulus were structurally and functionally normal. Coronary angiography showed normal coronaries. Cardiac magnetic resonance imaging (MRI) showed no evidence of structural heart disease, inflammation, or scar. The result of a comprehensive genetic panel of 30 proarrhythmic mutations was negative for channelopathy.

Regarding neurologic evaluation, an electroencephalogram after rewarming showed diffuse cerebral disturbance suggestive of anoxic brain injury. Head CT demonstrated preservation of gray-white matter differentiation and no acute intracranial pathologic changes. Brain MRI was attempted but was nondiagnostic because of motion artifact.

MANAGEMENT

The patient's course was complicated by rhabdomyolysis requiring intravenous fluids (thought

ABBREVIATIONS AND ACRONYMS

CPR = cardiopulmonary resuscitation

CT = computed tomography

ECG = electrocardiogram

ER = early repolarization

ICD = implantable cardioverter defibrillator

MRI = magnetic resonance imaging

SCD = sudden cardiac death

VF = ventricular fibrillation

FIGURE 1 Admission Electrocardiogram

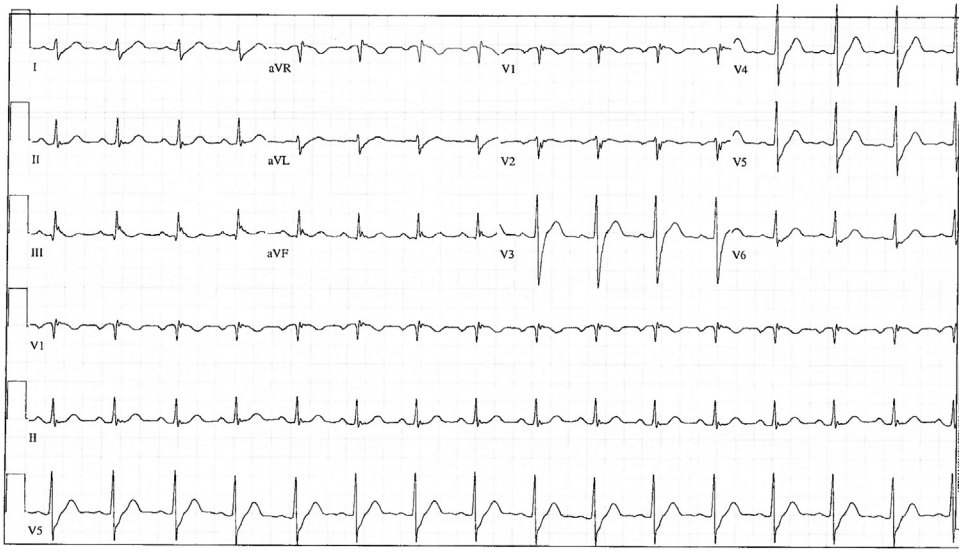
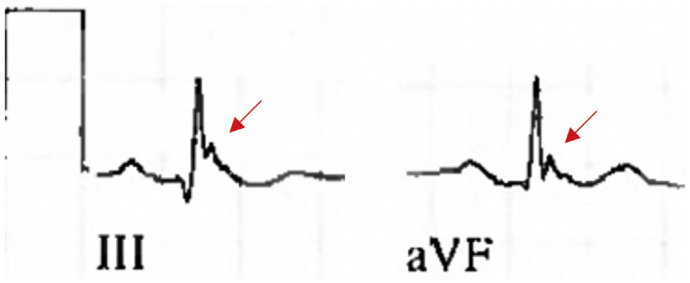


FIGURE 2 QRS Notching in Inferior Leads Highlighted



secondary to induced hypothermia and shivering, given the peak creatine kinase elevation during cooling, versus myocardial and skeletal muscle ischemia from prolonged CPR); methicillin-sensitive *Staphylococcus aureus* ventilator-associated pneumonia treated with oxacillin; and delirium, which resolved before discharge. In the absence of ischemic, structural, infiltrative, or reversible causes, he underwent placement of a secondary prevention, single-chamber, transvenous implantable cardioverter-defibrillator (ICD). He had no subsequent arrhythmic events during his hospitalization.

DISCUSSION

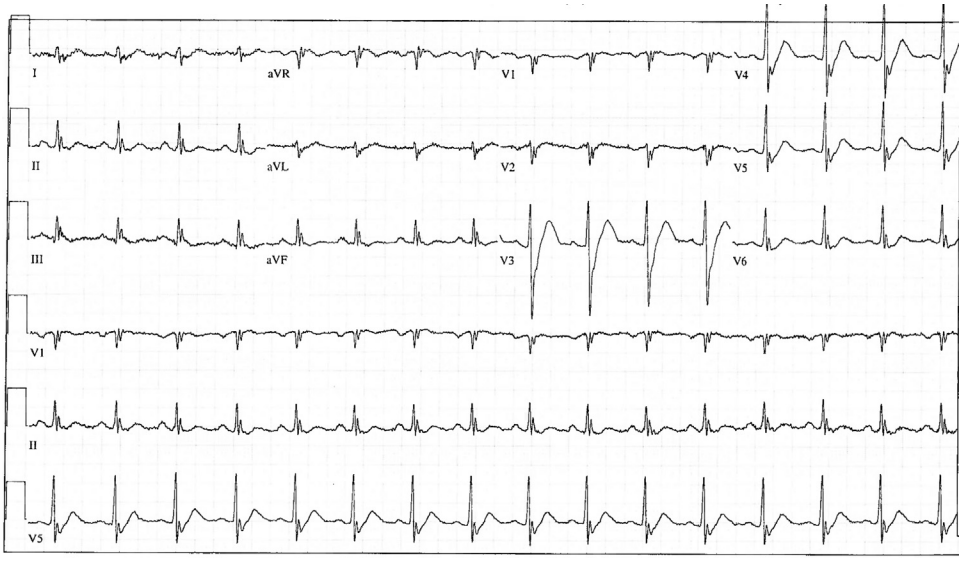
In the absence of ischemic and structural heart disease or another identifiable arrhythmogenic disorder, a presumptive diagnosis of VF secondary to ER syndrome was made. Various definitions for ER have emerged in clinical practice, which complicated the initial investigations of this ECG signature. When ER gained attention because of its associations with ventricular arrhythmias, efforts were made to explicitly define the criteria and standardize interpretation.

In 2015, Macfarlane et al (1) released a widely cited consensus definition of ER, emphasizing the presence of QRS notching or slurring predominantly in the inferior or lateral leads, the peaks of which must be at least 0.1 mV or more (**Figure 5**). Importantly, ER does not require ST-segment elevation, which is commonly described as benign early repolarization among young adults. The patient described here met the criteria for ER with QRS notching of 0.2 mV in the inferior and lateral leads.

Haïssaguerre et al (2) were the first to challenge the assumption that ER was a benign entity by establishing its high prevalence among idiopathic VF and cardiac arrest cases in a multicenter retrospective study of over 200 patients. The prevalence of ER was significantly higher among patients than matched control individuals (31% vs 5%, respectively). Importantly, patients with ER were noted to have twice the risk of VF recurrence.

Tikkanen et al (3) later established the prevalence and prognostic significance of ER among the general population in a Finnish cohort of over 10,000 patients followed up for 30 years. They found ER prevalence to be 5.8%, which portended a significantly higher risk of future cardiac death. Furthermore, the degree

FIGURE 3 QRS Notching Appreciated in Lateral Precordial Leads on Follow-Up Electrocardiogram



of J-point elevation correlated with the magnitude of risk; the relative risk of death was 1.3 among those with 0.1 mV J-point elevation and threefold in those with 0.2 mV elevation, as seen in this case.

Relevant to our patient's demographics, the literature further supports a higher prevalence of ER among South Asians, in up to 20% to 25% in one cohort (4), as well as a familial tendency, with ER found in over 50% of first-degree relatives in one South Indian population (5). Mitral valve prolapse is also more common among this population with ER, although it was not seen in this case. Advances in genetic screening may increase the diagnosis and prevalence of ER as mutations are further elucidated. Whereas the result of channelopathy testing was negative in our patient, current limitations of genetic screening are evidenced by one large prospective study identifying relevant mutations in only 27% of cases of idiopathic VF (6). Genetic differences might mediate the higher prevalence of ER seen in South Asian populations as compared with the Finnish cohorts.

The pathophysiology of ER is thought to be related to transmural heterogeneity in repolarization across the myocardium. Increased outward currents mediated by I_{to} channels prevent action potential propagation, causing localized conduction block. Concurrent alterations in calcium handling shorten the refractory period. The combination of localized block and shortened refractory periods can establish the substrate for phase 2 ventricular reentry arrhythmias (7). The pathophysiology informs the effectiveness of medical therapies in the short-term and long-term management of recurrent VF due to ER. In the short term, isoproterenol enhances inward calcium and decreases I_{to} currents, thereby reducing transmural voltage gradients and promoting termination. In the long term, quinidine directly blocks I_{to} to prevent recurrence (8).

FIGURE 4 QRS Notching in Lead V_6 Highlighted

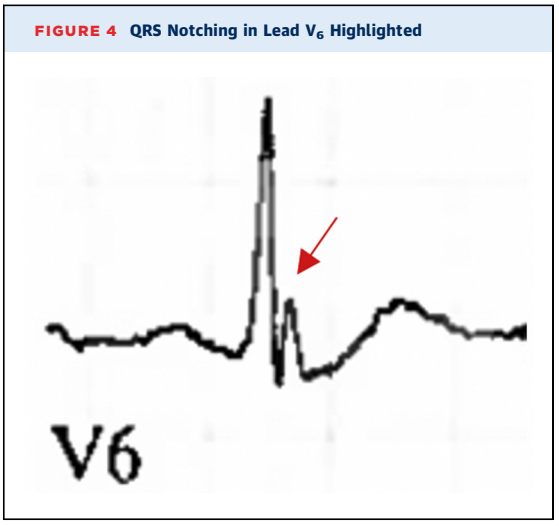


FIGURE 5 Definition, Epidemiology, and Significance of Early Repolarization

Definition:

Early repolarization is defined by the presence of QRS notching (A) or slurring (B), where the peak of the notch or slur onset (J peak or J_p) is at least 1mm or 0.1 mV or greater. Of note, early repolarization does not require the presence of ST segment elevation.

Distribution:

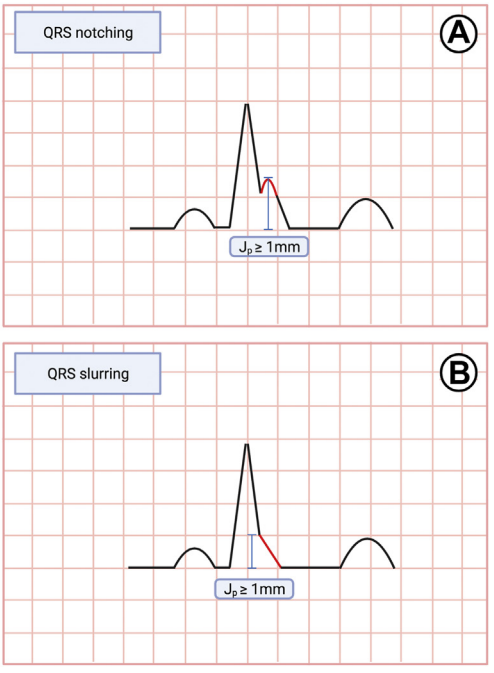
Most commonly seen in the lateral (V5, V6) leads, followed by inferior (II, III, aVF).

Epidemiology:

6-12% in the general population. Higher prevalence among males.

Significance:

Associated with 30% increase in relative risk of cardiac death compared to those without early repolarization, although the absolute risk remains small.



The American Heart Association (AHA) consensus statement acknowledged the difficulty in managing ER pattern because the overwhelming majority of patients will not experience ventricular arrhythmias. The AHA recommends detection of ER pattern should be coupled with: 1) close history taking that explores unexplained rest syncope or family history of SCD; and 2) ECG features associated with more arrhythmogenic variants of ER pattern, including greater amplitude of the J-wave and a horizontal or descending ST-segment; an ascending ST-segment is more often associated with "benign" ER (9). The role of ICD for primary prevention in ER pattern has yet to be established and requires further investigation.

Additional features of this case align with risk factors described in the literature. First, ER pattern is noted to be more prevalent among male individuals. Moreover, as seen in our patient, the development of VF during sleep has been described and is thought related to bursts of vagal and sympathetic tone during rapid eye movement sleep (10).

FOLLOW-UP

The patient demonstrated a remarkable neurologic recovery to baseline. He was cognitively intact, retained bilingual proficiency, and was independent with all activities of daily living at discharge. After being hospitalized for 13 days and free of recurrent arrhythmias, he was deemed safe for discharge after placement of a secondary prevention ICD. He did not have recurrent VF at his follow-up visits at 4- and 8-week intervals from discharge.

CONCLUSIONS

ER pattern is increasingly recognized as a risk factor for the development of SCD and should be in the differential diagnosis for those presenting with idiopathic VF. When ventricular arrhythmias occur, the presence of ER pattern is associated with recurrent events, emphasizing the need for secondary prevention and medical management if refractory. Future investigation is needed to inform risk assessment for primary prevention based on ECG features and high-risk genetic variants. Despite an initially devastating event, this case highlights the effectiveness of early bystander CPR, evidence-based postarrest care, multidisciplinary management, and recognition of ER as a risk factor for SCD.

ACKNOWLEDGMENTS The authors thank Biorender.com for creation of the figures.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS early repolarization, electrophysiology, sudden cardiac death