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CASE REPORT

ADVANCED

CLINICAL CASE

Autonomic Modulation for Treatment of Repolarization Alternans and Refractory Ventricular Electrical Storm

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ABSTRACT

Macroscopic T-wave alternans (TWA) is a rare finding on surface electrocardiogram and has been associated with an increased risk of impending sudden cardiac death. We highlight a case of macroscopic TWA in a patient with markedly prolonged QTc interval preceding ventricular electrical storm, which was refractory to medical management. Autonomic modulation of the stellate ganglion resulted in improvement in both TWA and QTc interval. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2021;3:1438–1443) © 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 60-year-old woman was admitted following witnessed ventricular fibrillation arrest with down time of approximately 30 min. Return of spontaneous circulation was obtained with defibrillation and she was intubated in the field. Admission electrocardiogram (ECG) showed sinus rhythm (rate 57 beats/min) with prolonged QTc (640 ms) (Figure 1). Serum K^+ was 3.0 mg/dL on admission. Serum Mg, Ca^{2+}, pH, and lactate were within normal limits. Coronavirus disease 2019 polymerase chain reaction test was negative. The patient self-extubated on hospital day 1. K^+ was repleted, and she was initiated on nadolol 20 mg orally daily and mexiletine 150 mg orally 3 times/day with improvement in QTc interval from 640 to 539 ms (Figure 2). On hospital day 3, olanzapine was administered for agitation. The patient experienced polymorphic ventricular tachycardia and was defibrillated. This was rapidly followed by 4 episodes of R on T phenomenon caused by long coupled ectopic beats resulting in torsades de pointes (TdP), and several external shock therapies (Figure 3). Macrovolt TWA developed on ECG (QTc 827 ms) (Figure 4).

LEARNING OBJECTIVES

- To identify macroscopic T-wave alternans as a rare but grave sign of ventricular electrical instability.
- To review the role of sympathetic nervous system modulation through stellate ganglion blockade as a useful adjunct for treatment of medically refractory ventricular electrical storm.
- To understand the role of stellate ganglion blockade in attenuating T-wave alternans.

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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.

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PAST MEDICAL HISTORY

The patient had a history of recurrent syncope thought to be caused by seizures. She was medicated chronically with levetiracetam. Her daughter had a history of sudden cardiac death (SCD) and implantable cardioverter-defibrillator (ICD) insertion at 30 years of age.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included congenital vs acquired long QT syndrome (LQTS) aggravated by QT prolonging factors, including electrolyte derangement and medications with early afterdepolarizations initiating recurrent TdP. T-wave morphology on admission ECG was suspicious for LQT3 phenotype.

INVESTIGATIONS

Initial transthoracic echocardiography revealed a structurally normal heart with preserved ejection fraction, normal diastolic function, and no significant valvular disease. After resuscitation of multiple episodes of TdP, transthoracic echocardiography revealed a left ventricular ejection fraction of 45%.

MANAGEMENT

Intravenous lidocaine, isoproterenol, and deep sedation reduced but did not eliminate ventricular ectopy (VE) burden, TWA or TdP. Autonomic modulation was considered in an effort to curtail adrenergic drive. Ultrasound-guided bilateral stellate ganglion blockade (SGB) (Figure 5) with 10 mL 0.5% bupivacaine eliminated VE and TWA. Five minutes following the procedure, the patient exhibited audible stridor and was intubated for airway protection. Subsequently laryngoscopy revealed left-sided vocal fold paralysis, which was felt to be caused by left recurrent laryngeal nerve paralysis. This resolved on hospital day 6. Bilateral thoracic sympathectomy was performed and the patient was successful extubated. ICD insertion implantation was performed for secondary prevention of SCD. Discharge medications included nadolol. QTc improved (597 ms) but did not normalize at discharge (Figure 5).

DISCUSSION

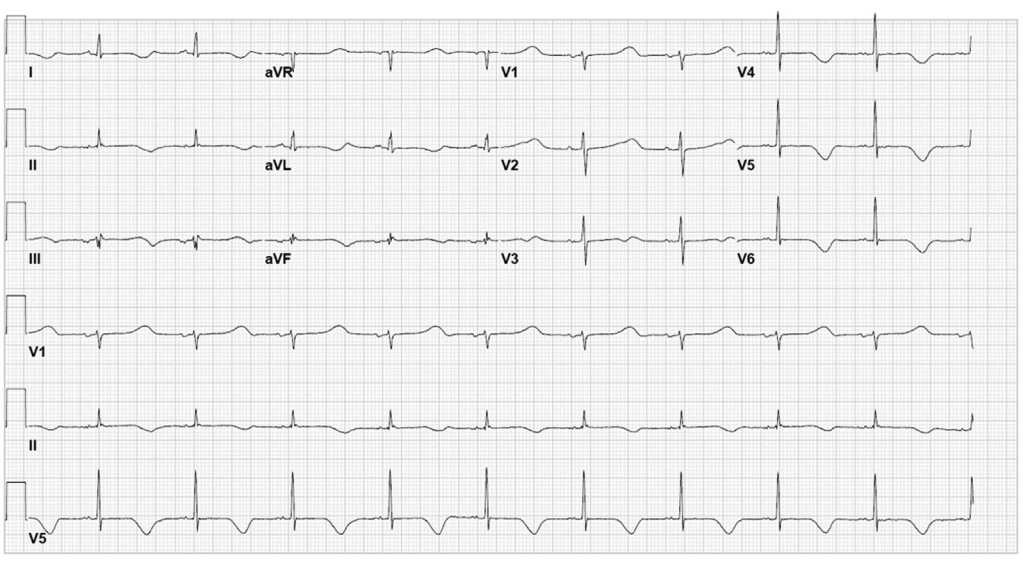
Electrical alternans was first described by Hering in 1908 and is characterized by beat-to-beat alterations in the shape of electrocardiographic waveforms. T-wave alternans, a manifestation of repolarization alternans (RA), has been associated with an increased risk of ventricular arrhythmias and SCD (1). Etiological hypotheses center around alternation of intracellular calcium (Ca^{2+}) concentration, either as a result of or as a driver of abnormalities in action

ABBREVIATIONS AND ACRONYMS

ECG = electrocardiogram

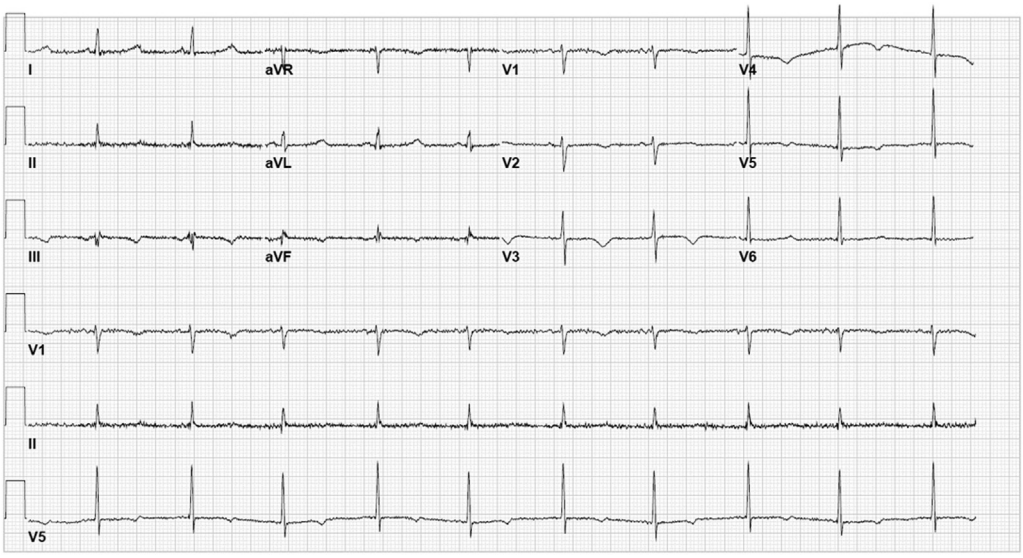
ICD = implantable cardioverter-defibrillator

FIGURE 1 Electrocardiogram on Day of Admission



Sinus rhythm rate 57 beats/min with prolonged QTc of 640 ms.

FIGURE 2 Electrocardiogram Following Nadolol and Mexiletine Initiation



Normal sinus rhythm rate 60 beats/min. QTc interval 539 ms.

potential duration, amplitude, or cellular sarcolemma currents in every other cardiac cycle (2). Localized cardiac alternans may lead to increased spatial dispersion of refractoriness (DR) and discordance of action potential duration in adjacent areas of the myocardium, which forms substrate for unidirectional conduction block and re-entrant arrhythmia (3). Prior investigations have shown that DR may be augmented under conditions such as LQTS, where repolarization reserve is reduced (4). This may likewise act as a trigger for VE, leading to re-entry-driven ventricular arrhythmias. The effect of autonomic modulation on RA is not certain. Clinical trials of parasympathetic tone modulation through vagal nerve stimulation have led to mixed results (5,6). Alternatively, beta-blockade has been shown to diminish RA amplitude by up to 35%, suggesting a role for sympathetic modulation.

The interaction between the sympathetic nervous system and the heart is complex and involves multiple hierarchical interfaces. Efferent sympathetic signaling has been shown to induce maladaptive electrophysiological changes within the ventricle. These include shortening of refractory periods and action potential duration, increased DR, increased heterogeneity of repolarization, as well as the induction of potentially arrhythmogenic early afterdepolarizations (7).

Medical management of VES may be limited by hemodynamic parameters, and VA is often refractory to beta-blockade and antiarrhythmic drug therapy. Notably, sympathetic signals are transmitted via the cervical and thoracic spinal cord to the stellate ganglion before synapsing with nerves of the intrinsic cardiac nervous system. Percutaneous stellate ganglion blockade represents a

FIGURE 3 Telemetry Rhythm Strip Demonstrating Prolongation of the QTc Interval With R-on-T Phenomenon Initiating Polymorphic Ventricular Tachycardia

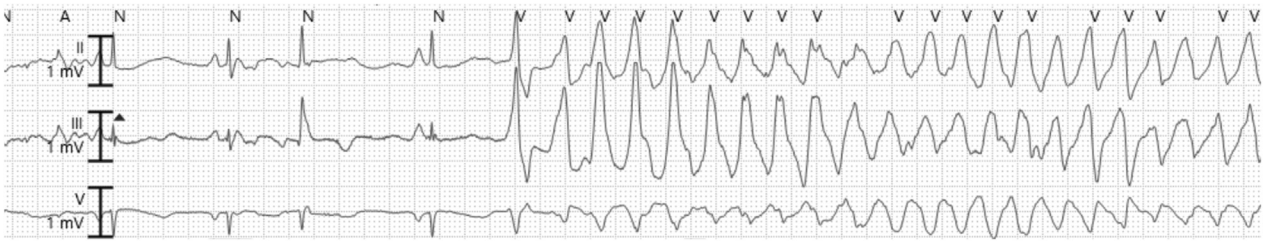
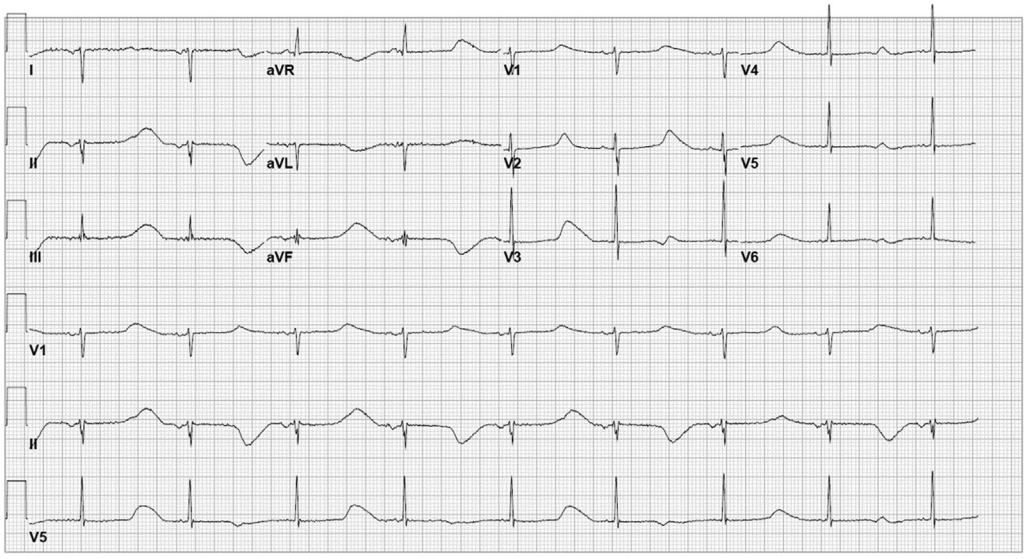


FIGURE 4 **Electrocardiogram Peri-Arrest Reveals Sinus Bradycardia at a Rate of 53 beats/min**

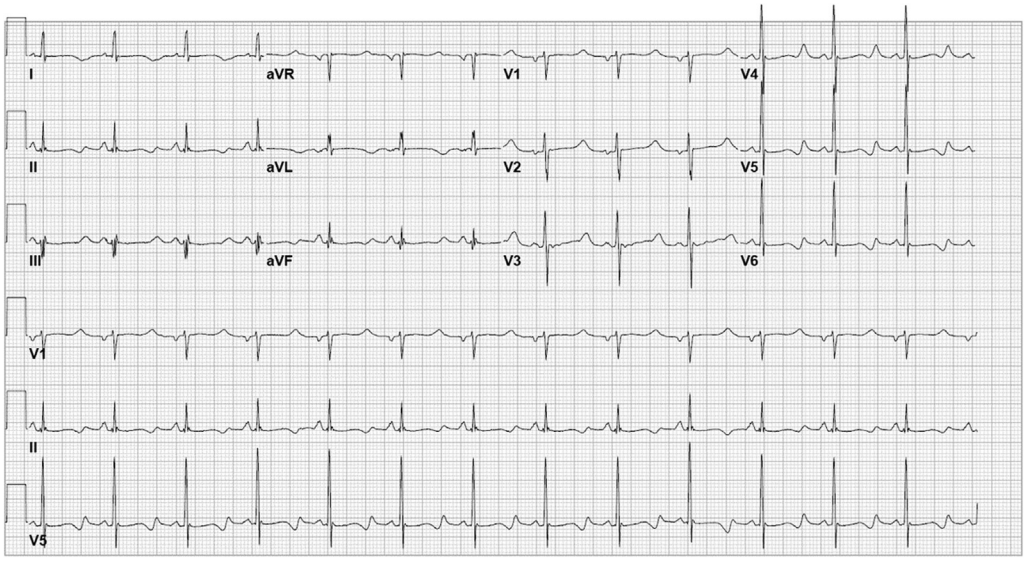


QTc interval 827 ms with macroscopic T-wave alternans.

minimally invasive approach for temporary cardiac sympathetic blockade, which may help determine a patient's response to operative (permanent) sympathectomy.

To perform SGB, ultrasound is utilized to visualize the longus colli muscle, hyoid and thyroid cartilages, internal jugular vein, carotid artery, and occasionally the stellate ganglion itself (Figure 6). The anterior

FIGURE 5 **Electrocardiogram Following Stellate Ganglion Blockade Shows Normal Sinus Rhythm at a Rate of 79 beats/min**



QTc interval 597 ms and T-wave alternans has resolved, although increased heart rate must be considered compared to prior electrocardiogram.

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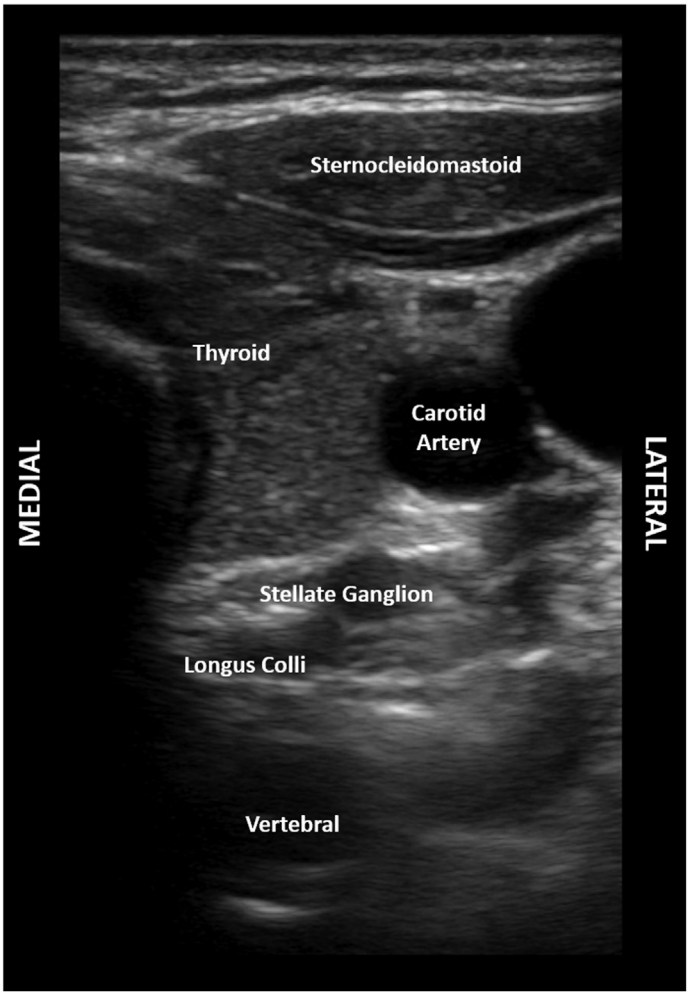
FIGURE 6 Relevant Anatomic Landmarks During Stellate Ganglion Blockade



tubercle of C6 is palpated between the left sternocleidomastoid muscle and trachea at the level of the cricoid cartilage. The carotid artery and sternocleidomastoid muscle are pulled laterally, and a 7-cm-long, 21-gauge micropuncture needle is inserted until it contacts the C6 transverse process. The needle is withdrawn approximately 2 mm and aspirated to avoid inadvertent intrathecal administration of anesthetics. 10 mL of 0.5% bupivacaine is then infiltrated around the stellate ganglion (8).

The role of unilateral left sided vs bilateral SGB continues to evolve. Prospective analyses have shown similar efficacy between the 2 (9). Although the left-sided SGB has been shown to reduce ventricular fibrillation threshold following myocardial infarction, functional asymmetry of the stellate ganglia suggest a role of the right stellate ganglion in influencing heart rate and arrhythmia vulnerability. Bilateral surgical sympathetic denervation may result in greater freedom from ICD shocks at 1-year follow-up than unilateral sympathectomy (10). However, it should be noted that the risk of phrenic nerve paralysis is higher in bilateral SGB, and care should be taken when this is performed in the unintubated patient. Indeed, the risk of palsy to surrounding nervous structures is highlighted in a recent retrospective analysis of 20 patients, where the only complication was 1 case of hoarseness, which was attributed to inadvertent recurrent laryngeal nerve palsy (11). This is mirrored in our case, where left-sided vocal fold paralysis resulted in inspiratory stridor and urgent orotracheal intubation. Possible signs of success and complications are outlined in the **Table 1**.

The impact of allelic variants for LQTS is well known. As outlined in the following text, this patient exhibited variants of unknown significance (VUS) in genes associated with LQTS. Polygenic mutations may represent an underlying substrate unmasked by aggravating factors including drugs and electrolyte disturbances (12). Acquired QT-prolonging risk factors such as inflammatory or autoimmune disorders should be considered (13). Due to a lack of historical or clinical evidence of autoimmune sequelae, serum markers such as anti-Ro/SSA antibodies and markers of inflammation were not assessed for and may represent a limitation of the current assessment.

TABLE 1 Signs of Successful SGB and Possible Complications

Signs of Successful SGB	Potential Complications of SGB
Horner's syndrome	Recurrent laryngeal and phrenic nerve block
Anhidrosis	Brachial plexus block
Nasal congestion	Pneumothorax
Venodilation in the hand and forearm	Generalized seizure
Increase in temperature of the blocked limb by at least 1° C	Total spinal anesthesia
	Severe hypertension
	Transient locked-in syndrome
	Paratracheal hematoma
	Soft tissue infection/osteomyelitis

SGB = stellate ganglion blockade.

FOLLOW-UP

The patient had no ICD shocks at 6-month follow-up. Genotyping revealed VUS in the *CACNAIC, KCNA1,* and *KCNQ1* genes. Family member screening is being pursued. The 12-lead ECG at time of outpatient follow-up was unavailable for analysis.

CONCLUSIONS

Macroscopic TWA is a grave marker of electrophysiological instability. Autonomic modulation of the

sympathetic nervous system may be effective in attenuating repolarization alternans and should be considered promptly as an adjunctive therapy in VES refractory to aggressive medical therapy.

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