Refractory ventricular arrhythmia in a patient with Lamin A/C (LMNA) cardiomyopathy successfully treated with thoracic bilateral stellate ganglionectomy

Eze Okeagu, MD,* Ahad Abid, MD,† Brian C. Jensen, MD, * Thomas G. Caranasos, MD,‡ Faisal F. Syed, MBChB*1

From the *Division of Cardiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, †Department of Internal Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, and ‡Division of Cardiothoracic Surgery, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina.

Introduction

Lamin A/C (LMNA) mutations cause familial dilated cardiomyopathy (DCM) with autosomal dominant inheritance and variable phenotypic expression,1 such as early-onset atrioventricular (AV) block, supraventricular and ventricular arrhythmia, progressive systolic heart failure, and frequent need for heart transplantation.2 LMNA cardiomyopathy has been associated with high incidence of malignant ventricular arrhythmia (MVA). In 25% of patients with LMNA cardiomyopathy, sudden cardiac death was the first presentation of MVA.3 MVA often occurs before the development of DCM.2 Sustained monomorphic ventricular tachycardia (VT) is seen in 35% of patients within 7 years of diagnosis.4 Ventricular arrhythmia in LMNA cardiomyopathy is invariably related to a basal septal intramural substrate.5 After VT ablation, there is a high rate of refractory ventricular arrhythmia (91% in 7 months) in patients with LMNA cardiomyopathy owing to the deep septal substrate.4

We present a case of a patient with LMNA cardiomyopathy who had a significant reduction in ventricular arrhythmia after receiving bilateral stellate ganglionectomy (also known as thoracic sympathectomy). There are no prior case reports that detail the clinical utility of this procedure for ventricular arrhythmia reduction in patients with LMNA cardiomyopathy. This case presents a novel therapy for management of refractory ventricular arrhythmia in this patient population.

Case report

A 41-year-old man with no significant past medical history, who was a competitive mixed martial arts athlete, had his index presentation to our cardiac intensive care unit after suffering an out-of-hospital ventricular fibrillation (VF) arrest while playing with his dog at home. He was successfully resuscitated in the field with cardiopulmonary resuscitation and defibrillation. During the course of his hospitalization, he was found to have nonischemic DCM (left ventricular ejection fraction [LVEF] of 15%). Admission electrocardiogram demonstrated sinus tachycardia and first-degree AV block with prolonged QTc500 (Figure 1), which subsequently normalized 5 days after admission. A left heart catheterization demonstrated no angiographic evidence of coronary artery disease. Cardiac magnetic resonance imaging demonstrated sinus tachycardia and first-degree AV block with prolonged QTc >500 (Figure 1), which subsequently normalized 5 days after admission. A left heart catheterization demonstrated no angiographic evidence of coronary artery disease. Cardiac magnetic resonance imaging demonstrated DCM with an LVEF of 30%–35%. (Figure 2A and 2B). There was no evidence of late gadolinium enhancement. Intravenous epinephrine challenge using the protocol described by Vyas and colleagues5 was negative. Procainamide challenge was deferred owing to frequent premature ventricular complexes present on the day of the study. Further nonischemic cardiomyopathy work-up with serum TSH, HIV, ANA, and iron studies was unremarkable. The patient was subsequently discharged with a Medtronic dual-chamber implantable cardioverter-defibrillator (ICD). Notably, the patient reported a significant family history of sudden cardiac death affecting his mother and multiple family members on his mother’s side in the fourth decade of life. Genetic testing with the Invitae Arrhythmia and Cardiomyopathy Comprehensive Panel identified no pathogenic mutations but reported a heterozygous c.618C>G (p.Phe206Leu) variant of uncertain significance in the LMNA gene.

KEYWORDS Cardiac sympathetic denervation; Lamin A/C (LMNA) cardiomyopathy; Stellate ganglionectomy; Sudden cardiac death; Ventricular fibrillation

(Heart Rhythm Case Reports 2022;8:110–113)

1Dr Caranasos and Syed contributed equally to this work and share senior authorship equally. Declarations of interest: None. Address reprint requests and correspondence: Dr Faisal F. Syed, MBChB, UNC Cardiology,160 Dental Circle, Burnett-Womack Building, CB #7075, Chapel Hill, NC 27599. E-mail address: faisal_syed@med.unc.edu.

2214-0271/© 2021 Heart Rhythm Society. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/). https://doi.org/10.1016/j.hrcr.2021.11.011
months after index presentation Invitae reclassified the mutation as pathogenic for LMNA cardiomyopathy.

The patient was treated initially with amiodarone therapy that subsequently was withdrawn owing to overall stability. Thereafter he was maintained on a beta-blocker. Overall, he fared well until suffering an ICD shock for VF 28 months after index presentation. Device interrogation also showed low paroxysmal atrial fibrillation burden. Sotalol and apixaban were initiated, but the patient could not tolerate the former owing to excessive fatigue. He suffered another ICD shock for torsades de pointes 29 months after index presentation. Sotalol was discontinued and he was subsequently transitioned back to amiodarone. Between 30 and 33 months

---

**KEY TEACHING POINTS**

- Lamin A/C (LMNA) cardiomyopathy is a familial dilated cardiomyopathy with a high incidence of malignant ventricular arrhythmia and possible need for cardiac transplantation.
- Ventricular arrhythmia can present before the onset of heart failure.
- Stellate ganglionectomy (thoracic sympathectomy) is a treatment option for malignant arrhythmia associated with LMNA cardiomyopathy.

---

**Figure 1** Baseline electrocardiogram after initial presentation demonstrating sinus rhythm with occasional premature ventricular contractions and first-degree atrioventricular block with evidence of prolonged QTc >500.

**Figure 2** Cardiac magnetic resonance imaging with short axis at the level of the papillary muscle (left) and long axis 4-chamber (right) demonstrating no evidence of late gadolinium enhancement.
after index presentation, ventricular pacing increased from 56.7% to 99.1%. Owing to concerns for pacing-induced deterioration in left ventricular function, he underwent upgrade to biventricular ICD 33 months after index presentation. The patient had another VF episode resulting in ICD shock. Ablation of VF triggers was considered. However, review of near- and far-field ventricular electrograms recorded by the ICD demonstrated that premature ventricular contractions triggering VF were of different morphologies, suggesting that such an approach would be unsuccessful. On account of recurrent ICD shocks despite antiarrhythmic therapy, the patient underwent bilateral stellate ganglionectomy 35 months after index presentation. The procedure was performed via a video-assisted thoracoscopic approach. A double-lumen endotracheal tube was utilized for lung ventilation to allow a video-assisted thoracoscopic approach. A double-lumen anterior thoracostomy was performed for sequential bilateral sympathectomy. The left side was approached first. With video-assisted thoracoscopic exposure the first, second, third, and fourth rib heads were identified. The sympathetic chain and stellate ganglion were identified prior to division from T2 to T4. At T3, accessory nerves of Kuntz were identified and divided as well. Amiodarone therapy was discontinued 36 months after index presentation. At the time of this manuscript preparation, 57 months after index presentation, the patient remains off antiarrhythmic medications, with only 2 episodes of monomorphic tachycardia that were successfully terminated with antiarrhythmia pacing and no episodes of VF or ICD shocks. He has frequent multifocal premature ventricular depolarizations. He is currently being treated with guideline-directed medical therapy for heart failure with reduced systolic function and has NYHA class I symptoms. We recommended exercise limitation.

**Discussion**

The Lamin A/C gene is mapped to the long arm of chromosome 1 (1q21.2-q21.3) and encodes 2 isoforms by alternative splicing, Lamin A and C.\(^6\) Lamin proteins are a type V intermediate filament that are major components of the scaffolding system of the inner nuclear membrane.\(^6\) Lamin mutations result in defects in the myocardium, skeletal muscles, and cardiac conduction system.\(^6\) LMNA cardiomyopathy has been associated with various arrhythmias, out of proportion to other heritable causes of DCM. They can range from relatively benign arrhythmia such as first-degree AV block and atrial fibrillation to such malignant arrhythmia as VT and VF. The 2017 AHA/ACC/HRS guidelines designate genetic overlap between LMNA cardiomyopathy and ARVC,\(^12,13\) Assis and colleagues\(^14\) demonstrated the success of BCSD in patients with ARVC. After BCSD, 63% of patients with ARVC had no recurrent ventricular arrhythmia within approximately 2 years of follow-up. This report demonstrates the clinical utility of BCSD in patients with other forms of arrhythmogenic cardiomyopathy.\(^15,16\) Its utility in LMNA cardiomyopathy has not previously been reported. Our patient’s predominant arrhythmias were VF, for which sympathetic modulation may have greater efficacy than that seen for scar-related reentrant VT. Future studies are needed to establish BCSD as a treatment option for patients with refractory ventricular arrhythmia from LMNA cardiomyopathy.

**References**

1. van Rijssinga IA, Nannenberg EA, Arabustini E, et al. Gender-specific differences in major cardiac events and mortality in lamin A/C mutation carriers. Eur J Heart Fail 2013;15:376–384.
2. Hasselberg NE, Haland TF, Saberniak J, et al. Lamin A/C cardiomyopathy: young onset, high penetrance, and frequent need for heart transplantation. Eur Heart J 2018;39:853–860.
3. van Rijssinga IA, Arabustini E, Elliott PM, et al. Risk factors for malignant ventricular arrhythmias in lamin a/c mutation carriers: a European cohort study. J Am Coll Cardiol 2012;59:493–500.
4. Kumar S, Androulakis AF, Sellal JM, et al. Multicenter experience with catheter ablation for ventricular tachycardia in lamin A/C cardiomyopathy. Circ Arrhythm Electrophysiol 2016;9:e004357.
5. Vyas H, Hejlik J, Ackerman MJ. Epinephrine QT stress testing in the evaluation of congenital long-QT syndrome: diagnostic accuracy of the paradoxical QT response. Circulation 2006;113:1385–1392.
6. Taylor MR, Pain PR, Sinagra G, et al. Familial Dilated Cardiomyopathy Registry Research Group. Natural history of dilated cardiomyopathy due to lamin A/C gene mutations. J Am Coll Cardiol 2005;41:771–780.
7. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS Guideline for Management of Patients With Ventricular Arrhythmias and the
8. Skjølsvik ET, Hasselberg NE, Dejgaard LA, et al. Exercise is associated with impaired left ventricular systolic function in patients with lamin A/C genotype. J Am Heart Assoc 2020;9:e012937.

9. Zipes DP, Barber MJ, Takahashi N, et al. Influence of the autonomic nervous system on the genesis of cardiac arrhythmias. Pacing Clin Electrophysiol 1983;6:1210–1220.

10. Schwartz PJ, Snebold NG, Brown AM. Effects of unilateral cardiac sympathetic denervation on the ventricular fibrillation threshold. Am J Cardiol 1976;37:1034–1340.

11. Richardson T, Lugo R, Saavedra P, et al. Cardiac sympathectomy for the management of ventricular arrhythmias refractory to catheter ablation. Heart Rhythm 2018;15:56–62.

12. Quarta G, Syrris P, Ashworth M, et al. Mutations in the Lamin A/C gene mimic arrhythmogenic right ventricular cardiomyopathy. Eur Heart J 2012;33:1128–1136.

13. Valtuille L, Paterson I, Kim DH, et al. A case of lamin A/C mutation cardiomyopathy with overlap features of ARVC: a critical role of genetic testing. Int J Cardiol 2013;168:4325–4327.

14. Assis FR, Krishnan A, Zhou X, et al. Cardiac sympathectomy for refractory ventricular tachycardia in arrhythmogenic right ventricular cardiomyopathy. Heart Rhythm 2019;16:1003–1010.

15. Vaseghi M, Barwad P, Malavassi Corrales FJ, et al. Cardiac sympathetic denervation for refractory ventricular arrhythmias. J Am Coll Cardiol 2017;69:3070–3080.

16. Elliott IA, DeJesus M, Dobaria V, et al. Minimally invasive bilateral stellate ganglionectomy for refractory ventricular tachycardia. JACC Clin Electrophysiol 2021;7:533–535.