Ganglionated plexi ablation to treat exercise-induced vasovagal syncope: A case report

Xu-Lin Hong, MD, Ru-Hong Jiang, MD, Jun-Hui Zhu, MD, Jia-Lin He, MD

From the Department of Cardiology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, China, and Key Laboratory of Cardiovascular Intervention and Regenerative Medicine of Zhejiang Province, Hangzhou, China.

Introduction

Vasovagal syncope (VVS) is the most frequent cause of a transient loss of consciousness in patients without apparent cardiac or neurological pathology. There are many triggers for VVS, including prolonged standing, changes in posture, medications, temperature, alcohol consumption, and mood changes. Exercise-induced VVS is rarely reported. The underlying mechanisms of VVS are not well understood. Dysregulation of the Bezold–Jarisch reflex, owing to the unbalance of vagal vs sympathetic tone, is considered to be part of the pathogenesis.[1]

Treatment for VVS is limited. Conventional treatments, such as tilt-training and medicine, have been shown to have limited efficacy[2–4]; pacemaker therapy may be beneficial in some patients.[5,6] Autonomic modification through catheter ablation of ganglionated plexi (GP) in the left atrium has been reported effective in several previous studies.[7,8]

Our case documents the manifestation and investigation of a young man who experienced several episodes of syncope after exercise and was treated successfully with left atrial GP ablation.

KEY TEACHING POINTS

- Triggers for vasovagal syncope are various; exercise-induced vasovagal syncope is rare.
- Exercise-induced vasovagal syncope requires systematic investigation to exclude structural heart disease, severe coronary artery disease, arrhythmogenic cardiac disorders, and noncardiac causes of syncope.
- Ganglionated plexi ablation might be considered as a therapeutic option for patients with exercise-induced vasovagal syncope given the lack of good outcome with conventional strategies.

Case report

A 31-year-old Chinese man presented to hospital after several episodes of syncope following strenuous exercise. On many occasions, he described dizziness lasting for several seconds before syncope. He regained consciousness on each occasion lying on the ground. Before admission, he had fallen down and sustained a minor laceration on the front of the head after carrying heavy objects. He described no chest pain or palpitations and there was no suggestive evidence of epileptic attack in the history. The patient was previously healthy. He had no medical history and was on no regular medication. He denied family history of sudden cardiac death or arrhythmias. He never smoked or drank alcohol.

On admission, his vital signs were stable, and he had a regular heart rate of 63 beats per minute (bpm). Physical examination was unremarkable. Systematic investigation was done to reveal the pathogenesis of the syncope:

Twelve-lead electrocardiogram (ECG): Sinus rhythm with a normal PR interval (126 ms) and narrow QRS complex (98 ms) with a normal corrected QT interval (393 ms) (Figure 1A).

Chest radiograph: No obvious abnormality of lung and heart size.

Transthoracic echocardiogram: The structure and function of the heart is normal; no left ventricular outflow tract obstruction was observed when performing the Valsalva maneuver.

Contrast-enhanced cardiac magnetic resonance imaging: Left ventricular thickness is normal and no systolic anterior motion of the mitral valve was detected.

Coronary angiography: No obvious stenosis or dysplasia in any main coronary artery.

Electrophysiologic study: Sinus and atrioventricular node function is normal, and no sustained ventricular tachycardia is induced.

KEYWORDS Exercise-induced syncope; Exercise test; Ganglionated plexi ablation; Head-up tilt test; Vasovagal syncope
(Heart Rhythm Case Reports 2020;6:854–857)

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Conflict of Interest: The authors have no conflicts to disclose. **Address reprint requests and correspondence:** Dr Xulin Hong, Department of Cardiology, Sir Run Run Shaw Hospital, Zhejiang 310016, China. E-mail address: 1028346604@zju.edu.cn.

https://doi.org/10.1016/j.hrcr.2020.08.009

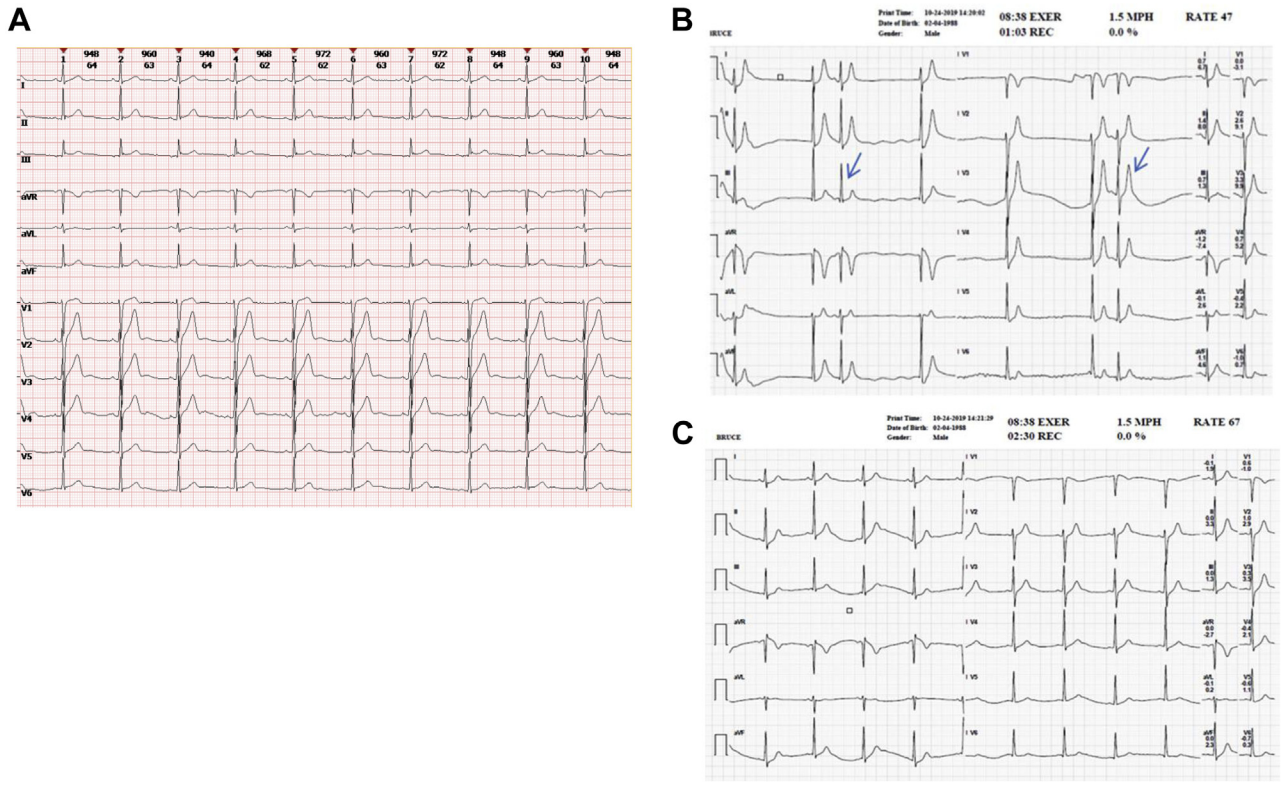

Figure 1 **A:** Resting 12-lead electrocardiogram (ECG) showed sinus rhythm with a normal PR interval (126 ms), a narrow QRS complex (98 ms), and a normal corrected QT interval (393 ms). **B:** ECG taken after 1 minute and 3 seconds during recovery demonstrated junctional escape rhythm, with occasional premature atrial contractions (marked by *arrow*). **C:** ECG taken after 2 minutes and 10 seconds during recovery (after regaining consciousness) demonstrated normal sinus rhythm.

Fifteen-minute Bruce protocol exercise test: The patient received a standard Bruce protocol exercise test. His resting heart rate of 63 bpm rose to a maximum heart rate of 172 bpm, representing 91% of the maximal, age-predicted heart rate. His resting blood pressure of 112/64 mm Hg rose to a maximum of 140/87 mm Hg. He felt tired and stopped. One minute and 3 seconds into recovery, he felt nauseous and dizzy and immediately lost consciousness. The subsequent electrocardiogram strip demonstrated junctional escape rhythm with occasional premature atrial contractions (Figure 1B), and his blood pressure dropped to 70/40 mm Hg. He was placed on the ground and physical stimulation was attempted while resuscitation drugs were being prepared. After about 1 minute he regained consciousness and his heart returned to sinus rhythm at a rate of 67 bpm (Figure 1C).

Head-up tilt test: No symptoms occurred in the passive phase. The patient experienced syncope during the provocative phase, demonstrating bradycardia (junctional ectopy, 40 bpm) and hypotension (76/50 mm Hg).

Treatment and follow-up

Our patient had tried to avoid exercise before and had been advised to maintain an adequate salt and fluid intake. However, he still suffered syncope occasionally. Pacemaker therapy may be inappropriate for the young man. After detailed discussion with him and his family, GP ablation was performed for him with an irrigated catheter (ThermoCool SmartTouch; Biosense Webster, Diamond Bar, CA) at 35–40 W with 17–25 mL/min irrigation and maximum temperature 43°C, guided by a 3D mapping system (CARTO; Biosense Webster). The ablation sites for GP were located anatomically as described in previous studies.[9] Superior left GP was ablated firstly; vagal reflex that R-R interval prolonged >50% was observed during ablation and then obliterated. Anterior right ganglionated plexi was targeted subsequently. The endpoint of GP ablation was elimination of atrial electrical activity (peak-to-peak bipolar electrogram <0.1 mV) at the ablation sites, as well as abolition of parasympathetic effects elicited by ablation (Figure 2).

The patient had attempted to take strenuous exercise after ablation. Bruce protocol exercise test (Figure 3A and B) and head-up tilt test (both passive and provocative phase were performed; isoproterenol was administered as a vasoactive medication) were reviewed after 1 month, and no bradycardia, hypotension, or syncope was induced. He never experienced exercise-induced syncope or near-syncope until now.

Discussion

Exercise-induced VVS is relatively rarely documented. Before making the diagnosis, several life-threatening diseases must be excluded, including structural heart disease (hypertrophic cardiomyopathy, aortic stenosis), severe coronary

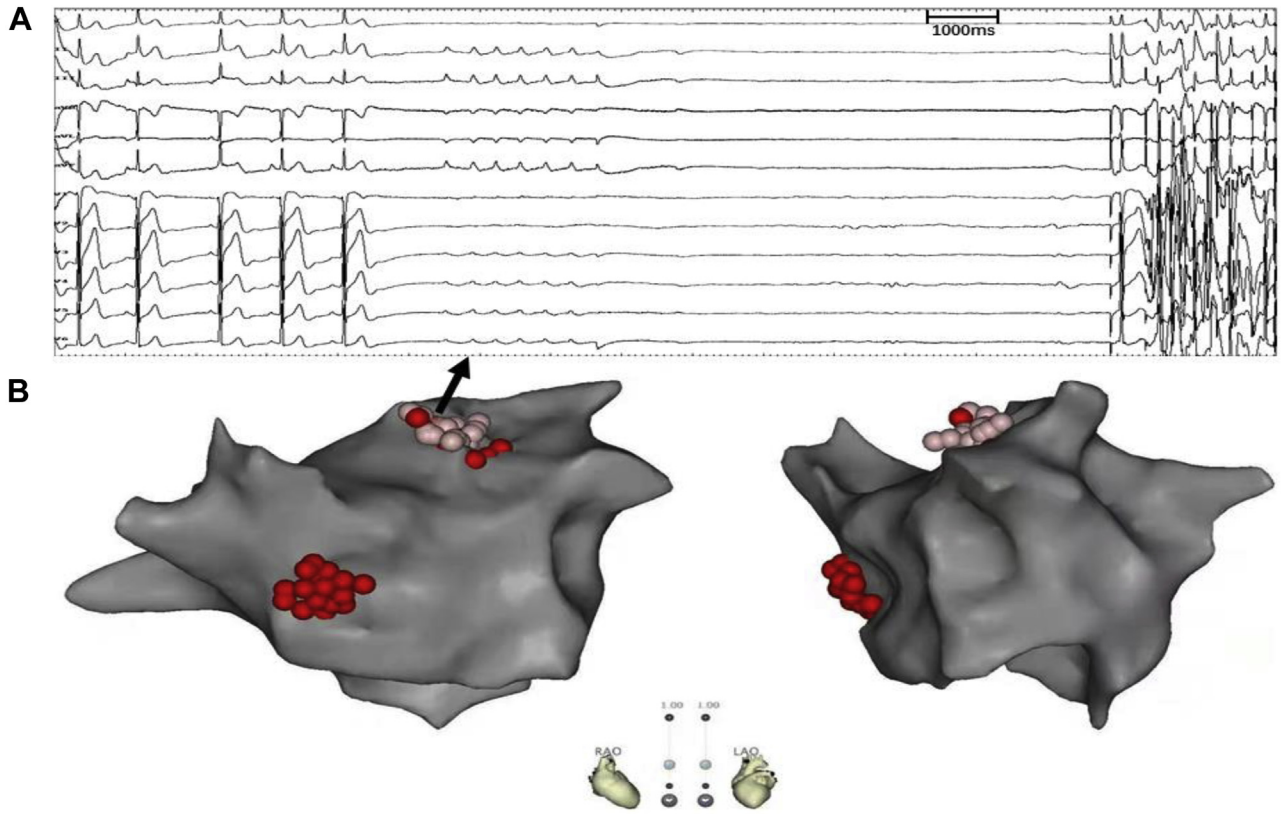

Figure 2 Left superior ganglionated plexi (GP) and right anterior GP were ablated for the patient. **A:** Vagal reflex with R-R interval prolonged (11 seconds) was observed during ablation at left superior GP. **B:** Ablation lesions on CARTO (Biosense Webster, Diamond Bar, CA) image.

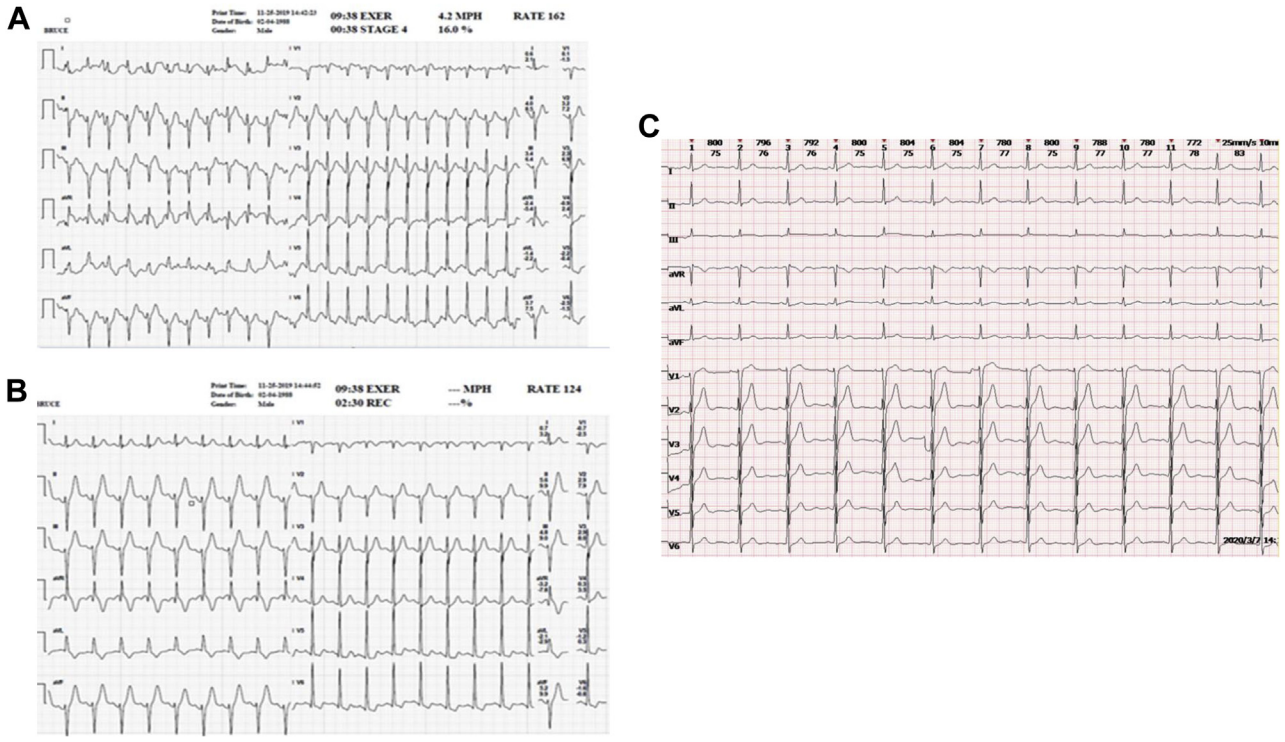

Figure 3 **A,B:** Bruce protocol exercise test showed normal electrocardiogram changes in 1 month follow-up after ablation. **C:** Resting heart rate rose to 75 beats per minute in 6 months follow-up after ablation.

artery disease, and arrhythmogenic cardiac disorders (Brugada syndrome, long QT syndrome, and catecholaminergic polymorphic ventricular tachycardia). A complete history and systematic examinations are crucial to clinical decision-making. For our patient, aggressive screening of the potential cardiac disease was implemented, and finally, the exercise tolerance test demonstrated junctional ectopy without any preceding arrhythmias, consistent with a diagnosis of exercise-induced VVS. A positive response to the head-up tilt test further supported the diagnosis.

Although previous reports confirmed that change in sympathetic tone is crucial to the vasodilatory response, the mechanisms through which VVS is mediated remain to be debated.[10] Several mediators are assumed to be responsible for VVS, such as ventricular baroreceptors (the Bezold–Jarisch reflex), serotonin, peripheral opioids and adenosine, and hypothalamic and brainstem autonomic nuclei.[10] Therefore, treatment for VVS becomes challengeable. Conventional strategies have failed to show good clinical outcomes.[2–4] As our patient cannot abandon physical labor because he has a family to raise, he was eager to seek an effective treatment to reduce the attack of exercise-induced VVS.

Cardiac innervation is composed of sympathetic, parasympathetic, and sensory systems. Only the parasympathetic innervation, which contains most of the postganglionic neurons, is located in the paracardiac ganglia (epicardial fat pads),[7] providing the feasibility of being affected by the endocardial radiofrequency energy. Many researchers have reported patients with VVS achieving symptomatic relief by vagal denervation (left atrial GP ablation).[7,8,11] The possible mechanism is that left atrial GP ablation may be capable of breaking both the afferent and efferent pathways of the abnormal Bezold–Jarisch reflex.[12] In this case, we just ablated anterior right and superior left GP, as these GPs were reported to be more relevant to the sinus and ventricular rate-slowing responses.[13–15] Another reason we did not routinely ablate inferior GPs is that ablation targeting the posterior left atrial wall may increase the risk of esophageal injury. One limitation of this case report is the relatively short follow-up. The patient did not experience syncope for 6 months postablation and the resting heart rate slightly rose (Figure 3C). Results with longer follow-up might be more conclusive, as reinnervation has been reported in documented studies.[7,11]

Conclusion

GP ablation might be considered as a therapeutic option for patients with exercise-induced VVS.

References

1. Chen-Scarabelli C, Scarabelli TM. Neurocardiogenic syncope. BMJ 2004; 329:336–341.
2. Tan MP, Newton JL, Chadwick TJ, Gray JC, Nath S, Parry SW. Home orthostatic training in vasovagal syncope modifies autonomic tone: results of a randomized, placebo-controlled pilot study. Europace 2010;12:240–246.
3. Sheldon RS, Morillo CA, Klingenheben T, Krahn AD, Sheldon A, Rose MS. Age-dependent effect of beta-blockers in preventing vasovagal syncope. Circ Arrhythm Electrophysiol 2012;5:920–926.
4. Romme JJ, van Dijk N, Go-Schon IK, Reitsma JB, Wieling W. Effectiveness of midodrine treatment in patients with recurrent vasovagal syncope not responding to non-pharmacological treatment (STAND-trial). Europace 2011;13:1639–1647.
5. Brignole M, Menozzi C, Moya A, et al. Pacemaker therapy in patients with neurally mediated syncope and documented asystole: Third International Study on Syncope of Uncertain Etiology (ISSUE-3): a randomized trial. Circulation 2012;125:2566–2571.
6. Turagam MK, Gopinathannair R, Park PH, et al. Safety and efficacy of leadless pacemaker for cardioinhibitory vasovagal syncope. Heart Rhythm 2020; 17:1575–1581.
7. Pachon JC, Pachon EI, Cunha Pachon MZ, Lobo TJ, Pachon JC, Santillana TG. Catheter ablation of severe neurally meditated reflex (neurocardiogenic or vasovagal) syncope: cardioneuroablation long-term results. Europace 2011;13:1231–1242.
8. Sun W, Zheng L, Qiao Y, et al. Catheter ablation as a treatment for vasovagal syncope: long-term outcome of endocardial autonomic modification of the left atrium. J Am Heart Assoc 2016;5:e003471.
9. Pokushalov E, Romanov A, Shugayev P, et al. Selective ganglionated plexi ablation for paroxysmal atrial fibrillation. Heart Rhythm 2009;6:1257–1264.
10. Fenton AM, Hammill SC, Rea RF, Low PA, Shen WK. Vasovagal syncope. Ann Intern Med 2000;133:714–725.
11. Scanavacca M, Hachul D, Pisani C, Sosa E. Selective vagal denervation of the sinus and atrioventricular nodes, guided by vagal reflexes induced by high frequency stimulation, to treat refractory neurally mediated syncope. J Cardiovasc Electrophysiol 2009;20:558–563.
12. Thompson GW, Collier K, Ardell JL, Kember G, Armour JA. Functional interdependence of neurons in a single canine intrinsic cardiac ganglionated plexus. J Physiol 2000;528:561–571.
13. Hou Y, Scherlag BJ, Lin J, et al. Ganglionated plexi modulate extrinsic cardiac autonomic nerve input: effects on sinus rate, atrioventricular conduction, refractoriness, and inducibility of atrial fibrillation. J Am Coll Cardiol 2007;50:61–68.
14. Yao Y, Shi R, Wong T, et al. Endocardial autonomic denervation of the left atrium to treat vasovagal syncope: an early experience in humans. Circ Arrhythm Electrophysiol 2012;5:279–286.
15. Mao J, Yin X, Zhang Y, et al. Ablation of epicardial ganglionated plexi increases atrial vulnerability to arrhythmias in dogs. Circ Arrhythm Electrophysiol 2014; 7:711–717.