CARDIONEU-ROABLATION

Cardioneuroablation for treating refractory vasovagal syncope

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ABSTRACT

Vasovagal syncope (VVS), also known as neurocardiogenic syncope, often presents significant management challenges in patients with frequent refractory episodes. Cardioneuroablation (CNA) targets ganglionated plexi (GP) through catheter ablation to mitigate excessive vagal tone. This case report demonstrates the successful application of CNA in a patient with recurrent neurocardiogenic syncope, initially characterised by a mixed response with a minimal cardioinhibitory component and subsequent electrophysiological evaluation, which revealed significant cardioinhibitory and vasodepressor components, prompting a targeted ablation approach. While future studies are required to evaluate the long-term safety and efficacy, this case adds to the growing evidence that supports CNA as a safe and effective intervention for select patients with refractory VVS.
Keywords: cardioneuroablation, vasovagal syncope, cardioinhibitory response, mixed response, vasodepressor response
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INTRODUCTION

VVS is the most common cause of transient loss of consciousness, accounting for a substantial proportion of syncope referrals.[1] Its underlying mechanism involves a reflex in response to a trigger that causes peripheral vasodilation and/or bradycardia, ultimately compromising cerebral perfusion.[2] Although VVS is often considered benign, affected individuals may sustain significant injuries and experience profound impairments in quality of life.[3] CNA is a technique that involves endocardial ablation and targets cardiac GP to mitigate excessive vagal activity.[4] This approach is effective in managing neurocardiogenic reflex syndromes with cardioinhibitory and vasodepressor responses.[3,5] We present a case that illustrates the successful application of CNA in managing recurrent neurocardiogenic syncope.

BACKGROUND

A 42-year-old female presented with recurrent syncope resulting in severe injuries. Most episodes were preceded by a prodromal phase of dizziness and transient cognitive changes, predominantly occurring upon standing or with postural changes. However, a subset of events arose without any discernible orthostatic triggers. Her symptoms, which began 1 year prior, had persisted despite treatment with midodrine, fludrocortisone, and lifestyle modifications. A loop recorder was implanted, revealing findings suggestive of a mixed response with minimal cardioinhibitory sinus slowing (Figure 1). Given the patient's refractory course, a multidisciplinary discussion was undertaken to explore invasive, catheter-based radiofrequency (RF) ablation of GP to modulate autonomic tone, with a subsequent assessment of procedural efficacy.

PROCEDURE

The procedure was performed under general anaesthesia. Following heparinisation, 2 decapolar steerable catheters (Dynamic XT 6 Fr, Boston Scientific, Marlborough, United States) were advanced from the femoral veins to both internal jugular veins at the base of the cranium, near the jugular foramen, directed medially towards the jugular ganglion of the vagus nerve. High-frequency stimulation (HFS) at 20 Hz, 20 mA, 20 microseconds (μs) pulse width, with a 4-second duration with Micropace EPS320™ (Micropace EP Inc., Santa Ana, United States) was performed, stimulating the vagus nerve and resulting in immediate hypotension and prolonged asystole from a single pole on the left side (Figures 2 and 3).

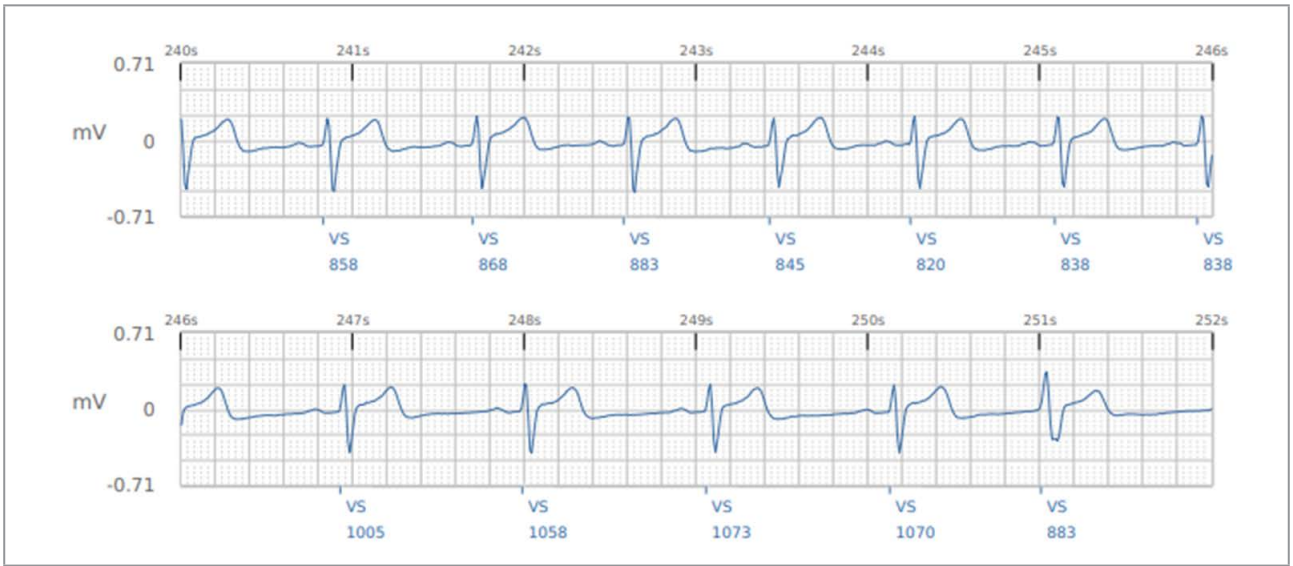

FIGURE 1: Implantable cardiac monitor tracing during a pre-syncopal episode, showing progressive sinus slowing without significant bradycardia or pauses consistent with mixed response.

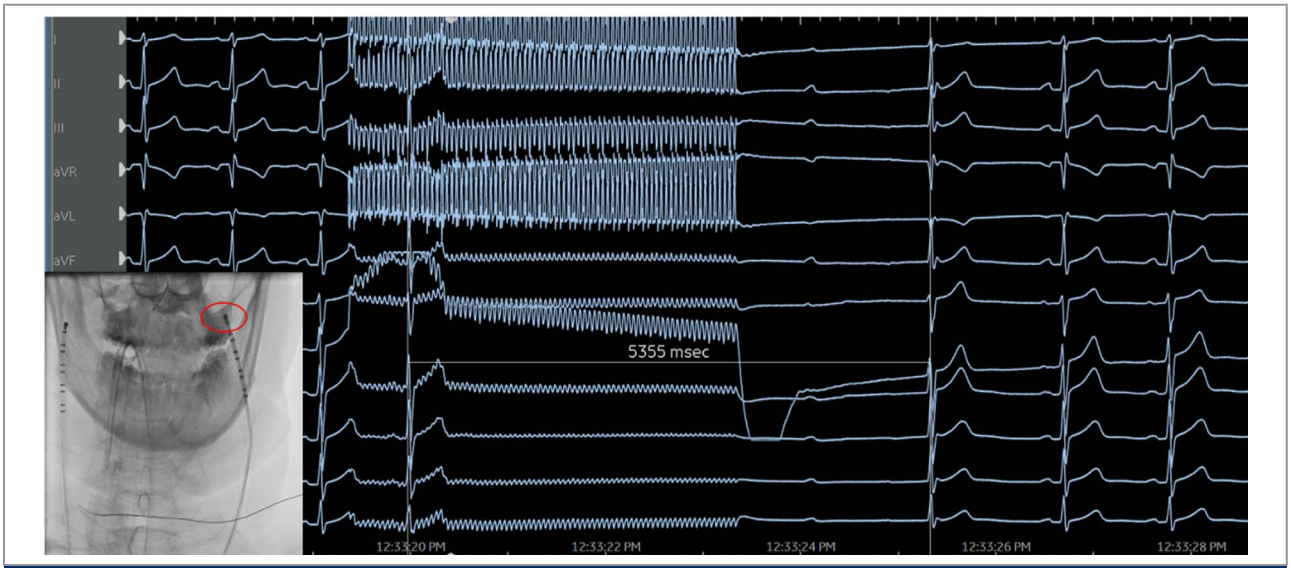

FIGURE 2: Pacing site at left cranial base (red circle) with cardioinhibitory and vasodepressor response.

A multipolar mapping catheter, Advisor HD Grid (Abbott HD, Abbott Park, United States), was utilised for mapping of the right and left atria, identifying areas of fragmentation and high-frequency signals with a bandpass filter set between 300 Hz and 500 Hz (Figure 4). Ablation was performed in all regions with high-frequency/fragmented electrograms, which are hallmarks of GP and targets for CNA. For our patient, this involved the ridge between the left superior pulmonary vein (LSPV) and the appendage, the right superior pulmonary vein, the superior vena cava, and the upper limbus of the interatrial septum (Figures 5, 6, and 7). Notably, ablation near the LSPV ridge elicited a profound bradycardic response with significant vasodepressor effects, necessitating temporary pacing. Pauses exceeding 10 seconds were observed, with each successive lesion resulting in progressive attenuation of both the cardioinhibitory and vasodepressor responses (Figure 8).

Following ablation of the atrial tissue adjacent to the GP, repeat HFS at the same jugular vein sites no longer elicited significant bradycardia or hypotension, indicating successful autonomic modification (Figure 9). The procedure concluded without complications.

FOLLOW-UP

At the 11-month follow-up, the patient reported 3 syncopal episodes – 2 within the first month and 1 isolated event at 9 months – reflecting a marked reduction from the 4 syncopal

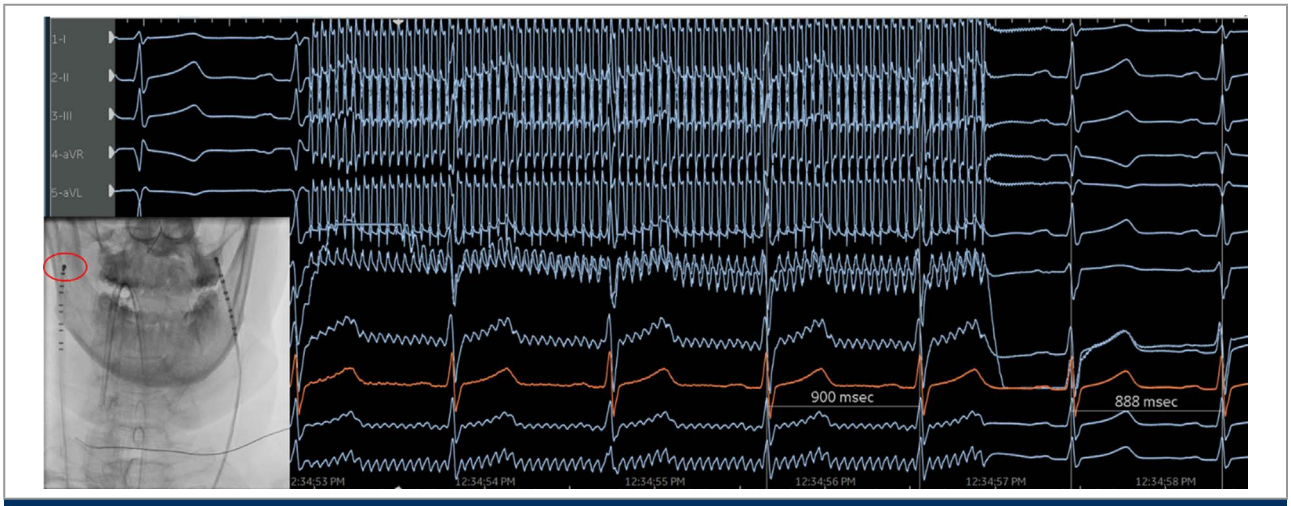

FIGURE 3: Pacing site at right cranial base (red circle) without cardioinhibitory or vasodepressor response.

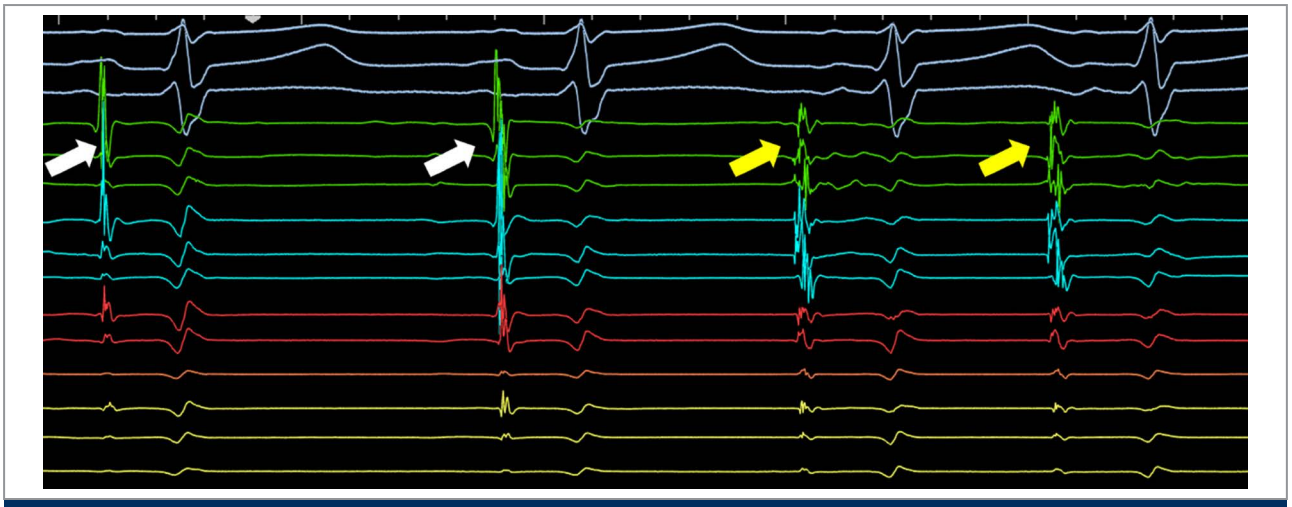

FIGURE 4: Intracardiac atrial electrograms during mapping. Normal electrograms (white arrows) show uniform, discrete deflections, while fragmented electrograms (yellow arrows) exhibit multiple high-frequency components – hallmarks of ganglionated plexi and targets for cardioneuroablation.

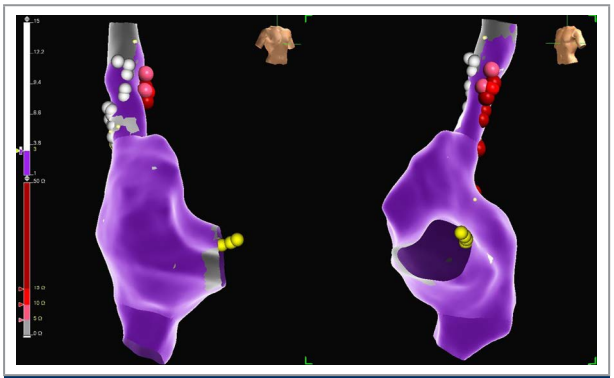

FIGURE 5: Three-dimensional electroanatomic map of the right atrium. Recorded sites of the His bundle are marked in yellow, diaphragm capture in grey, and radiofrequency ablation lesions in red.

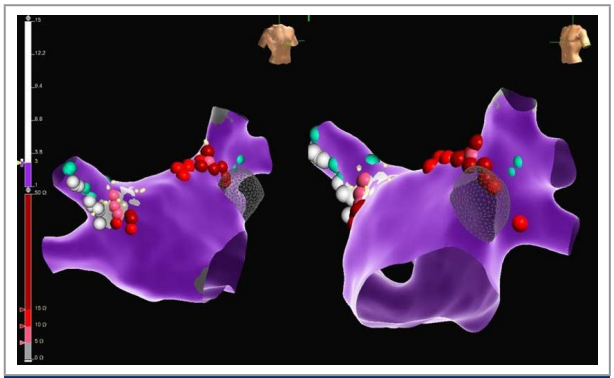

FIGURE 6: Three-dimensional electroanatomic map of the left atrium. Sites of diaphragm capture are shown in grey, and radiofrequency ablation lesions are marked in red.

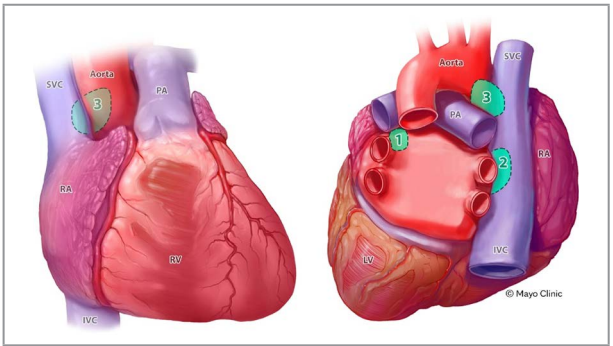

FIGURE 7: Schematic illustration of the ganglionated plexi targeted during cardioneuroablation. 1 – ridge between the left superior pulmonary vein and left atrial appendage, 2 – right superior pulmonary vein and upper limbus of the interatrial septum, 3 – superior vena cava region. RA – Right Atrium, PA – Pulmonary Artery, SVC – Superior Vena Cava, IVC – Inferior Vena Cava, RV – Right Ventricle, LV – Left Ventricle

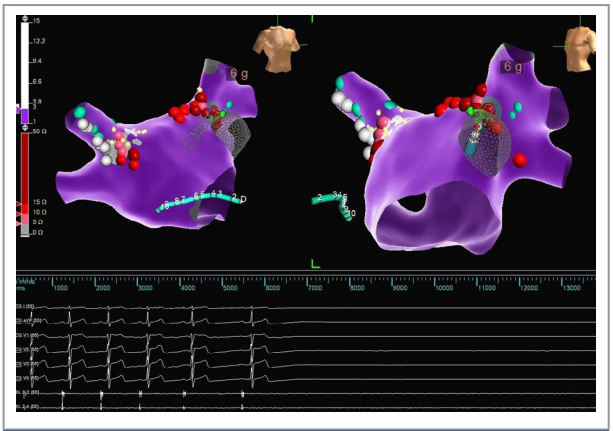

FIGURE 8: Radiofrequency ablation anterior to the left superior pulmonary vein eliciting a profound vagal response, evidenced by transient sinus arrest on intracardiac electrograms (bottom panel). The electroanatomic map demonstrates the ablation catheter position and the lesion set near the left superior pulmonary vein ridge.

events recorded in the 3 months before CNA. She also noted substantial improvements in her energy, mood, and overall well-being, stating that she "finally got her life back".

DISCUSSION

VVS arises from 2 primary pathophysiological mechanisms: vasodepression, manifested by vasodilation and resultant hypotension, and cardioinhibition, in which excessive parasympathetic activation leads to sinus bradycardia or pauses. When both responses are involved, the condition is classified as "mixed".[6] Clinical presentations often include dizziness or syncope secondary to hypotension, vagally mediated sinus node slowing or arrest, and/or atrioventricular block.[7] VVS predominantly affects younger individuals without underlying structural cardiac or neurological disorders.[8]

In more severe forms of VVS, where episodes of syncope are frequent and often occur with little or no prodrome, treatment can be particularly challenging.[3] Traditional VVS management includes counterpressure manoeuvres and the use of pharmacologic agents, like midodrine and fludrocortisone.[6] In cardioinhibitory VVS, permanent pacing may be considered, especially in individuals over 40 with documented asystolic episodes.[9] Importantly, pacemakers have limited sustained benefit as they do not address the vasodepressor reflex and have a risk for short- and long-term complications.[6,7]

CNA has emerged as a promising alternative treatment for VVS, using RF ablation to target cardiac vagal ganglia, effectively reducing excessive vagal activity.[3] Several observational studies and 1 randomised controlled study reported excellent short- and long-term outcomes for patients with VVS, functional atrioventricular block, and sick sinus syndrome treated with CNA.[10]

CNA is performed with RF energy and irrigated catheters to deliver current into the tissue to induce resistive and conductive heating.[11] Ablation parameters commonly include 25–35 W for 40–60 seconds, with shorter durations (< 20 seconds) for the

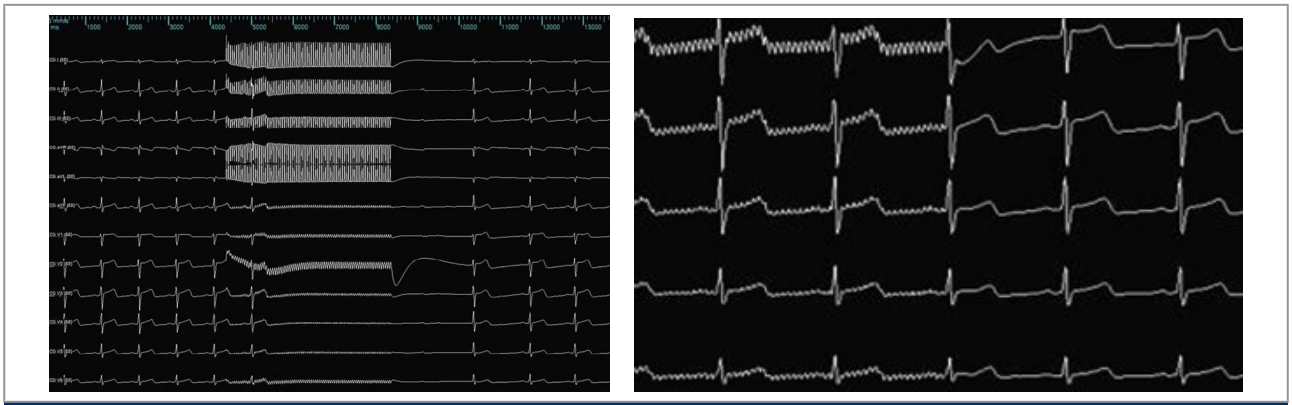

FIGURE 9: High-frequency stimulation at the left cranial base before (left) and after (right) cardioneuroablation. Pre-ablation stimulation induced a significant vagal response with bradycardia and hypotension, while post-ablation stimulation failed to elicit any notable autonomic effect, indicating successful parasympathetic modulation.

posterior wall, and avoiding lesion stacking while monitoring the oesophageal temperature.[12] Procedural endpoints vary but generally fall into three categories: (1) elimination of vagal response to HFS, (2) targeting of high-frequency or fractionated atrial electrograms, and (3) empiric anatomical ablation at established GP sites.[13] In this case, we used a physiology-guided approach incorporating both HFS and electrogram mapping to guide targeted ablation.

Emerging technologies, such as pulsed field ablation (PFA), are also being explored for CNA in atrial fibrillation, as autonomic input from GP can abbreviate atrial refractoriness and promote re-entry.[14] In pre-clinical studies, PFA selectively ablated cardiomyocytes via electroporation while preserving myelinated structures, such as the phrenic and sciatic nerves.[15-17] GP ablation with PFA was initially shown to be safe and feasible from an epicardial approach via substernal access in canine models.[18] While human data are limited for epicardial ablation, a trial of epicardial RF GP ablation during thoracoscopic pulmonary vein isolation showed no benefit in atrial fibrillation suppression and was associated with increased adverse events.[19]

Outcomes of CNA for VVS are encouraging. However, there have been concerns, including attenuation of vagal tone, resting tachycardia, exercise intolerance, atrial arrhythmias, and, in animal models, increased susceptibility to ventricular arrhythmias.[13,20] Intra-procedural risks are similar to those of left atrial ablation and include oesophageal injury and thromboembolic events.[12]

While CNA is gaining traction in patients with cardioinhibitory VVS, its role in vasodepressor-predominant syncope remains controversial, as cardiac parasympathetic denervation is believed to improve bradycardia without directly affecting vasodepressor response.[9] However, a recent case series compared 13 patients with vasodepressor VVS and 19 with mixed-type VVS who underwent CNA, and found no significant difference in syncope recurrence at 11 months.[21] Another study reported similar benefits in patients with vasodepressor responses on tilt table testing.[22]

CONCLUSION

This case adds to the emerging literature by highlighting a patient with minimal cardioinhibitory findings on a loop recorder that demonstrated both cardioinhibitory and vasodepressor responses with HFS and benefited from CNA. This vagal response to HFS was eliminated after ablation, suggesting the effective modulation of autonomic tone.[23] This finding aligns with anatomical studies showing that GP contain both afferent and efferent parasympathetic neurons, which have mechanoreceptors and chemoreceptors.[24] Efferent signals drive bradycardia, while afferent GP activation may provoke a vasodepressor reflex. This duality may explain how CNA benefits patients who have mixed syncope with a minimal cardioinhibitory component. Further study is warranted in this subset of patients.

DISCLOSURES

The authors do not have any funding to disclose.

Conflict of interests: none declared.

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