Repeat Cardioneuroablation for Recurrent Syncope

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Abstract

Introduction: Some patients suffer recurrent syncope following cardioneuroablation (CNA) for vasovagal syncope (VVS), yet no cases of repeat CNA have been described in detail. Methods and Results: Our present patient suffered a recurrence seven months following successful CNA and wished for a repeat CNA. Pre-procedurally, she lacked an atropine response. During CNA, high-frequency stimulation (HFS) at ganglionated plexi (GP) would not trigger cardioinhibitory events. Ablation was delivered based on anatomy and fractionation mapping, producing characteristic tachycardia at 2 GP sites. Conclusion: Repeat CNA is feasible and safe, and characterized by unique physiology.

Introduction

Cardioneuroablation (CNA) is emerging as a compelling new management option for vasovagal syncope (VVS), one which has grown increasingly prevalent since the first US case was described only three years ago (1,2). The largest CNA cohorts have reported promising success, describing recurrent syncope at rates ranging from only 0-27% on long-term follow up (3-6). Many patients suffering from VVS are young, and standard-of-care management is often ineffective or overly burdensome. CNA may be a promising new option for this segment of the VVS population; however, the question of how to treat the minority who faint again post-CNA must be confronted. To this point, there have been no published reports in the literature describing in detail a repeat CNA procedure in patients with recurrent syncope post-CNA. Herein we describe such a case, our diagnostic findings, and procedural approach.

Case Report

A 20-year-old woman with VVS suffered recurrent cardioinhibitory syncope seven months after successful CNA (see Fig 1), the details of which are published elsewhere (7). Evaluation of her ILR data at the time of recurrence revealed both HRV and average ventricular rate gradually trending back toward baseline pre-CNA levels, after having initially dropped off following CNA (see Fig 2). On her subsequent clinic visit, a thorough discussion was held with the patient and her mother, during which time she expressed a strong desire to re-attempt CNA.

She presented to the EP suite again in a fasting state, and the same preparations were made. She was administered atropine 0.5 mg; however, her HR increased from 51 beats per minute (BPM) to only 60 BPM. After ruling out administration errors and waiting approximately 20 minutes, a second dose of atropine 0.5 mg was administered, and again no significant HR response was observed. These findings were in stark contrast to those of her index procedure, when a single dose of atropine 0.4 mg increased her HR by 81% (7). A transseptal puncture was performed in the usual fashion. Fractionation mapping was then undertaken, resulting in the same annotated fractionation areas as in the first CNA (see Fig 3A). High-frequency stimulation (HFS) was applied to each of the ganglionated plexi (GP); however, this time, slow junctional responses could not be reliably elicited from any GP sites, except for a single junctional beat

following HFS from the posterior RA GP. Ablation at both the posterior RA GP and along the anterior RSPV acutely increased the HR by approximately 10 BPM, suggestive of further vagal denervation (see Fig 3B). Of note, the anterior RSPV lesions covered a broader area than in the index CNA. RF ablation was applied at each of the GP sites, due to sparse new diagnostic data in support of any given site, and with cognizance that this was a repeat procedure (see Fig 3C). Atropine was again administered at the end of ablation, and the patient's HR paradoxically dropped from 78 BPM to 40 BPM in response. Isoproterenol 10 mcg was given as a bolus, and HR increased to >100 BPM. A 12-lead ECG obtained in the post-procedural recovery area recorded normal sinus rhythm, HR 65 BPM, with all measured intervals within normal range.

On follow up 2 months after her repeat CNA, she reported feeling quite well, with no further syncope events. Her ILR again demonstrated an abrupt decrease in HRV, although its ensuing ascent was steeper than the pattern following her initial procedure (see Fig 2B). Further, there was not a sustained increase in her average ventricular rate, unlike her spike following her first CNA (7).

Discussion

While VVS in young patients represents a management challenge, recurrent VVS post-CNA poses an even greater dilemma. Repeat CNA has not yet been reported in the nascent literature on this novel approach; the present case is the first such report to our knowledge.

The first interesting aspect of the present case was the inability to pharmacologically suppress vagal tone in pre-procedural testing, despite both her ILR data and clinical recurrence demonstrating its return (see Figs 1 and 2). This "reinnervation" phenomenon has been previously described in AF populations treated via GP ablation, including the same HRV trend back to pre-procedural values (8). However, AF suppression in these patients remained durable despite recovery of GP inputs. The underlying mechanism is not well understood; indeed, our present patient was autonomically denervated, after which her ILR data exhibited gradual reinnervation (Fig 2). Unlike the AF cohorts, however, she suffered clinical relapse.

As such, one might expect to find at least one endocardial site behaving similarly to her GP in the initial procedure, perhaps suggesting that ablation had been incomplete, or that some GP connections had been missed. Yet after she failed to generate a tachycardic response to serial doses of atropine, she could not reproduce her junctional responses to HFS at GP sites. The significance of this finding is not entirely clear, although one explanation is that her reinnervation process may have been characterized by a "re-growth" of injured vagal inputs, perhaps with altered functional properties, or possibly a scenario where alternative plexi gradually took over cardiac vagal function. Yet during the RF phase of the procedure, in which her GP were largely targeted anatomically due to lack of a response to HFS, it was notable that two of her GP (posterior RA and right anterior GP) exhibited accelerated sinus rates in response to RF. During her first procedure, all five GP had clearly accelerated.

One limitation of our present report is that current protocols favoring atropine administration for vagal testing may be fallible, and one practice favors administration of atropine 1-2 days in advance of the procedure. Given her lack of chronotropic response to atropine on this second CNA, it is not clear that advance administration would have changed the responses, nor is it clear that the absent junctional responses to HFS at previously-responsive GP were simply blunted pharmacologically, by the same rationale. One promising albeit primitive alternative to atropine testing is extracardiac vagal stimulation (ECVS), performed by applying high-amplitude, high-frequency pulses from within the lumen of the right internal jugular vein to achieve transient asystole or atrioventricular block. A report from a Brazilian group found GP-ablated patients significantly less responsive to the maneuver at the end of the procedure than a control group, suggesting significant vagal denervation (9). It is of course theoretically possible that, had our present patient been tested either at the end of her first CNA or the beginning of her second, ECVS might have revealed some lingering vagal inputs, perhaps at the GP which produced HR increases on second CNA, although this is only speculative.

A second limitation in the present case may have been simply related to patient selection, the optimal approach to which is widely acknowledged to be an enigma in CNA. Early work in a post-CNA population

with recurrent syncope found nocturnal deceleration capacity, calculated from interval differences in R waves from signal-averaged ECGs, to be predictive of recurrent VVS in post-CNA patients (6).

The pace of progress in CNA is encouraging; however, larger prospective studies are needed to better understand the post-CNA population with recurrent VVS.

Conclusion

Herein we report the first detailed case of repeat CNA in a patient with recurrent VVS despite successful CNA seven months prior. Repeat CNA after recurrent VVS is both feasible and safe. It may be characterized by a blunted chronotropic response to atropine and a failure to redemonstrate bradycardic responses to HFS. It may reproduce chronotropic evidence of vagal denervation after prior post-CNA recovery of the same. Repeat CNA lacks well-defined patient selection criteria and consensus procedural protocols, including optimal means of vagal denervation testing. The present case underscores the importance of elucidating these measures.

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Figures and Legends

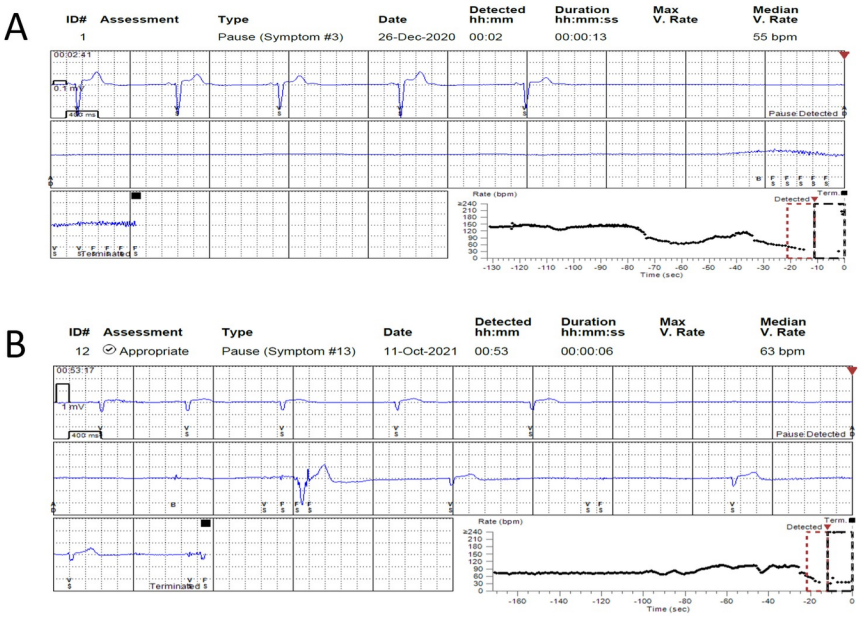

Figure 1: Syncopal events. A) *Pre-cardioneuroablation (CNA) syncope:* The patient's implantable loop recorder (ILR) recorded gradual sinus slowing followed by 13 seconds of sinus arrest with asystole, causing syncope. B) *Post-CNA syncope:* 7 months after successful CNA, the ILR recorded gradual sinus slowing leading to junctional beats followed by 7 seconds of sinus arrest with asystole, causing syncope.

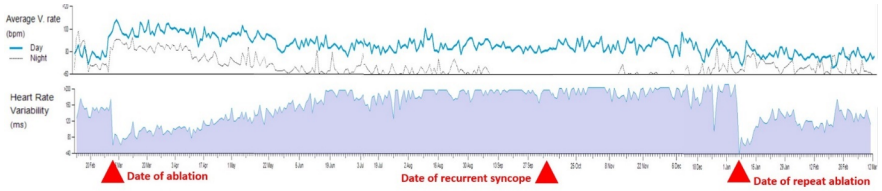

Figure 2: Ventricular Rate and Heart Rate Variability (HRV). The patient's implantable loop recorder (ILR) recorded an abrupt increase in her average ventricular rate and an abrupt decrease in her HRV upon initial cardioneuroablation (CNA). In the months following, the patient's ILR recorded a gradual regression to pre-procedural values in both average ventricular rate and heart rate variability, culminating in her recurrent syncopal event over 7 months later. On repeat CNA, she again exhibited an abrupt drop in HRV, though without a sustained rise in her average ventricular rate.

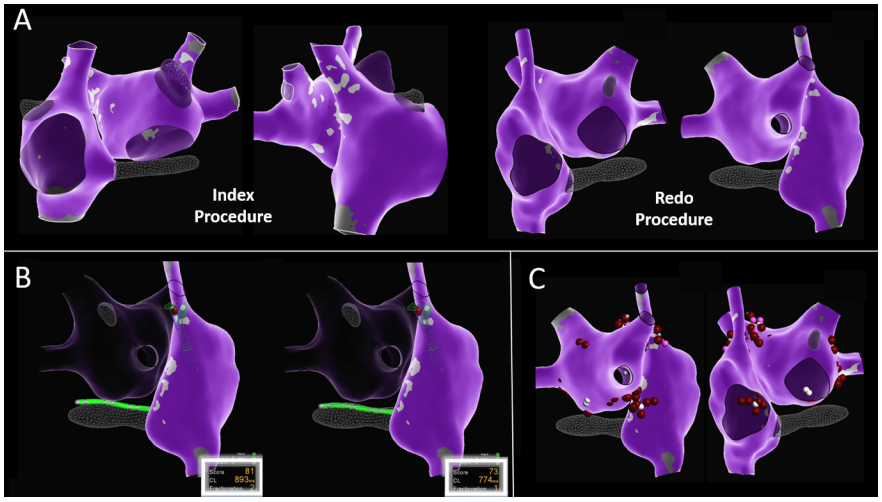

Figure 3: Procedural Data. A) *Fractionation maps:* The ganglionated plexi (GP) were found in the same locations as in her first cardioneuroablation (CNA), at the posterior right atrial (RA) GP, posteromedial RA GP, left anterior GP, left inferior GP, and right anterior GP, correlating with expected anatomy. B)*Radiofrequency (RF) ablation:* At the posterior RA GP, she exhibited a tachycardic response to RF characteristic of vagal denervation. C) *Final lesion set:* Due to a lack of high-frequency stimulation (HFS) responses, repeat CNA was performed based on anatomy and fractionation mapping.

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