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ADVANCED

CASE REPORT: CLINICAL CASE

Single Ectopy-Triggering Ganglionated Plexus Ablation Without Pulmonary Vein Isolation Prevents Atrial Fibrillation

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ABSTRACT

A 58-year-old woman with drug-refractory symptoms of paroxysmal atrial fibrillation (AF) was referred for AF ablation. A single site of ganglionated plexus triggering pulmonary vein ectopy and AF was ablated, without pulmonary vein isolation. This procedure led to long-term freedom from AF. (**Level of Difficulty: Advanced.**)

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HISTORY OF PRESENTATION

A 58-year-old woman presented with paroxysmal atrial fibrillation (AF) and a report of symptomatic episodes occurring at least once a month and lasting several days at a time. Because of her drug-refractory symptoms, she was referred for AF ablation and underwent ganglionated plexus (GP) ablation as part of a pilot study.

LEARNING OBJECTIVES

- To understand how specific GP can be stimulated to trigger PV or non-PV ectopy and AF (ET-GP) with HFS.
- To understand that ET-GP ablation without PVI can provide a more patient-centric approach to AF ablation and achieve long-term freedom from AF.

PAST MEDICAL HISTORY

The patient had hypertension, good left ventricular systolic function, and a left atrial diameter of 3.6 cm. Flecainide was used as “pill-in-the-pocket” therapy. She previously had an electrophysiology study, which detected a concealed septal accessory pathway but no inducible tachycardia. This condition was left untreated.

DIFFERENTIAL DIAGNOSIS

The differential diagnoses included atrial tachycardia, atrial flutter, and AF.

INVESTIGATIONS

A 12-lead electrocardiogram confirmed AF (**Figure 1**).

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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 *JACC: Case Reports* author instructions page.

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MANAGEMENT

The procedure was performed while the patient was under general anesthesia. Access to the left atrium was guided by fluoroscopy and transesophageal echocardiography. A 3-dimensional electroanatomic map of the left atrium was created using the CARTO system (Biosense Webster, Irvine, California).

At the beginning of mapping, frequent and spontaneous AF episodes were seen, and they became sustained. We then commenced mapping of GP sites with high-frequency stimulation (HFS) delivered to the left atrial endocardium by using the ablation catheter. Continuous HFS (10-s stimulation at 10V, 20 Hz) delivered during AF identified atrioventricular dissociating GP (AVD-GP). AVD-GP are defined as causing asystole during HFS, or >50% prolongation in the average RR interval during HFS (compared with baseline) secondary to atrioventricular dissociation (1). After approximately 50 min, AF spontaneously reverted to sinus rhythm. Therefore, the remaining left atrium was mapped with synchronized HFS to identify ectopy-triggering GP (ET-GP). ET-GP cause pulmonary vein (PV) or atrial ectopy and atrial arrhythmia when stimulated with synchronized HFS (2) (100-ms, 10-V, 40-Hz bursts synchronized to atrial-paced stimuli, delivered within the local atrial refractory period to capture GP and not myocardium). A total of 64 sites were tested with HFS, which identified 19 GP (30%); 2 ET-GP, and 17 AVD-GP.

Figure 2 shows the effect of synchronized HFS identifying an ET-GP near the left inferior PV (LIPV) ostium. Multiple repeat tests at this site consistently triggered PV ectopy from the LIPV, thus causing AF. Radiofrequency ablation at this ET-GP immediately triggered AF (Figure 3A), and during ablation AF terminated to sinus rhythm (Figure 3B). In total, 197 s of ablation were performed in a cluster at this ET-GP. The ablated ET-GP was tested again with synchronized HFS, which did not trigger ectopy or AF (Figure 4). There was no further spontaneous AF (which had occurred frequently before ablation). Other GP were not ablated. All PVs at the end of the procedure remained electrically connected. There were no complications.

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

AVD-GP = atrioventricular dissociating ganglionated plexus

ET-GP = ectopy-triggering ganglionated plexus

GP = ganglionated plexus

HFS = high-frequency stimulation

LIPV = left inferior pulmonary vein

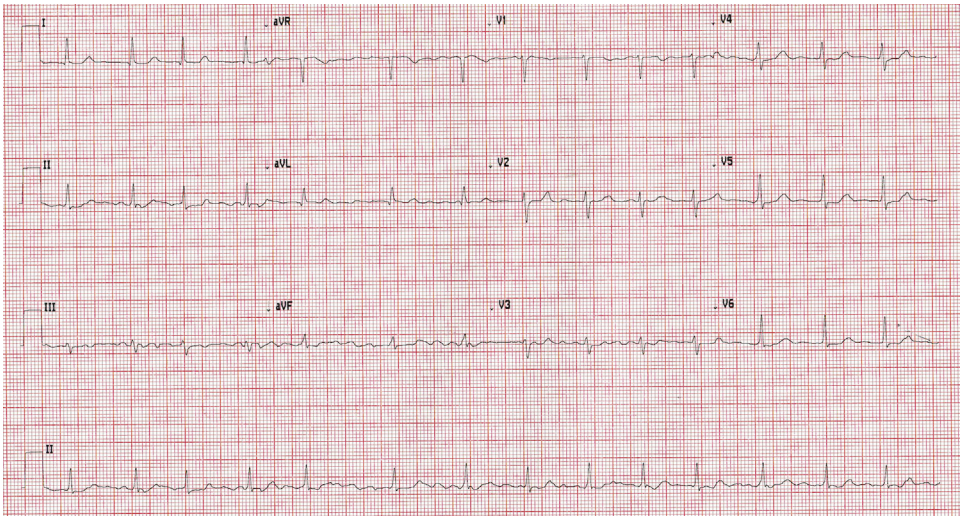
PV = pulmonary vein

PVI = pulmonary vein isolation

DISCUSSION

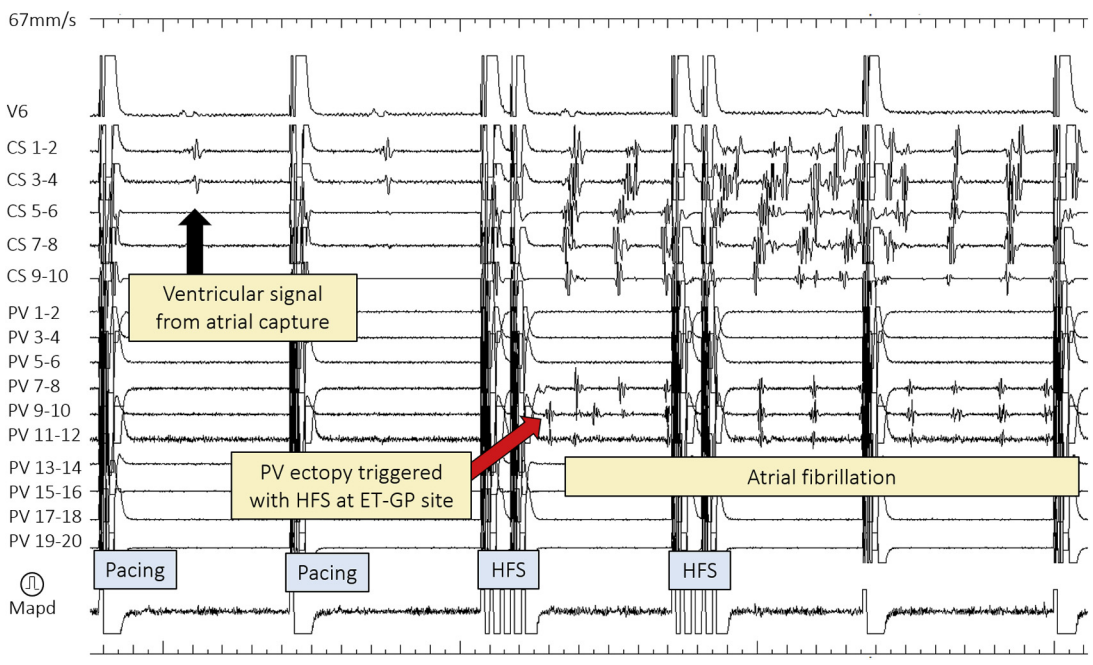
This is the first report of a single site of ablation outside the PV, without PV isolation (PVI), resulting in sustained freedom from AF. The landmark study by Haïssaguerre et al. (3) first described focal PV ectopy triggering AF. However, because of difficulties with mapping these PV foci and the unpredictable nature of AF initiation, PVI became established as the

FIGURE 1 12-Lead Electrocardiogram



A 12-lead electrocardiogram confirmed atrial fibrillation before the ablation procedure.

FIGURE 2 Initiation of PV Ectopy-Triggering Atrial Fibrillation From ET-GP Stimulation



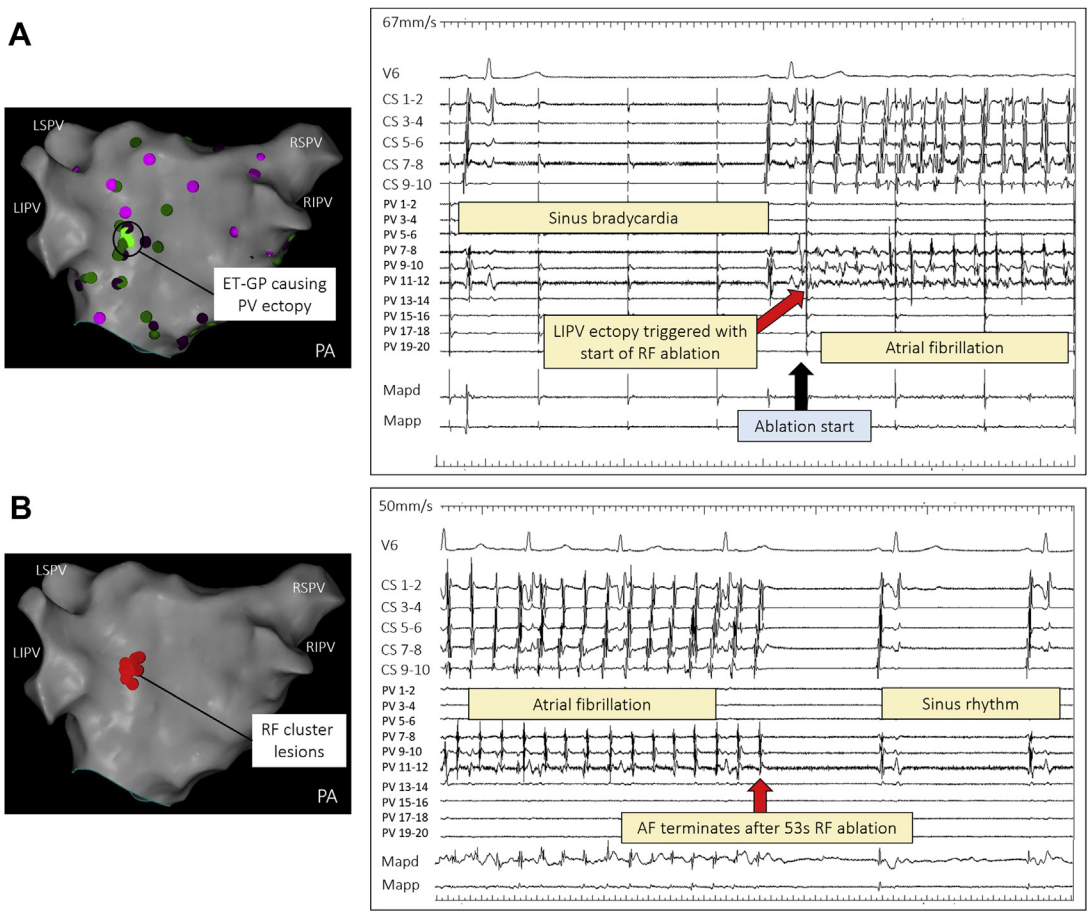
The ablation catheter (Mapd) was used to pace and deliver high-frequency stimulation (HFS). The pulmonary vein (PV) catheter was inserted into the left inferior PV. No recordings were obtained from the first 3 pulmonary vein channels because of poor tissue contact of PV poles 1 to 6 of the Lasso catheter. The first 2 artifacts are from pacing the left atrium at 10 V with atrial capture. The third and fourth artifacts are high-frequency stimulation (10-V, 35-Hz, 85-ms duration), delivered immediately after pacing from the ablation catheter (within the local atrial refractory period). After the first train of high-frequency stimulation, PV ectopy is triggered in the left inferior PV, with the earliest activation signals in PV 9 to 10 and PV 11 to 12. This led to atrial fibrillation, which terminated to sinus rhythm after 24 s. ET-GP = ectopy-triggering ganglionated plexus.

recommended empirical therapy for AF treatment (4). Despite improvements in catheter ablation techniques, the success rate of PVI is only modest, at 50% to 60% (5). Incomplete PVI has also been associated with freedom from AF (6). Therefore, other mechanisms and therapeutic approaches need consideration.

The autonomic nervous system plays an important role in both triggering and maintenance of AF. The importance of "vagally mediated" AF is well established historically (7). The human intrinsic cardiac autonomic nervous system contains a complex network of GP, located abundantly in the atrial epicardium. However, different GP mapping and ablation techniques have produced mixed results: HFS-mapped AVD-GP ablation prevented AF in 42.5% of patients (8), and anatomically identified left atrial GP ablation prevented AF in 48% of patients (9). Targeting the GP alone did not confer greater benefit over standard PVI. The previous GP ablation series indicated that GP ablation can prevent AF, but not as well as PVI. Our case report illustrates that GP ablation can be specific and limited to a single triggering site. Further studies are needed to determine whether this was an isolated phenomenon or whether it is possible in other patients with AF.

Another HFS technique synchronizes to the local atrial refractory period to identify ET-GP (2). It is not known what role ET-GP have in prevention of AF without PVI. The ET-GP identified in this report was a reproducible trigger for LIPV ectopy. After ablating this site, we were no longer able to trigger LIPV ectopy or AF. Subsequent 48-h Holter monitors did not show recurrence of atrial arrhythmia, and the patient remained symptom free after several years. This finding suggests that the upstream focal PV trigger responsible for the paroxysmal AF was exclusively from the ET-GP situated at the LIPV antrum. It

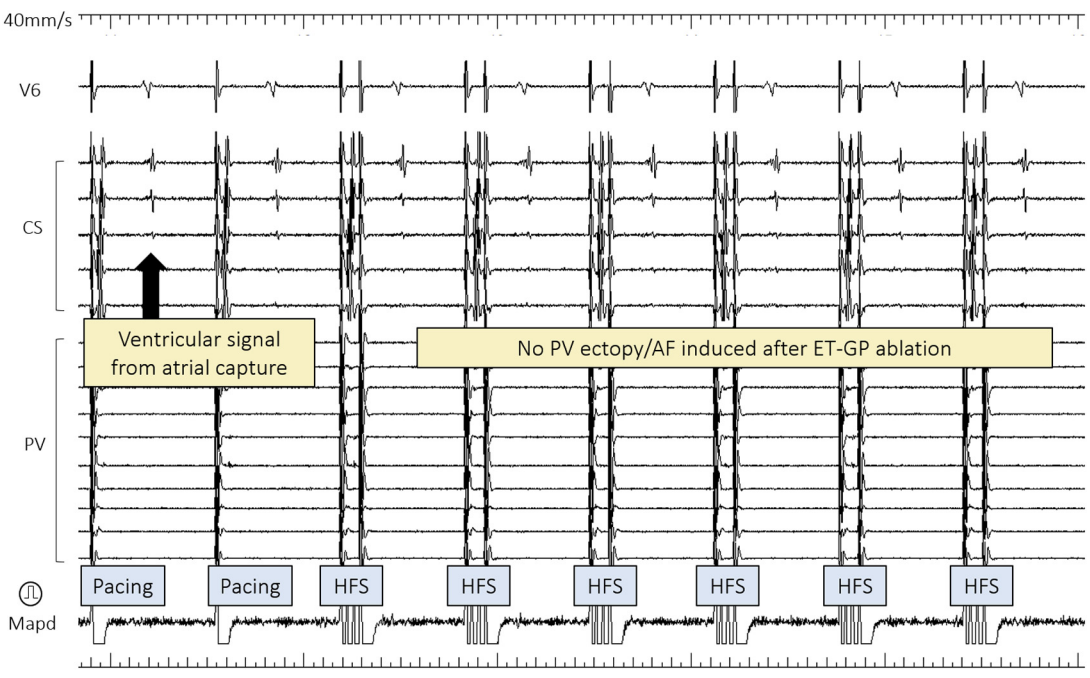
FIGURE 3 **Ablation of ET-GP Leading to Acute Termination of AF**



(A) Posteroanterior (PA) view of left atrium demonstrating locations of high-frequency stimulation (HFS) testing (**purple** represents a negative high-frequency stimulation response with synchronized high-frequency stimulation, **pink** is a negative high-frequency stimulation response with continuous high-frequency stimulation, **light green** is ectopy-triggering ganglionated plexus [ET-GP] with synchronized high-frequency stimulation, and **dark green** is atrioventricular dissociating ganglionated plexus with continuous high-frequency stimulation). The adjacent electrograms show that the patient was in sinus bradycardia before ablation. The pulmonary vein (PV) catheter (Lasso, Biosense Webster, Irvine, California) was situated in the left inferior pulmonary vein (LIPV). Low-output pacing artifact was inadvertent. Ablation started over the ectopy-triggering ganglionated plexus site as depicted. The onset of radiofrequency (RF) immediately triggered left inferior pulmonary vein ectopy and atrial fibrillation (AF). **(B)** Posteroanterior view of the left atrium demonstrating the location of cluster radiofrequency ablation performed over the ectopy-triggering ganglionated plexus from **(A).** The adjacent electrograms show that after radiofrequency ablation at the ectopy-triggering ganglionated plexus for 53 s, atrial fibrillation acutely terminated to sinus rhythm. LSPV = left superior pulmonary vein; Mapp = proximal mapping catheter; RIPV = right inferior pulmonary vein; RSPV = right superior pulmonary vein.

is possible that interrupting this specific site of neural connection also affected other PVs in the left atrium. This is the first report of a single site of ET-GP ablation without PVI in a patient who achieved long-term freedom from AF. In this case we stopped ablation after a single ET-GP because there were no further spontaneous AF episodes after ablating this GP site. This an important, but fortuitous, observation because it implies that the other GP sites that were identified were not part of the AF triggering mechanisms. We cannot compare this with previous GP studies because data on the exact ablation performed

FIGURE 4 Synchronized HFS at Ablated ET-GP Inducing No Further AF



After ablation of the ectopy-triggering ganglionated plexus (ET-GP) near left inferior pulmonary vein (LIPV), repeat synchronized high-frequency stimulation (HFS) was performed at the same ablated site. The pulmonary vein (PV) catheter remained in the left inferior pulmonary vein. The first 2 artifacts are from pacing the left atrium at high output, thus confirming atrial capture. Subsequently, synchronized high-frequency stimulation was performed; it did not trigger pulmonary vein ectopy or atrial fibrillation (AF) again. Abbreviations as in Figures 2 and 3.

in successful patients are limited. Current guidelines still mandate PVI, and a large case-series is needed before ET-GP mapping and ablation can be incorporated into routine clinical practice.

FOLLOW-UP

After the procedure, the patient had 3 separate 48-h Holter monitor sessions: after 74 days, 262 days, and 483 days. None revealed any atrial arrhythmia. The patient has been completely free of AF symptoms for more than 4 years. However, we cannot rule out asymptomatic AF without continuous monitoring.

CONCLUSIONS

A single ET-GP site was identified and ablated as the upstream trigger for this patient's PV-mediated AF. This acutely terminated sustained AF and led to long-term AF prevention without requiring an empirical PVI. Successful targeting of a specific ET-GP without PVI warrants further investigation to understand the role of ET-GP in AF. Mapping and ablating specific ET-GP in patients with AF may provide a more patient-centric approach to treatment and help improve our ablation strategy.

AUTHOR RELATIONSHIP WITH INDUSTRY

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KEY WORDS **atrial fibrillation, atrial fibrillation ablation, autonomic nervous system, ganglionated plexus, pulmonary vein ectopy**