Prolonged asystole after conversion to sinus rhythm during pulmonary vein isolation with pulsed field ablation: A case report

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Introduction

Pulsed electric field (PEF) ablation is a novel method for pulmonary vein isolation (PVI). It does not address the issue of heating and allows myocardium-specific ablation.[1] PEF ablation has been reported to avoid collateral damage to surrounding structures, including the esophagus, nerves, and vessels. The safety of the procedure has been reaffirmed in recently published multinational surveys.[2,3] However, already in 2018, Reddy and colleagues[1] described vagal responses in 33% (5/15) of patients undergoing PEF pulmonary vein ablation.[1] So far, the mechanisms of these severe vagal responses remain unclear.

We report a case of a total atrial asystole following PEF ablation in a patient with symptomatic paroxysmal atrial fibrillation. In this patient, persistent sinoatrial and atrioventricular conduction delay could be excluded before hospital discharge.

Case report

A 59-year-old male patient presented to our arrhythmia outpatient clinic with symptomatic paroxysmal atrial fibrillation. There was no evidence of structural heart disease; both atria were normal in size and function. He had a history of arterial hypertension but no further comorbidities and was already on oral anticoagulation (CHA_2DS_2-VASc 1; edoxaban). The body mass index was 25 kg/m^2. Antiarrhythmic drug therapy had to be discontinued owing to symptomatic sinus bradycardia, and catheter ablation was planned for rhythm control. As there was no documentation of atrial flutter, the patient was scheduled for PEF PVI. The preprocedural computed tomography scan was unremarkable, with only a right median pulmonary vein as standard anatomical variant.

KEYWORDS Atrial fibrillation; Atropine; Autonomic nervous system; Case report; Electroporation; Pulmonary vein isolation; Pulsed field ablation; Vagal response

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KEY TEACHING POINTS

- Atropine should be administered in each patient before pulsed electric field application to avoid severe vagal responses. Appropriate doses should be considered.
- Pulsed electric field does not seem to cause irreversible damage of the cardiac autonomic nervous system.
- As in this case, prolonged but eventually reversible atrial asystole can occur. Sustained sinoatrial and atrioventricular conduction delay should be ruled out before hospital discharge.

At the beginning of the procedure the patient presented in sinus rhythm with a heart rate of 62 beats per minute (bpm) (AA interval 975 ms) (Figure 1A). The procedure was performed under unconscious sedation with fentanyl and propofol. Anticoagulation was established with 70 IU/kg of unfractionated heparin. After groin puncture, 2 6F and 1 8F sheaths were inserted into the right common femoral vein and right ventricular (RV) and coronary sinus (CS) catheters were placed as usual. RV threshold was tested (1 V), where we also observed poor retrograde conduction properties (Figure 1B). The left atrium was accessed by transseptal puncture without complications. During transseptal puncture atrial fibrillation started with a cycle length of 200 ms (Figure 1C). The transseptal sheath (SL0) was exchanged for a larger steerable sheath (Faradrive®, Boston Scientific, Marlborough, MA). The ablation catheter (Farawave®, 31 mm, Boston Scientific, Marlborough, MA) was inserted into the left atrium after confirmation of an activated clotting time greater than 300 seconds.

PVI, starting with the left superior pulmonary vein (PV), was performed 1 minute after the administration of 1 mg of atropine. The current rhythm was atrial fibrillation (AF), when we administered atropine. The AF cycle length decreased from 200 ms to 144 ms, and the average ventricular rate increased from 110 to 124 bpm (Figure 1D).

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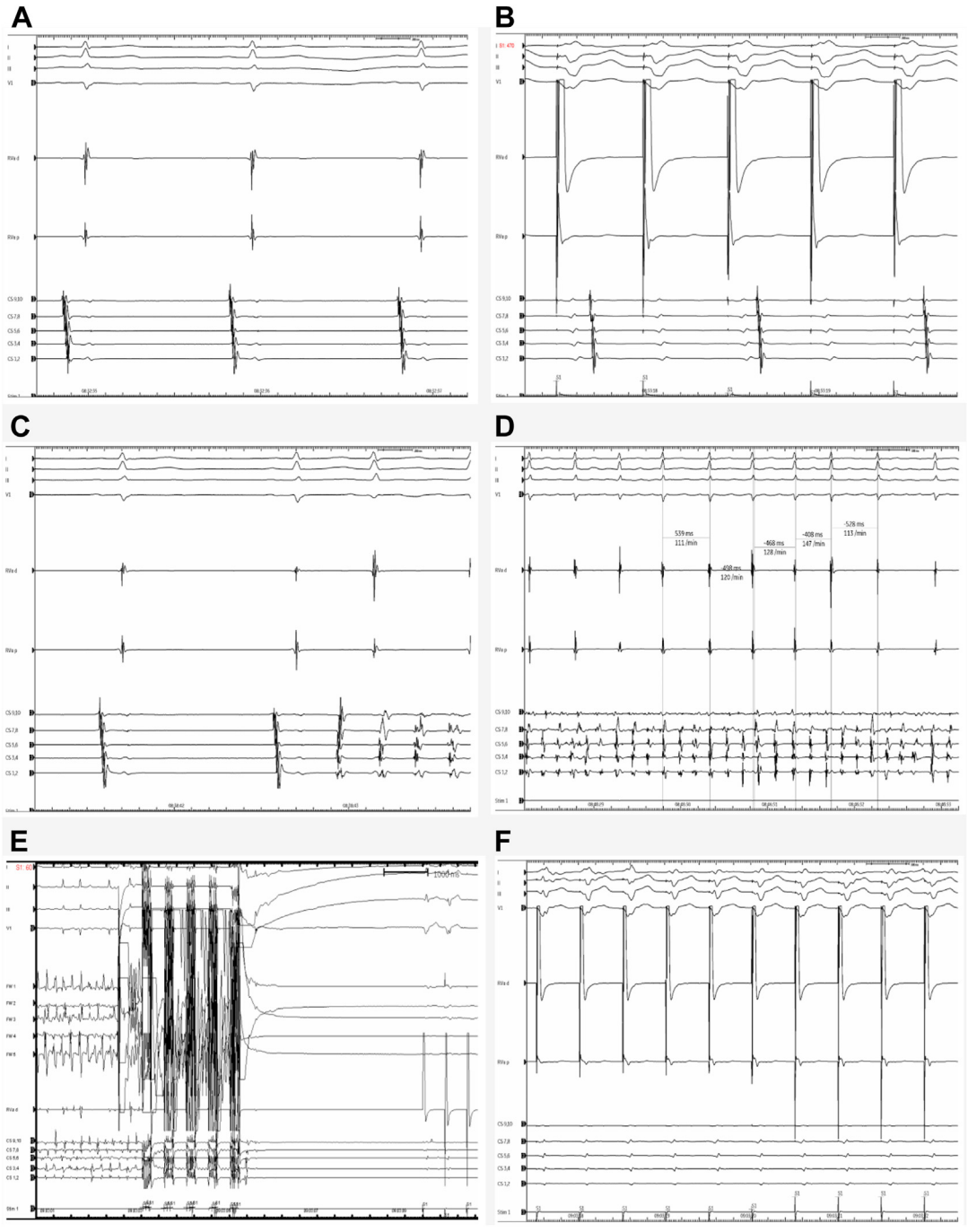

Figure 1 Tracings during pulsed electric field ablation. **A:** Basal heart rate at the beginning of the procedure (AA 975 ms). **B:** Incremental ventricular pacing shows bad retrograde conduction properties with 2:1 block already at S1 470 ms. **C:** Start of atrial fibrillation (AF) during transseptal puncture. **D:** Acceleration of AF after atropinization. V-V interval 124 beats/min on average. **E:** Asystole after first flower application at right superior pulmonary vein. **F:** No ventriculoatrial conduction (pacing cycle length 500 ms), no spontaneous atrial excitation. **G:** Sinus node restores only after >48 seconds. Sinus rate 60 beats/min. **H:** Antegrade conduction even during recurrent asystole, seen during coronary sinus pacing. **I:** Supraventricular extrasystole with normal atrioventricular conduction during ventricular pacing. **J:** Recurring spontaneous atrial asystole.

The left superior PV and the left inferior PV were treated with 8 applications (4 in basket, 4 in flower configuration) (Figure 2) per vein, followed by total extinction of the local PV signals. The right superior PV (RSPV) was then treated with 4 applications in basket configuration. The fifth application (first flower application for RSPV) terminated AF with consecutive asystole (Figure 1E and 1F) and a corresponding drop in systolic blood pressure (Δ20 mm Hg). RV pacing was started, causing the blood pressure to rise again. Atrial conduction recovered only very slowly—after >48 seconds, the sinus node recovered with a sinus rate of 60 bpm. We still paced the ventricle, but by this time a constant concentric CS signal appeared on the intracardiac electrocardiogram, CS 9/10 leading (Figure 1G). We suspect that there was

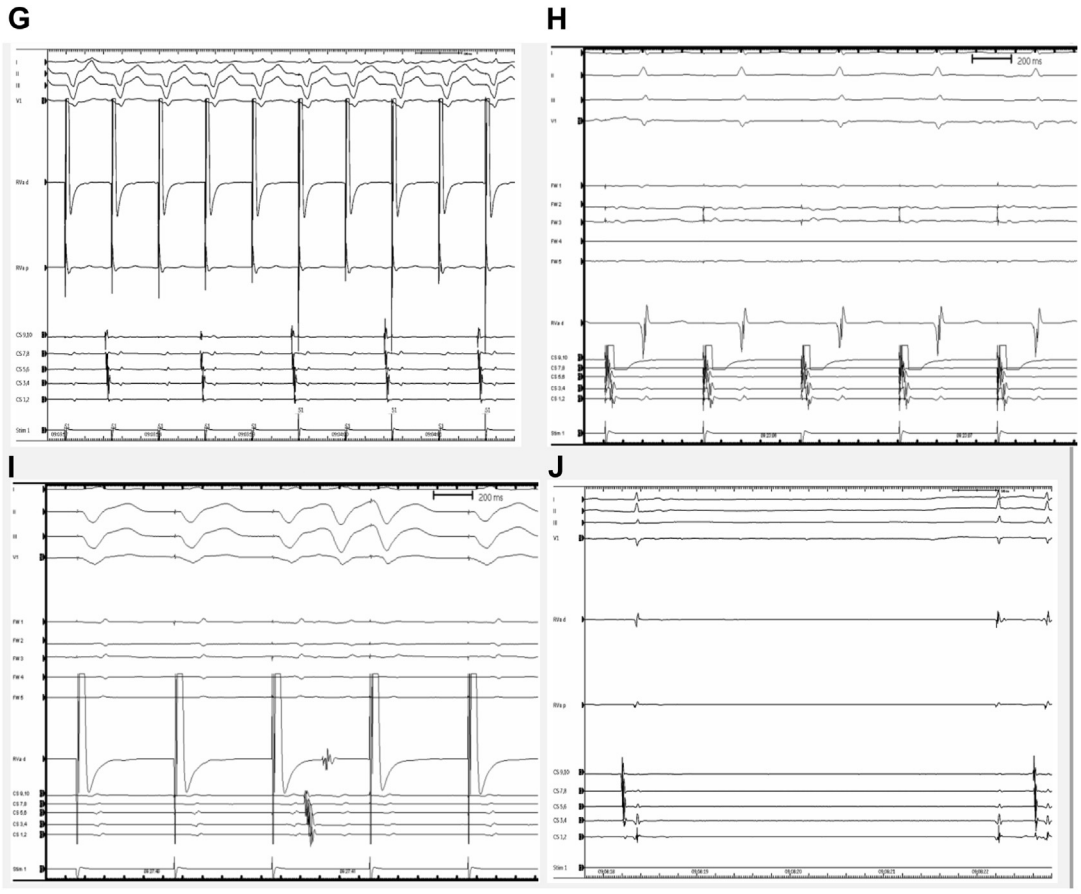

Figure 1 Continued

unimpaired antegrade AV conduction. This was observed when pacing from the proximal poles of the CS catheter (Figure 1H). Poor retrograde AV conduction properties could have been demonstrated already at the beginning of the procedure and we did not interpret this as a sign of vagal response in the AVN. As further evidence of normal AV conduction, we recognized some spontaneous supraventricular extrasystoles, which were normally conducted via the AV node during ventricular pacing without ventriculoatrial conduction (Figure 1I). During the following 10 minutes there were repeated atrial pauses of 3.5–4.5 seconds (Figure 1J). Therefore, we decided to treat the right inferior PV according to the protocol (2 × 2 basket, 2 × 2 flower) under continuous RV pacing, which could be done without any further complications. The RSPV was not treated with any additional applications beyond the 5 already submitted. All 4 veins were checked for entrance and exit block, which confirmed PVI.

After PVI the patient had stable sinus rhythm again. We tested sinus node recovery time (SNRT), which was significantly prolonged (22 seconds). However, asystole could not be reproduced, and after a few junctional beats, sinus rhythm was restored. For safety reasons a temporary pacemaker (VVI 40 bpm) was placed through 1 of the 3 femoral sheaths that we left in the femoral vein. All others were removed. The patient was monitored in the cardiac care unit, and we scheduled a diagnostic electrophysiological study (EPS) for the following day.

The patient did not require pacing with the temporary pacemaker at any time from the end of the index procedure until the following day. The patient was not sedated for the EPS. Intrinsic rhythm was sinus rhythm with an AA interval of 700 ms. The temporary pacemaker was removed, and a His catheter was placed through the remaining sheath at the His, RV, and high right atrium position to measure conduction intervals and SNRT, which showed normal characteristics (AH 80 ms, HV 46 ms, ERP AVN 380 ms; SNRT600: 1258 ms, SNRT500: 1100 ms) (Figure 3A and 3B). One milligram of atropine was then administered, followed by an adequate increase in heart rate from 67 to 100 bpm.

We concluded that the patient had a severe vagal response to PVI with PEF. There was no indication for permanent pacemaker implantation. At the 1-year follow-up, the 24-hour electrocardiogram showed no conduction abnormalities or AF recurrence.

Discussion

Persistent atrial asystole would potentially lead to serious hemodynamic consequences, which may result in heart failure, syncope, and sudden cardiac death.[4] To the best of our

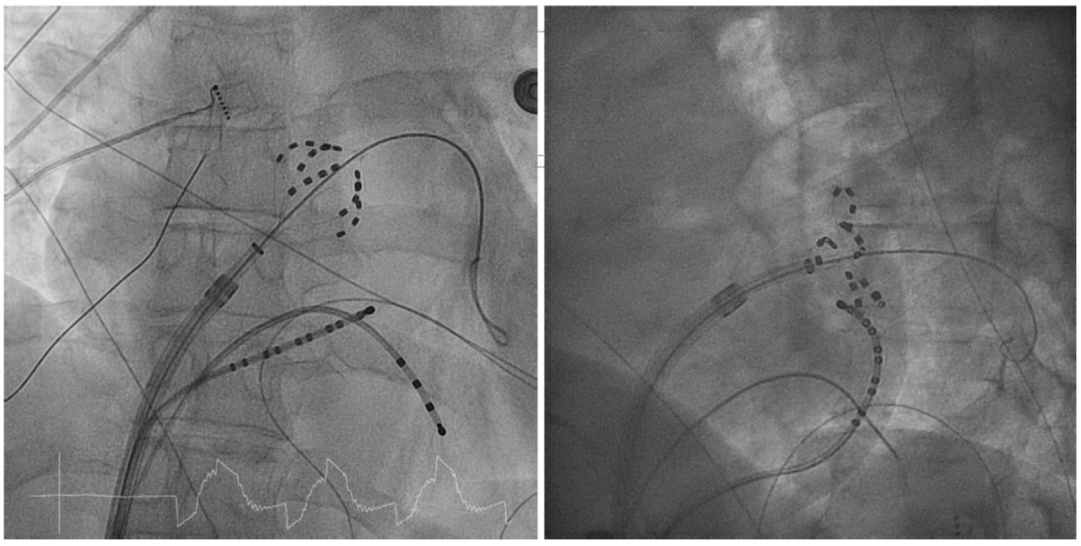

Figure 2 Basket and flower configuration of Farawave® ablation catheter (Boston Scientific, Marlborough, Massachusetts).

knowledge, there are no reports of atrial asystole of such a long duration (>48 seconds) or of EPS following a severe vagal response during PVI with PEF ablation.

When PEF is used for PVI, the myocardium is exposed to short pulses of a high-amplitude direct current electric field,[5–7] which may trigger severe vagal responses.[3,8] We and others believe that PEF-induced asystole and heart block can be preserved in most cases by administering 1 mg of atropine prior to ablation.[2,8] However, despite this procedural step, we observed a small number of severe vagal responses (3%, n = 5/230).

As the EPS showed normal conduction properties the next day, it can be assumed that the observed events were of a functional transient nature. Several possible reasons should be discussed: (1) Was vagal action due to intense stimulation of the vagus nerve during PEF ablation, causing sinus node arrest, owing to insufficient atropinization? (2) Was it caused by direct stunning of the sinoatrial node owing to the pulsed electric field? (3) Was it because of additional ablation of the cardiac autonomic nervous system (CANS), as known from thermal ablation modalities?

Vagus nerve stimulation because of insufficient atropinization

When we administered atropine, the patient was already in AF. The AF cycle length decreased from 204 ms to 144 ms and the ventricular rate increased from 110 to 124 bpm after atropinization, which should be questioned as an adequate response. Asystole occurred 15.3 minutes after atropine administration. The blood level of atropine falls rapidly and then slowly within 10 minutes. The half-life of atropine is 3 ± 0.9 hours in adults and is slightly shorter (about 20 minutes) in women than in men. It is mainly eliminated by the kidneys.[9] In our patient, renal function was normal (creatinine 1.07 mg/dL). The patient's body weight was 80 kg (body mass index 25). The recommended dose of atropine is 0.02–0.04 mg/kg, which in this case would have been 1.6–3.2 mg. Therefore, despite the initial response to atropine, we should consider inadequate atropinization as a possible reason for this severe vagal response. Intense stimulation of the vagus nerve during PEF ablation resulted in a release of acetylcholine, which, acting on the M2 muscarinic receptors, led to arrest of the sinus but—in this case—not the AV node. Given that we were

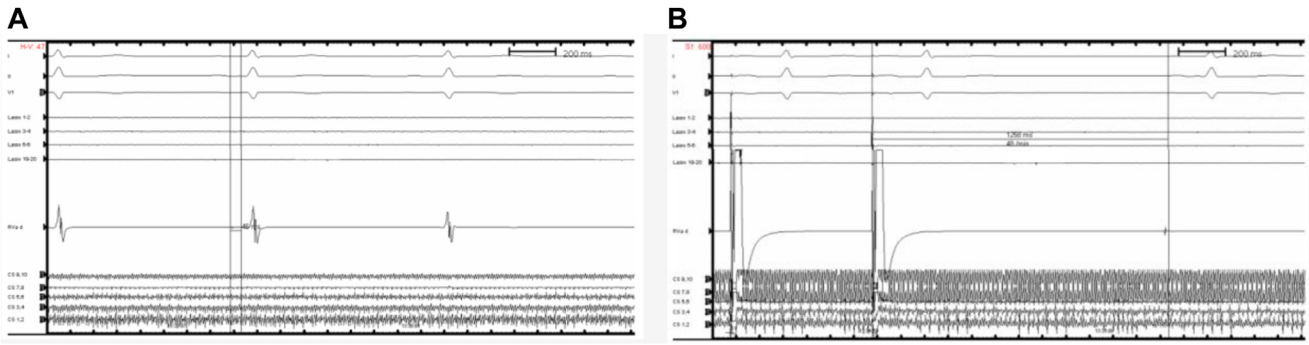

Figure 3 Tracings during electrophysiological study the following day. **A:** HV time 46 ms (normal, 35–55 ms). **B:** Sinus node recovery time 1258 ms.

ablating at the right inferior PV, which is very proximal to the right vagus nerve, this is even more likely.

Direct stunning of the sinus node

The RSPV is in close proximity to the sinus node. When ablating in the flower configuration, the catheter comes even closer to the sinus node, which could have led to direct stunning and subsequent atrial asystole. Another hypothesis is PEF causing transient sinus node ischemia owing to spasm of the sinus node artery. We suggest that this can be considered if the ramus nodi sinuatrialis originates from the circumflex artery, which occurs in approximately one-third of patients. As a coronary angiogram was never performed, we do not know the anatomy of the arteries in this case.

The impact of the CANS

Thermal energy sources affect the CANS.[10] In a recently published paper, Stojadinović and colleagues[11] demonstrated that the reduction in cardiac vagal response is considerably less in PEF compared to radiofrequency ablation; moreover, it appears to be preserved after PEF ablation. Guo and colleagues[12] could show that PEF does not affect levels of nerve injury biomarkers or the cardiac sympathetic or parasympathetic tone, as assessed by measuring heart rate variability before and 30 days after ablation. Despite the small sample size, these data could give another hint, that PEF PVI at least does not have a lasting effect on the CANS. Musikantow and colleagues[13] demonstrated only a minimal effect of PEF on the ganglionated plexi, although vagal response was not uncommon. There were no differences in vagal responses based on catheter configurations and PVs. However, among PVs that displayed a vagal effect after the initial PEF application, an 83% recurrence of vagal response was observed at additional applications.[13]

According to the current knowledge, vagal response is not caused by irreversible damage of the CANS. Evaluation of different effective ablation times on either the left or right pulmonary vein, as well as optimizing PEF energy, could potentially lead to decreased rates of vagal responsiveness.

Conclusion

Vagal response with prolonged asystole exceeding 3 seconds is a rare complication during PEF procedures. Nevertheless, in this case prolonged yet reversible total atrial asystole occurred despite the administration of atropine. The most probable cause could have been transient vagal stimulation, because of incomplete atropinization, during PEF ablation at the RSPV, which is situated in direct proximity to the right vagus nerve. Further investigation is required to evaluate the mechanisms, duration, and severity of potential PEF effects on the cardiac nerve ganglia, respective to the sinoatrial and AV node.

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