INNOVATIVE COLLECTIONS

COMPLEX CASE STUDY

Late Arrhythmic Risk with Biventricular Pacing

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ABSTRACT. Cardiac resynchronization therapy has been a tremendous advance in the management of systolic heart failure patients, with proven efficacy in the reduction of heart failure symptoms and mortality. However, there have been reports of biventricular pacing induced proarrhythmia resulting in episodes of ventricular tachycardia and fibrillation within the first 24–72 hours after initial implantation. We present a case of biventricular pacing-induced ventricular tachycardia storm 7 years after the patient was implanted with his biventricular device. Resolution of the arrhythmia only occurred after terminating left ventricular pacing. A review of the current literature on possible mechanisms for this phenomenon and potential therapeutic options are discussed.

KEYWORDS. biventricular pacing, cardiac resynchronization therapy, implantable cardioverter-defibrillator therapy, transmural dispersion of repolarization, ventricular tachycardia.

Introduction

Cardiac resynchronization therapy (CRT) has been a tremendous advance in the management of chronic congestive heart failure in patients with systolic dysfunction. This therapy has been proven to improve ventricular function, exercise tolerance, quality of life, and, most importantly, decrease mortality. However, there have been rare case reports of proarrhythmia that manifests soon after CRT implantation. These proarrhythmic events include polymorphic ventricular tachycardia, torsade de pointes (TdP), and monomorphic ventricular tachycardia (MMVT). Typically, the arrhythmia is evident within 24–72 hours after initial implantation. In this article, we report a case of MMVT storm perpetuated by biventricular pacing 7 years after implantation of the CRT device.

Case presentation

The patient is a 78-year-old man with longstanding history of ischemic heart disease, coronary artery bypass followed by subsequent angioplasty and stenting, and NYHA Class III symptoms at baseline on good medical therapy. His arrhythmic history includes permanent atrial fibrillation and symptomatic ventricular tachycardia, which reportedly was successfully ablated 3 years previously. A biventricular defibrillator had been implanted 7 years before. The patient presented on high-dose β-blocker therapy, mexiletine, aspirin, clopidogrel, atorvastatin, furosemide, and warfarin. Recent cardiac evaluation included an echocardiogram revealing a left ventricular (LV) ejection fraction of 25% with known extensive wall motion abnormalities and no significant valvular disease. A recent nuclear stress test performed several months earlier revealed no inducible ischemia, dilated left ventricle with an ejection fraction of 13%, and akinesis of the anterior, apical, lateral, and inferior walls.

The patient reported repetitive defibrillator discharges on the day of admission and one discharge 2 weeks previously that he had not sought care for. He also reported worsening heart failure symptoms despite compliance with his medications. Device interrogation revealed five episodes of sustained MMVT requiring defibrillator discharge; all therapies were successful. The patient was admitted for heart failure and arrhythmia management. While on the telemetry floor, he had recurrent MMVT resulting in multiple defibrillator discharges. The ventricular tachycardia storm resulted in hemodynamic deterioration necessitating intubation.
The patient was loaded with intravenous amiodarone and lidocaine, which resulted in slowing but not suppression of the ventricular tachycardia. Repeat interrogation of the device revealed a repetitive pattern of MMVT terminated by either antitachycardia pacing (ATP) or defibrillation followed by a biventricular paced impulse which triggered a premature ventricular contraction (PVC) resulting in reinitiation of ventricular tachycardia (Figures 1 and 2). Accordingly, biventricular pacing was discontinued, resulting in immediate cessation of ventricular tachycardia. Right ventricular pacing only did not reinitiate ventricular tachycardia, whereas LV pacing only did. Therefore, the patient was programmed with right ventricular pacing only. The patient’s heart failure was managed with adequate diuresis. There was no evidence of ongoing myocardial ischemia. He was maintained on intravenous amiodarone and lidocaine and eventually transitioned to oral amiodarone and mexiletine.

The patient had been a clinical responder to CRT, so we opted for a strategy that would allow reactivation of the LV lead in the future. Unfortunately, the LV lead could not be repositioned since there were no other adequate branches for lead placement. Also, we could not solely rely on antiarrhythmics for prevention of recurrent ventricular tachycardia upon reactivation of the LV lead. As a result, the patient was scheduled for ventricular tachycardia ablation. LV pacing in the electrophysiology (EP) laboratory no longer triggered a PVC so this could not be targeted. Scar mapping of the left ventricle revealed dense scar along the anterior, apical, posterior, and lateral walls. The patient was inducible for the clinical ventricular tachycardia which was successfully ablated in the basal to mid-anterolateral LV wall (Figure 3). He was also inducible for four additional ventricular tachycardias. All induced ventricular tachycardias were not addressed due to worsening heart failure during the case necessitating early termination.

The patient continued to remain ventricular tachycardia free with right ventricular pacing. He was discharged on amiodarone and mexiletine with LV pacing temporarily turned off. He was scheduled for outpatient reassessment of his clinical status after completing a full amiodarone load to determine whether LV pacing could be reinitiated. Antiarrhythmic therapy was continued post ablation to prevent any further ventricular tachycardia from presenting given the patient’s marginal ability to compensate during arrhythmic storm. During follow-up, the patient decided that he did not want to take the risk of recurrent arrhythmic storm and opted not to have LV pacing turned back on.

Discussion

The literature on CRT and arrhythmia predominantly supports the antiarrhythmic properties of CRT which is

**Figure 1:** Biventricular paced impulse (black arrow) triggers a premature ventricular contraction (red arrow) that initiates NSVT. A second biventricular paced impulse again triggers a PVC resulting in reinitiation of ventricular tachycardia.

**Figure 2:** Antitachycardia pacing successfully terminates ventricular tachycardia (VT). However, the following biventricular paced impulse (black arrow) triggers a premature ventricular contraction (red arrow) and reinitiates VT.
thought to be secondary to reverse LV remodeling.\textsuperscript{4–6} The literature on CRT-induced ventricular arrhythmia remains sparse. Case reports have described CRT-induced ventricular fibrillation, TdP, and ventricular tachycardia with these events typically occurring within 24–72 hours of device implantation.\textsuperscript{7–11} However, ventricular arrhythmic storms have been reported as far as 1 month after initial implantation.\textsuperscript{12} To our knowledge, this is the first reported case of CRT-induced ventricular tachycardia storm years after device implantation.

Several theories have been postulated to explain why CRT may be proarrhythmic. Most events occur in patients with ischemic cardiomyopathy. The initiation wavefront from epicardial LV pacing may approach the critical isthmus in LV scar allowing for unidirectional block and initiation of re-entrant MMVT. Transmural dispersion of repolarization (TDR) may provide the electrophysiologic basis for biventricular pacing-induced ventricular arrhythmia. The ventricular myocardium consists of at least three electrophysiologically distinct cells: the endocardial, M (middle), and epicardial cells. M cells are noted to have longer action potentials (APs) than endocardial and epicardial cells. TDR refers to the difference in timing of final repolarization between these electrophysiologically distinct myocardial layers.\textsuperscript{13} Normal ventricular activation spreads from endocardium to epicardium, which results in the epicardial layers depolarizing last but repolarizing first due to their shorter APs than M cells. This difference in timing of final repolarization creates voltage gradients within the myocardium that are responsible for the inscription of the T-wave on the surface electrocardiogram.\textsuperscript{14}

Under particular circumstances TDR may be augmented, which may lead to arrhythmogenesis.\textsuperscript{15,16} A prolonged TDR may facilitate transmural propagation of phase 2 early after depolarization (EAD). To review, EADs are oscillations of the transmembrane potential that usually occur in the M cells during phase 2 or 3 of the AP under circumstances that prolong the AP duration.\textsuperscript{17} If upon generation of the EAD the adjacent epicardial tissue is fully repolarized, which is often the case during TDR prolongation, then the generated ectopic beat is able to propagate resulting in a cascade of depolarization and potential ventricular arrhythmia. Moreover, the myocardial structure may allow for anisotropic re-entry in the setting of prolonged TDR, which can also serve as substrate for ventricular arrhythmia.\textsuperscript{18}

Prevailing theory for CRT-induced proarrhythmia surrounds work by Medina-Ravel et al.\textsuperscript{8} Biventricular pacing results in a reversal of normal LV depolarization initiating from the epicardium and spreading to the endocardium. The delayed activation of the M cells coupled with early activation and repolarization of the epicardial cells can lead to the augmentation of TDR and subsequent arrhythmogenesis. Medina-Ravell et al. demonstrated an accentuated TDR with LV epicardial pacing using a perfused rabbit-wedge tissue model. When tissue specimens were perfused with an APD-prolonging agent coupled with LV pacing, multiple R on T extrasystoles were noted as well as recurrent TdP. The authors concluded that in a subset of patients with augmented TDR, CRT can pose a potential risk for development of TdP. Fish et al.\textsuperscript{19} replicated similar findings using a canine LV wedge preparation. However, equivocal data exist on the extent epicardial pacing contributes to increasing TDR in the whole heart. Van Huysduynen et al.\textsuperscript{20} used a simulation whole heart model, and measured normal ventricular activation and variations in TDR during different pacing modes. They

\textbf{Figure 3:} Twelve-lead electrocardiogram of the clinical ventricular tachycardia.
reported no significant change in TDR during LV only and biventricular pacing versus right ventricular only pacing. They noted a modest increase in TDR between normal ventricular activation and different pacing modes mainly localized to increases in TDR anatomically under the LV and right ventricular pacing sites. However, the dispersion dissipated as the depolarization wavefront propagated longitudinally along the myocardial fibers. Furthermore, Santagelo et al.21 demonstrated a reduction in the TDR as measured by the T_peak – T_end interval on the electrocardiogram during biventricular pacing compared with native intrinsic conduction. Management of CRT-induced ventricular arrhythmia can be challenging. Acute management involves turning off LV pacing, which typically results in immediate cessation of the arrhythmia. Long-term management may include antiarrhythmic drug therapy, ablation of the ventricular tachycardia or ablation of the triggered PVC, repositioning of the LV lead or deactivation of the LV lead.7,9,12 Combes et al.10 reported echocardiogram-guided optimization of the atrioventricular delay which resulted in cessation of the ventricular tachycardia. The authors hypothesized that changing the atrioventricular delay resulted in variation in the degree of fusion between intrinsic and paced ventricular activation thereby altering the amount of ventricular dispersion. More recently, Itoh et al.11 managed CRT-induced ventricular arrhythmia by adding a second right ventricular lead to the high right ventricular outflow tract near the anterosepum. They theorize that the resulting alteration in ventricular activation fronts prevented the required ventricular dispersion needed to induce ventricular tachycardia. It remains unclear as to why our patient developed CRT-induced ventricular tachycardia so many years after being upgraded to a biventricular device. Possible explanations include alteration of ventricular dispersion in the setting of acute-on-chronic heart failure; progressive negative remodeling of the ventricular myocardium in a patient with chronic ischemic disease; or a possible prior subclinical ischemic event that altered the patient’s ventricular substrate. Whatever the cause, termination of the ventricular tachycardia storm was only achieved after cessation of LV pacing.

Conclusion

This case serves as a reminder that CRT remains a powerful tool in treating patients with congestive heart failure; however, practitioners must remain ever vigilant of the potential proarrhythmic effects of this therapy.

References

