Case Report

Effects of Cardiac Resynchronization Therapy on the Arrhythmic Substrate in a Patient with Long QT and Torsades de pointes

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We describe a patient with torsades de pointes (TdP) who was implanted with cardiac resynchronization therapy defibrillator (CRT-D). At the time of CRT-D implantation, left ventricular (LV) epicardial pacing exacerbated TdPs and developed into electrical storm, which was triggered even by biventricular pacing. We needed to inactivate the LV lead for 2 weeks. At the next device check testing of LV pacing still induced TdPs, whereas biventricular pacing did not. After starting the continuous biventricular pacing no ventricular arrhythmias happened, and furthermore the QT intervals prolonged by LV pacing were obviously shortened only after 2 weeks as ventricular systolic function recovered. Then even continuous LV alone pacing induced no TdP. These findings indicate novel electrical effects of cardiac resynchronization therapy.

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Key words: Cardiac resynchronization therapy, Torsade de pointes, Long QT, QT dispersion, Epicardial pacing

Introduction

Cardiac resynchronization therapy (CRT) is an established therapy in selected symptomatic patients with systolic heart failure, improving symptoms and reducing mortality.1,2) It is controversial at to whether CRT also reduces ventricular tachyarrhythmias.3–5) The antiarrhythmic effects of CRT are reported in several small studies6,7) and are logically attributed to reverse anatomical remodelling,8) with concomitant decrease in myocardial wall tension and neurohormonal activation.9) On the other hand, there have been a few reports of ventricular tachycardia storm following cardiac resynchronization therapy,5,10,11) raising the concern of pro-arrhythmia from this therapy.4,12) Theoretically, this could be due to increased dispersion of refractoriness with biventricular pacing or to initiation of arrhythmias with left ventricular (LV) pacing close to a region of slow conduction.13) The best type of management for this can be the acute cessation of LV epicardial pacing.12) Here, we present a patient who developed multiple torsades de pointes (TdP) which was initiated by LV epicardial pacing. However, after starting continuous
biventricular pacing TdP disappeared and QT intervals shortened.

An 81-year-old female was referred to our hospital with repeated syncope attacks. She was implanted with a pacemaker to treat a complete atrioventricular block 20 years previously. Also she had been treated with a diuretic for the past few weeks because of the symptoms characteristic of functional NYHA class III heart failure. On the admission the device was programmed in VDD mode (50–120 bpm) (Figure 1A). Intermittent atrial fibrillation events were detected by electrocardiography (ECG) upon admission. Some of them developed short-long-short sequences and TdP, with syncope. While confirming the capture threshold of the device, a prolonged QT interval and enhanced QT dispersion resulted in TdP (Figure 1B). The arrhythmic events disappeared after changing the device programming to right ventricular (RV) overdrive pacing in the rapid VVI mode. A few days later the device was reprogrammed to the VDD mode without the recurrence of ventricular arrhythmias. Blood analyses found no electrolyte abnormalities or other specific changes. Echocardiography showed non-hypertrophied left ventricular (LV) systolic dysfunction based on wall dysynchrony and coronary angiography did not reveal any obstructive lesions. She had no family history of heart disease and also there were no typical imaging or laboratory data suggesting secondary cardiomyopathy. We suspected an idiopathic cardiomyopathy and a cardiac resynchronization therapy defibrillator (CRT-D) was implanted to ameliorate cardiac function and prevent lethal arrhythmias. For the implantation, firstly the old VDD pacemaker was removed and new right atrial (RA) and defibrillator leads were introduced to the RA appendage and RV apex. Secondary the LV lead was smoothly placed to the posterolateral branch of the coronary sinus (CS). However, activation of the LV lead remarkably exacerbated the QT interval and dispersion, and several paced events resulted in incessant TdP (Figure 2). Notably, TdP occurred in response to either LV pacing alone or biventricular pacing, but not to isolated RV pacing from the defibrillator lead. Although we repeatedly changed the LV lead positions in all other CS branches, TdP was unavoidable. We thus placed the LV lead in the anatomically appropriate position in the CS branch and finally a CRT-D generator (Medtronic, Concerto) was implanted. After the procedure the device setting was programmed to maintain RV-only pacing using the new defibrillator lead for 2 weeks. At the next device check, LV and biventricular pacing still induced similar QT prolongation. LV pacing induced TdP, whereas biventricular pacing did not. We thus switched the setting to biventricular pacing (VVI mode, rate 70 bpm), which has allowed the patient to remain free of ventricular arrhythmias. Furthermore, the QT prolongation and dispersion that were previously exacerbated by LV pacing were obviously improved during 9 days of biventricular pacing (Figure 3) and pacing only the LV no longer induced TdP. Echocardiography revealed an obvious improvement of cardiac function (ejection fraction, from 48 to 66%; LVDd, from 52 to 49 mm) and NT-proBNP scores decreased from 419 to 214. Her symptom of heart failure was improved to NYHA class II on discharge. Ventricular arrhythmias has never developed and the improvements in QT abnormalities and LV function have persisted. At every follow-up device check even constant LV pacing or RR prolongation for the capture threshold test has not induced TdP.

Discussion

Some evidence indicates that ventricular function improved by cardiac resynchronization therapy (CRT) exerts an antiarrhythmic effect and reduces the incidence of malignant ventricular tachyarrhythmias or mortality.6–9,14) Also one meta-analysis showed no effect of CRT on appropriate shock rates.3) In contrast, some reports indicate that LV epicardial pacing has proarrhythmic potential5,10,11,13) and the best type of management for this can be the acute cessation of LV epicardial pacing.12) According to the guideline of The Japanese Circulation Society, CRT is indicated for the patient with an LV ejection fraction <35% and a QRS duration >130 ms, in NYHA class III or IV. Although CRT was off-label use in this case, we selected it because the symptom of heart failure strongly limited her activities of daily living and the many cardiac tests indicated the dyssynchrony of the LV wall motion significantly exacerbated LV systolic function.

Medina-Ravell et al. first described that reversing the normal sequence of activation from the epicardium prolongs the QT interval and significantly increases existing transmural dispersion of repolarization, creating a substrate for re-entrant arrhythmias as well as a trigger in the form of an early afterdepolarization-induced extra systole under long QT conditions.13) The proarrhythmic effect of epicardial pacing was obvious in our patient and TdP was unavoidable without temporal cessation of LV pacing. This patient showed a relatively long QT interval even during constant RV pacing (Figure 1A),
Figure 1 Twelve-lead ECG upon admission (A) and at the time of device check (B).
A. Underlying rhythm is sinus with AV block. Pacemaker is programmed in the VDD mode (50–120 bpm). All QRS complexes are preceded by pacing spikes. QRS and QT intervals are 160 and 460 ms, respectively.
B. Regular P waves and AV block are evident after first two RV paced beats during a test of ventricular lead capture threshold. A ventricular escape beat occurs, the QT interval is obviously prolonged and TdP follows. Max QT interval is 700 ms. Overdrive RV pacing completely suppressed these arrhythmic sequences.
and her TdP was easily induced by a slightly prolonged RR interval. Although we did not perform genetic testing or myocardial biopsy, some genetic or acquired abnormalities to produce long QT interval are highly suspected. Under such a condition of prolonged repolarization, abrupt change in the propagation of an excitation wave front induced critical QT prolongation and increased dispersion of repolarization to facilitate TdP.

After maintaining RV pacing for 2 weeks we were able to start CRT with no TdP events. It can be speculated that using the new defibrillator lead to pace the RV instead of the old RV pacing lead changed repolarization enough to make CRT safe.

Figure 2 Twelve-lead ECG during CRT-D implantation.
A. Underlying rhythm is sinus with AV block. RV and LV pacing differ. First two and last four pacing spikes are activation at RV apex lead, and middle four are at LV lead in coronary sinus (programmed with VVI 70 bpm). QT intervals are prolonged and dispersion is enhanced during LV pacing and T wave alteration is evident. B. Underlying rhythm is sinus with AV block. LV pacing results in short-coupled premature ventricular beat and TdP. Biventricular, but not RV pacing elicited same premature beat and TdP. *(L), pacing spikes from LV lead in CS and (R) from RV apex lead.
Actually T-wave morphologies were changed by switching the pacing site in 2 weeks. Of note, the prolonged QT intervals were significantly improved by only 2 weeks of CRT without a change in the QRS morphology. Shortening of QT was pronounced between peak and end of T wave. Medication was not changed. A’ and B’ are magnifications of A and B, respectively.

Figure 3 Changes in QT interval and dispersion before and after CRT. A. Twelve-lead ECG recorded 14 days after CRT-D implantation. Underlying rhythm is atrial tachycardia. LV pacing is programmed in VVI mode rate of 70 bpm. QT interval is prolonged (660 ms) and dispersion is enhanced (180 ms). B. Twelve-lead ECG recorded 28 days after CRT-D implantation. Underlying rhythm is sinus standstill. LV pacing is programmed in VVI mode rate of 70 bpm. Device setting was switched to biventricular pacing programmed with VVI mode rate of 70 bpm during the final 14 days after recording shown in A. QT interval significantly shortened (to 580 ms) and dispersion was reduced (to 80 ms) during that period. The QT shortening is pronounced between peak and end of T wave. Medication was not changed. A’ and B’ are magnifications of A and B, respectively.

Aiba et al. described the molecular and cellular basis of electrical remodelling in heart failure with dyssynchronous LV contraction and its restoration by CRT in a canine model of heart failure with tachypacing. They found that CRT partially restores ion channel remodelling and abnormal Ca²⁺ homeostasis, and attenuates the physiological consequence. Aiba et al. described the molecular and cellular basis of electrical remodelling in heart failure with dyssynchronous LV contraction and its restoration by CRT in a canine model of heart failure with tachypacing. They found that CRT partially restores ion channel remodelling and abnormal Ca²⁺ homeostasis, and attenuates the...
regional heterogeneity of action potential duration.\textsuperscript{15} Some reports have also indicated relationships between the anti-arrhythmic CRT effect and LV structural improvement or favorable neurohumoral changes.\textsuperscript{8,9} In fact, the echocardiographic findings and NT-proBNP score were improved in our patient.

Epicardial LV pacing exacerbates the transmural dispersion of repolarization and may precipitate TdP.\textsuperscript{13} The cessation of LV pacing is initially required under these conditions\textsuperscript{12} and defibrillator backup is essential due to this potential proarrhythmic effect.\textsuperscript{4} In this case, time-related benefits of CRT on LV function were associated with reduced dispersion of refactoriness and proarrhythmia. This may be an electrical reverse remodeling effect of CRT.

References