Case Report

Short-Coupled Variant of *Torsade de Pointes* as a Cause of Electrical Storm and Aborted Sudden Cardiac Death: Insights into Mechanism and Treatment

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This case report describes a 50-year-old woman with normal repolarization duration who survived multiple electrical storms and cardiac arrest related to recurrent short-coupled *torsade de pointes* (TdP). Overdrive ventricular pacing could not prevent malignant TdP, but exposed a pause-related TdP initiation pattern. Isoproterenol and atrial pacing completely suppressed TdP, suggesting that ventricular pacing may entail vulnerability to this condition.

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Torsade de pointes (TdP) meaning "twisting of the points", is a potentially life-threatening form of polymorphic ventricular tachycardia which displays on the electrocardiogram (ECG) as a characteristic feature of beat-to-beat varying QRS morphology prone to revert spontaneously.[1,2] Prolongation of the QT interval as a consequence of congenital or acquired pathophysiological states is the common determinant for the development of TdP. On the ECG, a "short-long-short" sequence pattern is the typical initiating mode of TdP.[2,3] Occasionally, the clinical presentation of TdP is electrical storm, i.e. a cluster of arrhythmia episodes that sometimes degenerate into ventricular fibrillation.

The uncommon short-coupled variant of TdP is characterized by a short initiation sequence of the first coupling interval, mimicking the R-on-T phenomenon.[4,5] We report a patient without structural heart disease and with a normal QT interval who survived a short-coupled TdP storm and was successfully treated with isoproterenol infusion and continuous atrial pacing.

Case presentation

A 50-year-old female presented to the community hospital after several episodes of loss of consciousness which were treated by her husband with resuscitative efforts and chest compressions. The initial 12-lead ECG was reported to show sinus rhythm with normal QRS and QT intervals in the absence of abnormal TU waves or conduction abnormalities. Upon admission to the emergency room, continuous ECG monitoring had showed recurrent episodes of TdP with a uniform twisting pattern, which were not sustained in most cases, but some of them degenerated to ventricular fibrillation requiring repeated direct current shocks for termination. The continuous infusion of lidocaine and amiodarone did not prevent arrhythmia recurrences. Owing to the patient's persistent critical clinical condition, she was referred to our hospital, where she was admitted 10 hours later.

The patient had no history of chest pain, or alcohol or drug abuse. She did not smoke, was not taking any medications, and

did not report any family history of syncope, or premature or sudden death. The patient had experienced her first syncopal episode one month prior to hospital admission, but outpatient investigation, including echocardiography and Holter examination, was considered normal. Overall, recurrent syncope presented in our patient late in life, while she was awake, and was unrelated to obvious emotional or physical stress or to any other stimuli.

On her arrival at our hospital, the patient's 12-lead ECG showed sinus rhythm with a normal PR interval of 160 ms, QRS duration of 84 ms and QT interval of 440 ms (Figure 1). Using Bazett's formula the corrected QTc interval was calculated to be 416 ms (heart rate 54 beats/min). In the telemetry unit the ECG showed repeated short-coupled ventricular premature beats and TdP episodes. The initiating mode of TdP was initially uniform. The arrhythmia occurred during sinus rhythm and was introduced by a premature ventricular beat falling early (<300 ms) on the T wave peak of the last sinus beat (Figure 2). The TdP episodes were not precipitated by significant sinus bradycardia, pauses or an increased sinus rate. Numerous TdP episodes deteriorated into ventricular fibrillation requiring defibrillation to restore sinus rhythm (Figure 3A).

Physical and laboratory examinations, including thyroid function and serological tests, were normal. In particular, there were no cardiac enzyme elevations, with magnesium at 2.0 mg/mL, calcium at 9.1 mg/dL, and potassium at 4.4 mmol/L. Transthoracic echocardiography revealed normal left and right ventricular dimensions and function. Despite prompt discontinuation of both lidocaine and amiodarone, further attempts to terminate the ventricular arrhythmias by cardioversion and magnesium sulfate given intravenously as bolus as well as continuous infusion failed again, with the patient having spontaneous TdP relapses. Other drugs were not used.

A temporary transvenous pacemaker was then inserted with the electrode placed in the right ventricle. However, continuous ventricular pacing at 90 beats/min not only did not suppress, but even exacerbated the malignant arrhythmia. Short-coupled TdP repeatedly recurred even when the heart rate was increased with regular ventricular pacing. Although arrhythmia episodes exhibited the same twisting morphology, their initiation pattern was not more consistent. Short-coupled TdP episodes began during regular ventricular paced rhythm without preceding pause (Figure 3B), but also followed "short-long-short" cardiac cycles induced by premature atrial beats (Figure 3C). Once it was recognized that pacing exaggerated TdP, ventricular pacing was stopped and isoproterenol infusion was started. The acceleration of the heart rate to approximately 100 beats/min by isoproterenol (2 μg/min) completely and immediately suppressed ventricular ar-

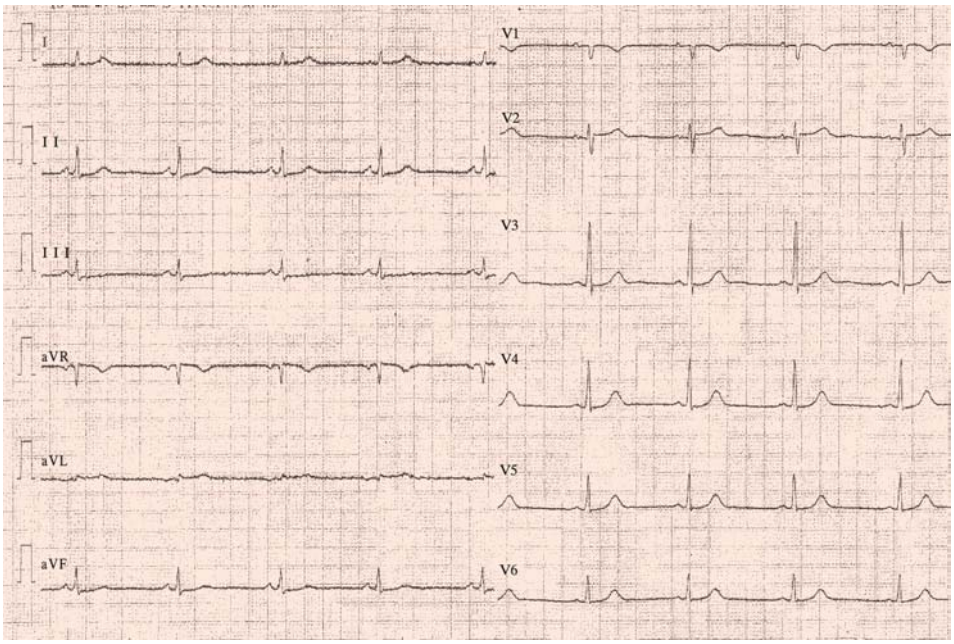

Figure 1. Twelve-lead ECG during sinus rhythm. Note the normal durations of QT interval (440 ms) and QTc interval (416 ms) interval at a mean heart rate of 54 beats/min. Paper speed 25 mm/s.

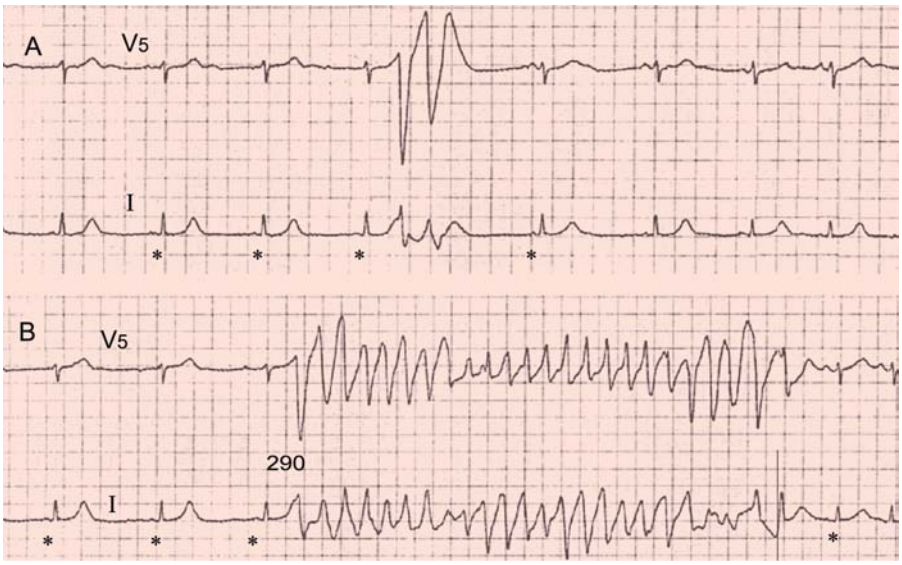

Figure 2. Simultaneous electrocardiographic recordings showing a short-coupled premature ventricular beat (A) and self-terminating short-coupled torsade de pointes (TdP) (B), without significant preceding bradycardia or pauses. Short-coupled ventricular extrasystoles do not correspond to the timing of U waves on the surface ECG. The two ECG channels are recorded simultaneously and continuously in both A and B, and represent leads V5 and I. Because p waves are not well visualized in lead V5 it could be argued that there is atrioventricular conduction disturbance. This speculation is not supported, however, by the recording of lead I, which shows sinus rhythm with always 1:1 conduction (*) and a normal PR interval before arrhythmia. The QT interval preceding arrhythmia is normal. The coupling interval of the ventricular beat initiating TdP is always short (<300 ms).

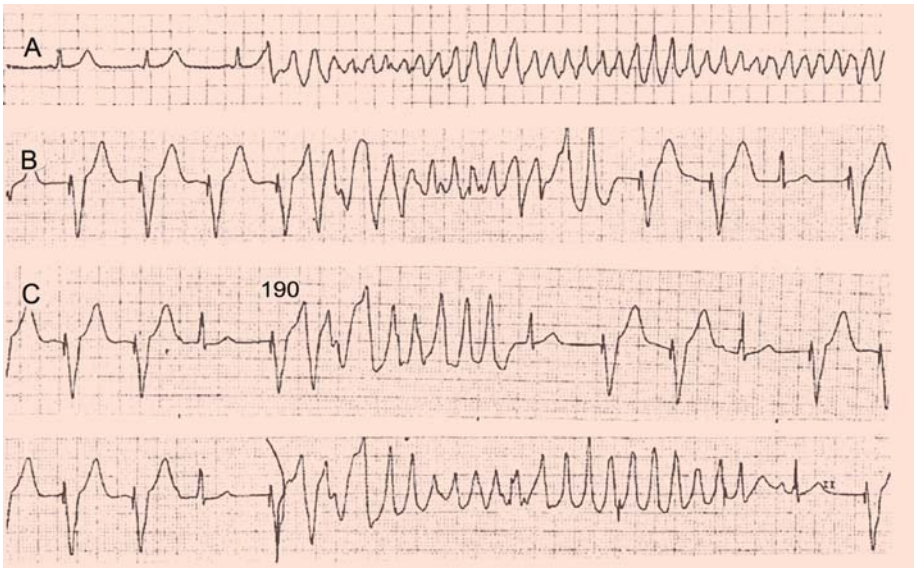

Figure 3. Short-coupled torsade de pointes (TdP) (A) degenerating into ventricular fibrillation during sinus rhythm and (B and C) during regular ventricular pacing at 90 beats/min. Short-coupled TdP with a coupling interval of 190 ms of the first ventricular beat initiating TdP in association with a preceding atrial post-extrasystolic pause (B and C). Note that ventricular pacing yields a QT interval of 470 ms, whereas the QT interval of the atrial beat is 400 ms.

rhythmia. A second temporary electrode was then inserted and placed in the right atrium. With continuous atrial pacing at 85 beats/min, and despite isoproterenol discontinuation, ventricular arrhythmia did not recur in the following days. Coronary angiography revealed normal coronary arteries. One week later a dual-cham-

ber cardioverter defibrillator was implanted. Follow-up 12-lead ECGs disclosed normal sinus rhythm without ventricular repolarization or conduction abnormalities. With continuous atrial pacing at 85 beats/min, the patient is free of symptoms and has no evidence of arrhythmia recurrences during a 3-month follow up.

Discussion

Torsade de pointes, aside from congenital long-QT syndromes, usually occurs in the setting of identifiable pathological conditions such as structural heart disease or ischemia, or other precipitating iatrogenic and metabolic risk factors, and particularly drug therapy.[1,2,6,7] Despite the varying clinical presentations, there is a major criterion which defines typical TdP, namely the long coupling interval of the initial beat of the arrhythmia (>600 ms). Both congenital and acquired TdP share several other key electrocardiographic features, such as exaggerated TU wave changes and characteristic arrhythmia-initiating patterns, which manifest as pauses, or deceleration, or acceleration in the ventricular rhythm.[3] Notable differences exist in the methods that are effective in controlling the arrhythmia.[1] Eliminating pauses in the pause-dependent acquired form by increasing the heart rate, such as with isoproterenol or pacing, eliminates recurrences of the arrhythmia. In contrast, the increase in heart rate in the adrenergic-dependent idiopathic form can provoke TdP. There is also an intermediate group of patients with TdP who may exhibit features of both forms, or even atypical TdP unrelated to repolarization abnormalities, reflecting the challenging complexity surrounding this phenomenon.

Our patient presented with new onset syncopal episodes unrelated to exertion or excitement in the absence of any currently appreciated inciting factors. Recurrent TdP episodes were not associated with obvious QT interval prolongation or specific initiation patterns. This constellation of clinical and electrocardiographic findings does not fit into the common forms of the long QT syndromes, whether congenital or acquired, or even atypical. The finding of increased heart rate variability, which was documented before TdP onset, suggesting autonomic instability, has been acknowledged as common in the described short-coupled variant entity of TdP.[4]

As early as 1994, Leenhardt et al[4] introduced the short-coupled variant of TdP, which occurs with an extremely short first coupling interval (<300 ms) of the initial beat of *torsade*, in a series of 14 healthy adults with normal QT interval. One third of these patients had a familial history of sudden death, and a significant number of them (approximately 70%) manifested malignant TdP prone to deteriorate into ventricular fibrillation. In that report, the lack of increased arrhythmia inducibility with programmed stimulation, as well as the short refractory periods, were viewed as evidence against the existence of an electrophysiological substrate favoring re-entry. Conversely, Shiga et al[5] did propose facilitated re-entrant excitation in light of observations that Nifekalant, a pure potassium channel blocker that potentially inhibits the rapid I_{kr} channel, significantly prolonged the ventricular effective refractory period and inhibited TdP, without, however, affecting the frequency of ventricular premature complexes. Those potential inciting short-coupled ventricular extrasystoles, i.e. the first ectopic beats to instigate the progress of arrhythmia, could be only abolished by the intravenous infusion of verapamil. In light of these data, the authors recognized the cellular arrhythmogenic role of early afterdepolarizations in the genesis of short-coupled TdP, since these features, which account for the onset of arrhythmia if the slow inward current is abnormally responsive, may be suppressed by verapamil.[8]

Of course, the entity of short-coupled variant of TdP does not exclude interrelations with silent ion channel mutations responsible for unusual or transient repolarization behavior.[9] This must be considered in the differential diagnosis, including a possible association with rarely reported cardiomyopathy-related TdP,[10] but in our patient all such conditions were ruled out by the clinical presentation and the laboratory tests. In this regard, a possible explanation for the origin of the U waves observed in our patient in Figure 2A may be attributed to the amiodarone treatment[11] in the community hospital, since no QT-U abnormalities were visible before referral. Moreover, those U waves appeared not to be directly related to the arrhythmia, given the fact that the ventricular extrasystoles initiating TdP emerged before the apex of the T wave, appearing much earlier than the timing of the U waves.

In the present case, following unsuccessful drug therapy, and since there was no underlying bradycardia, our next therapeutic measure was to accelerate the basic heart rate by temporary ventricular pacing. Increasing the heart rate by continuous ventricular pacing not only did not prevent arrhythmia recurrences, but exposed a second TdP initiation pattern. Short-coupling *torsade* recurred as long as the ventricu-

lar rhythm was regular (Figure 3B), but also following perturbation in the ventricular cycle length by occasional premature atrial complexes that produced long pauses (Figure 3C). This initiating mode of short-coupled TdP may be considered analogous to the pause-dependent TdP pattern, where the arrhythmia is accentuated by pauses or slower pre-pause rates. Several other observations in this case deserve attention, since they provide added insight into the mechanisms of short-coupled TdP. First, the QT interval during pacing was longer (470 ms) than that of the premature atrial beat (400 ms). It could be argued that increased dispersion in ventricular activation times, caused by right ventricular stimulation itself,[12] may increase the heterogeneity of repolarization, which has been shown to be critical in facilitating a re-entrant mechanism. In addition, one could speculate that the altering repolarization sequence—i.e. subsequent paced and atrial beats producing short-long cycles—might even serve to amplify transmural repolarization dispersion. Enhanced transmural dispersion in repolarization has been shown to facilitate afterdepolarization propagation, leading to R-on-T ventricular extrasystoles capable of initiating *torsade*.[13] The afterpotential hypothesis could be considered in our patient with normal repolarization, since it could be argued that focal activity might not be sufficient to generate visible surface wave abnormalities, but could result in the triggering of malignant arrhythmia. It is therefore likely that post-pause ventricular pacing promotes and accentuates early afterdepolarization-induced triggered activity under conditions of increased dispersion of refractoriness. The complete suppression of TdP by the heart rhythm increase in response to isoproterenol and overdrive atrial pacing supports our view that the pauses were critical for the initiation of TdP, and on the other hand argue against an adrenergic-dependent form. Moreover, as demonstrated here, it could be argued that, compared to ventricular pacing, atrial activity provides a substantial degree of protection against short-coupled TdP by limiting both dispersion of repolarization and the formation of early afterdepolarization. However, since permanent pacemakers and verapamil treatment have not been proven effective in preventing sudden death, only implantable defibrillators should be considered for the long-term management of these high-risk patients with the short-coupled variant of TdP.[4]

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