# Torsade de pointes in a patient with VVI pacemaker dysfunction

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ABSTRACT

*Torsade de pointes* is a clinically important ventricular tachyarrhythmia that typically appears in the presence of a long QT interval and which, without prompt identification and treatment, can lead to sudden cardiac death. The prolongation of QT and corrected QT intervals significantly increases the chance of this arrhythmia to appear in congenital or acquired long QT syndromes. In almost all patients, these intervals are markedly long in the period prior to the arrhythmic event. We describe a case of a female patient with a pacemaker who presented this arrhythmia and suffered several syncopal events.
*Keywords:* Torsades de pointes, Long QT syndrome, Sudden cardiac death

### Torsade de pointes en una paciente con disfunción de marcapasos VVI

RESUMEN

*La torsade de pointes es una taquiarritmia ventricular de gran importancia clínica que aparece típicamente en presencia de un intervalo QT prolongado y que, sin identificación y tratamiento puntual, puede conducir a la muerte súbita cardíaca. La prolongación de los intervalos QT y QT corregido aumenta significativamente la posibilidad de que aparezca esta arritmia en los síndromes de QT largo congénitos o adquiridos. En casi todos los pacientes, dichos intervalos se encuentran marcadamente prolongados en el período previo al evento arrítmico. Se describe un caso de una paciente con marcapasos que presentó esta arritmia y sufrió varios episodios sincopales.*
*Palabras clave:* Torsades de pointes, Síndrome de QT largo, Muerte súbita cardíaca

## INTRODUCTION

Cardiac arrhythmias represent a wide and heterogeneous group of electrical anomalies of the heart, with or without underlying structural heart disease. They can be innocuous, influence the development of potentially deadly strokes or embolism, or represent a life-threatening emergency that

can lead to sudden cardiac death (SCD), one of the common causes of death in developed countries[1-3].

Most of the SCD in young people or adults are attributable to cardiovascular structural anomalies, which are identified during the autopsy[1-2], although in a 30-50% of these people, the sudden death remains unexplained, even after a full autopsy and the corresponding forensic investigation[1].

The QT interval is the electrical representation of the ventricular systole, both of the depolarization and repolarization period; it goes from the beginning of the QRS complex to the end of the T wave. The leads with the highest positive predictive value to measure the QT are: $V_5$, $V_6$ and $D_{II}$. In order to accurately determine the QT interval, it is calculated as it is evidenced in the electrocardiogram, and it is corrected according to the heart rate (corrected QT [cQT])[3-5]. Women present a QT interval longer than men, and also a greater susceptibility to its prolongation facing the same factors that determine its prolongation in an acquired manner[6].

This QT prolongation, induced by drugs and other factors, as well as the *torsade de pointes* (TdP), provoked by this causes, are a constant concern for the doctors that prescribe medications which carry the risk of generating these unwanted and potentially deadly side effects. The estimated impact of this type of (drug-induced) TdP oscillates between 1 and 8%, depending on the drug and the dose[7]. Although the occurrence of the SCD due to this cause is uncommon, there is a long list of "torsadogenic" or with "QT sensitivity" drugs that, not only includes antiarrhythmic drugs like quinidine, sotalol and dofetilide, but also others, like antipsychotics, methadone, antihistaminics and cisapride, among others; as well as electrolytic disorders, hypokalaemia, hypomagnesemia and hypocalcaemia[8]. More than 100 drugs with the potential of prolonging the QT and generating this type of arrhythmias have been generally described, as well as central nervous system affections and important bradyarrhythmic events. When this arrhythmia appears in patients with bradycardia, it can be a result of the inverse heart rate dependency phenomenon, with which there is a decrease on the local extracellular potassium and block of the $I_{Kr}$ channels, with the subsequent QT prolongation[9].

The term TdP was introduced in 1966 by Dessertenne *et al*[10,11], in order to describe the particular characteristic of the QRS complexes (pointes) that seem to spin around the isoelectric line. In its original description[11], the heart rate ranged from 160 to 280 beats per minute (average of 220). Generally, the *torsades de pointes* end spontaneously; however, eventually, they can degenerate in ventricular fibrillation. Its electrophysiological mechanisms are not very well known, but almost all data point out that the early postdepolarizations give account of the long QT syndrome and the TdP or, at least, of its beginning. Its perpetuation can be a result of the induced activity, the re-entry by dispersion of the repolarization caused by the early postdepolarizations, or an anomalous automatism. Nevertheless, most of the current data point out the transmural re-entry like the most plausible mechanism of the perpetuation[12].

The secondary TdP to acquired long QT syndrome presents a typical morphology and way of starting. In 1983, Kay *et al*[13] described a characteristic way of starting named "short-long-short" ventricular cycle sequence. In this case, the first ventricular complex is a premature beat or the last of a run of premature ventricular contractions, that is followed by a pause and a subsequent supraventricular contraction; later, another premature ventricular contraction takes place at a relatively short cycle's length and it provokes a TdP event.

## CASE REPORT

A 76-year-old patient, with a history of high blood pressure and type 2 diabetes mellitus, being on a treatment with amlodipine 10 mg/day, hydrochlorothiazide 25 mg/day and glibenclamide 30 mg/day, who also has a monocameral pacemaker (VVI, Medtronic, USA), implanted five years earlier due to a third-degree atrioventricular block (complete AVB), and who presented two events of loss of consciousness lasting a few minutes each, accompanied of paleness, coldness and prominent sweating, without remembering what had happened when she recovered the consciousness after these events. For these reasons, she was referred to our Department, where, once her admission was decided, she presented another event with similar clinical manifestations.

At physical examination, during the third syncopal event, the patient presented −besides the symptoms described before− light tachypnea, low blood pressure 70/50 mmHg, irregular and filiform peripheral pulse and 28 breaths per minute.

An electrocardiogram was performed, where the following data was found: pattern of stimulation, detection and capture by monopolar VVI pacemaker,
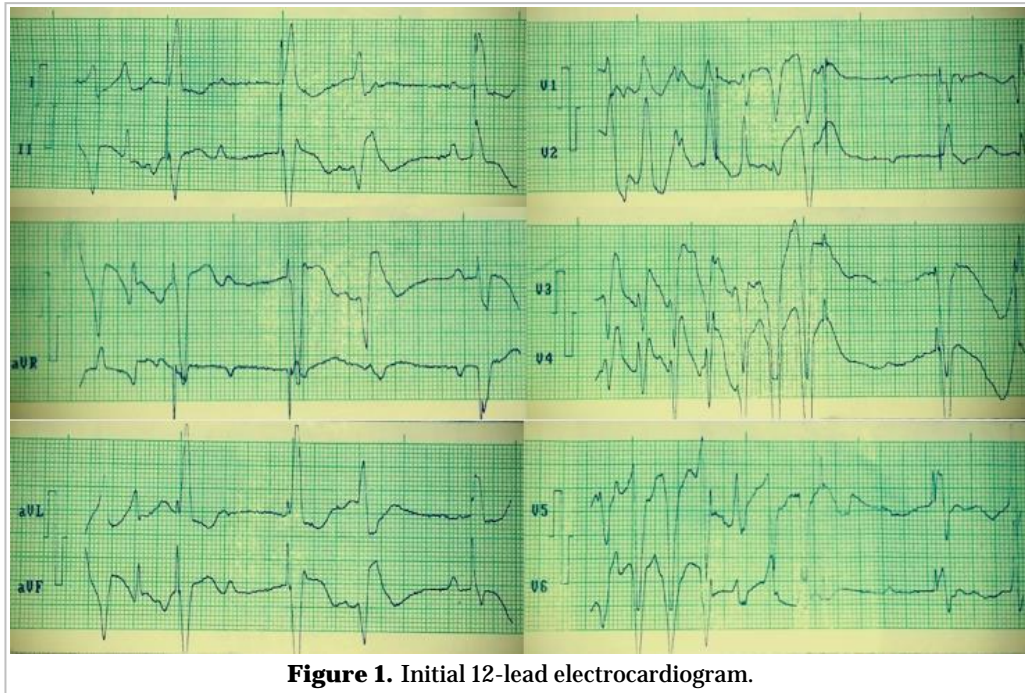
**Figure 1.** Initial 12-lead electrocardiogram.

with left bundle block branch (LBBB) pattern, superior QRS axis, pattern of appropriate discordance in precordial leads, complete AVB with atrioventricular dissociation; basic interval, from the first spike observed until the second one, of 1000 ms in standard and limb leads, escape interval from premature ventricular contraction located next to the second paced beat until the third one with its spike of 1000 ms; besides, at the beginning of the registration it is appreciated, in standard and limb leads, rhythms consistent with polymorphic ventricular tachycardia TdP type, better registered in precordial leads (first seven beats); later it is observed a detection failure with spike of pacemaker that falls on the T wave of the TdP last beat, that coincides with the absolute refractory period and, therefore, it is not capable of producing ventricular capture, but between this spike and the next one, the basic interval is of 1000 ms again. Alternance and notches of the T wave with normal QT and cQT are appreciated (**Figure 1**).

Next, a long D$_{II}$ lead was recorded, where the following elements were found: in the superior trace (**Figure 2**), three beats of ventricular bigeminism with short-coupling intervals are observed, the two first bigeminated complexes present a QT interval of 520 ms and cQT of 631 ms −calculated using the Fridericia´s formula−, QT dispersion higher than 60 ms and subsequent to the last bigeminated premature ventricular complex, two premature ventricular contractions of different focal spots that start a short torsadogenic event that continues in the inferior trace are observed; later, a paced beat is observed,
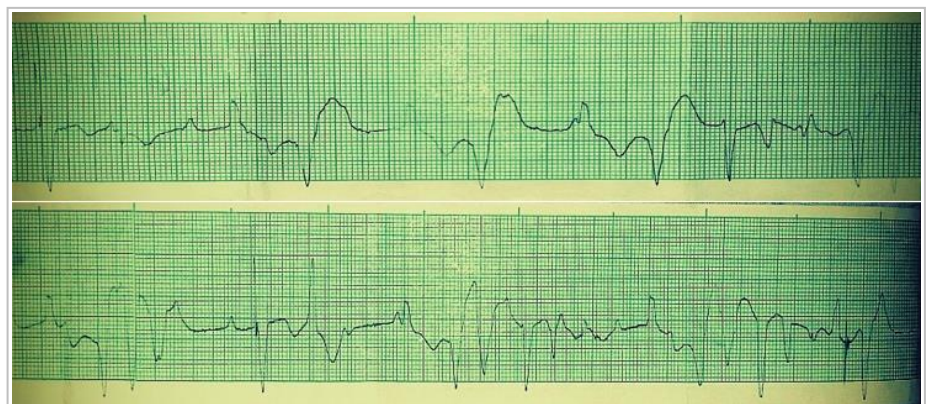


**Figure 2.** Long D$_{II}$ during the syncopal event.

another premature ventricular contraction with short-coupling that provokes a longer TdP event of 13 complexes, that stops when the device captures the ventricle again, but with detection failure; the spike at the ST level of the last ventricular complex must be noticed. There is also atrioventricular dissociation by complete AVB.

A blood sample for ionogram and other tests was taken (**Table**), where moderated hypokalemia and hyperglycemia were observed, and an echocardiogram was also performed, where remarkable structural or functional anomalies were not appreciated.

Since no clinical, enzymatic, imaging or electrocardiographic elements were found, which might suggest severe myocardial ischemia, since there were no personal or family history of congenital long QT syndrome, and since moderated hypokalemia was observed, besides knowing about the usage of the maximum dose of the orally administered glucose-lowering drug glibenclamide, plus the described electrocardiographic elements, an acquired long QT syndrome was diagnosed, secondary to the electrolytic disorder and, presumably, to the usage of sulfonylureas in the treatment of diabetes mellitus, with the subsequent emergence of syncopal events and TdP type ventricular tachycardia. Due to these reasons, the following therapeutic measures were established: acute correction of the hypokalemia condition, 10% magnesium sulfate was intravenously administered as well as positive inotropic therapeutic with dobutamine, the glucose-lowering drug was initially replaced by insulin, the intracardiac stimulation device was reprogrammed, increasing the basic heart rate and optimizing the amplitude and duration thresholds of the impulses, correcting therefore the capture and detection failures −that also contribute to the ventricular tachyarrhythmical events− and, with all these measures, the syncopal condition and the TdP events disappeared.

Once the arrhythmical condition was corrected, the enalapril was associated to the antihypertensive treatment, substituting the thiazide diuretic, with the objective (also) of saving the maximum potassium level offered by this drug.

A further electrocardiogram was recorded (**Figure 3**), that confirmed the absence of arrhythmogenic events, with presence of her own rhythm, followed by ventricular stimulation and capture by monopolar VVI pacemaker, with equidistant basic and escape (800 ms) intervals at a heart rate of 75 bpm, with isolated monomorphic premature ventricular contractions.

The patient was asked for her consent to be re-operated with placement of the atrial lead and changing the generator to bicameral, in order to

**Table.** Blood tests' results.

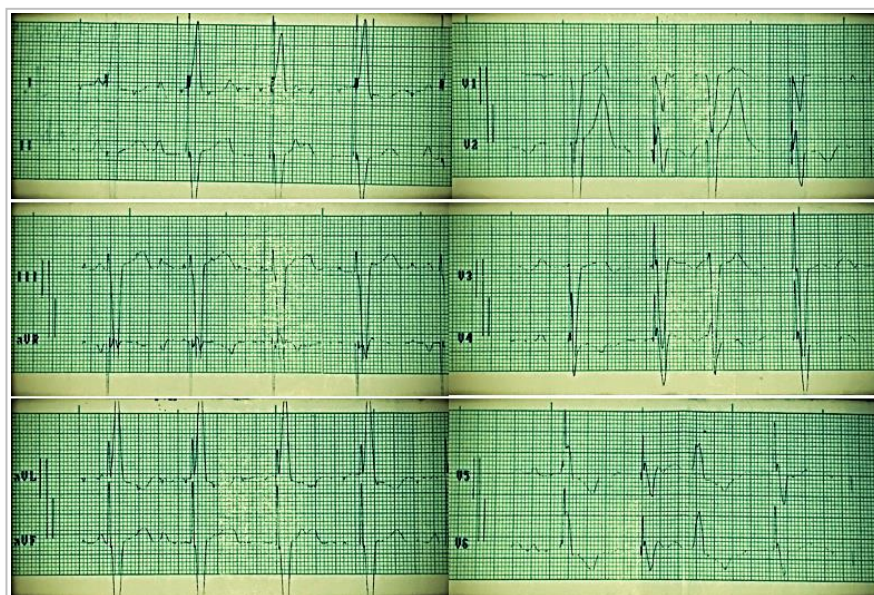| Parámetro | Valor |
|---|---|
| Potassium | 2.3 mEq/l |
| Sodium | 142 mEq/L |
| Chlorine | 90 mEq/L |
| Ionic Calcium | 1.25 mmol/l |
| CK-MB | 18 U/l |
| CK (phosphocreatine kinase) | 97 U/l |
| Glycaemia | 12.6 mmol/l |
| Creatinine | 124 µmol/l |

CK-MB, creatine kinase isoenzyme MB



**Figure 3.** 12-lead electrocardiogram after establishing the treatment and reprogramming the device.

achieve a sequence of synchronized atrioventricular activation, but she refused this procedure.

After being asymptomatic during 72 hours, without recurrence of the ventricular tachyarrhythmia, the patient was discharged from our Department and was transferred to the Department of Internal Medicine to continue with the study of the fluid and electrolyte imbalance, and to readjust the treatment for the diabetes mellitus, with the suggestion of not using sulfonylureas.

## COMMENTS

In the described case, it can be appreciated how the convergence of the fluid and electrolyte factors (hypokalemia), pharmacological factors (usage of glibenclamide) and the permanent pacemaker's dysfunction, gave place to the emergence of an acquired long QT syndrome with TdP and syncopes, in a patient without any other biochemical, clinical or congenital elements that might explain this situation.

Besides its function and specific action, most of the drugs with potential side effects predisposing to TdP development are $I_{kr}/K_v11.1$ channel blockers, also called HERG (human ether-a-go-go-related) channel blockers. In fact, the drugs prolonging the QT create a phenotype similar to the type 2 long QT syndrome by decreasing the effectiveness of the repolarization and ulterior prolongation of the cardiac action potential[9].

Since a long time ago it is known that the electrolytic disorders like the hypokalemia, hypomagnesemia and hypocalcemia promote the emergence of this proarrhythmical manifestation. If on top of this, potential torsadogenic drugs are added, then the emergence of long QT syndrome could become more frequent, with symptoms that can go from syncope to sudden death, due to TdP or ventricular fibrillation, if early diagnosis and treatment are not carried out[14,15].

Leonard *et al*[16] demonstrated, in a recent study, that the sulfonylureas, like glibenclamide and glimepiride, potentially block the ATP-dependent potassium channels, that might reduce or eliminate the ischemic preconditioning, and prevent and shorten the duration of the action potential, as well as inhibit the channel sustained by the HERG gene, which would be related to the electrocardiogram's QT interval prolongation.

Other authors state as well that the glibenclamide, besides being the second-generation sulphonylurea with the highest risk of hypoglycemia, can provoke the described effects about the channel sustained by the HERG gene and the ATP-dependent potassium channels, which minimize the natural response to the myocardium's excitability to the acute ischaemia and increases the risk of arrhythmias caused by the delays in the depolarization, but it can block the re-entrant arrhythmias[16,17].

It is valid to appreciate that our patient with a VVI pacemaker, with complete AVB, developed TdP because of the intermittent stimulation failure; due to the same reasons premature ventricular contractions took place, which induced short-long-short ventricular sequences. These facts, associated to the hypokalemia and the usage of glibenclamide, might have been combined to result in irregularities of the R-R interval, which subsequently reduced the repolarization reserve and started the TdP. In the complete AVB, when the escape rhythm is slow, the more irregular the R-R interval is, the longer the refractory periods and the duration of the action potential are, and as a result, the possibilities of generating TdP re-entrant arrhythmias increase.

Similar cases of TdP events in patients with complete AVB and implanted pacemakers have been published. Palanca *et al*[18] described syncopal events due to this type of malignant ventricular arrhythmia in 3 patients with complete AVB after an implantation of a unique lead wire in a VDD pacemaker. The defective intermittent atrial detection may lead to a change to VVI mode in this modality, which can induce the bradycardia and sudden oscillations of the R-R interval, that act as a precipitating factor to start the TdP.

The cQT measuring, in our case, was made according to the Fridericia's formula, since it is considerably superior to the Bazett's one for measuring this electrocardiographic parameter, when the heart rate is out of the physiological range[19].

It should be mentioned that the electrocardiographic elements of a very high risk of sudden death that this patient presented, which were registered during the third syncopal event, were identified in the $D_{II}$ lead trace with the event of bigeminated premature ventricular contractions, and apart from the remarkable prolongation of the QT interval, with obvious dispersion, there were observed notches in the T waves, alternant in their duration, and multifocal and polymorphic premature ventricular complexes with short-coupling intervals; all of them are elements of poor prognosis and high probability of ventricular arrythmogenesis.

Electrocardiographic signs suggesting SCD should be always taken into account when examining an electrocardiogram, it is a valuable complementary method to stratify the risk that a patient might have of presenting malignant arrhythmias, in order to offer him/her the best therapeutic options to prevent major adverse −or even deadly− events.

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