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Case Report

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Incessant right ventricular outflow tract tachycardia – Tachycardiomyopathy? The enigma

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Abbreviations
CMP: cardiomyopathy
LV: left ventricle
RVOT: right ventricular outflow tract
RVOTT: right ventricular outflow tract tachycardia
TIC: tachycardia-induced cardiomyopathy
VT: ventricular tachycardia

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ABSTRACT

Long-lasting or incessant ventricular tachycardias may cause heart failure, left ventricular dysfunction, and cardiomyopathy; conditions that reverse once the arrhythmias have been solved. This is a diagnosis of exclusion: there may be a basic heart disease that worsens with the tachycardia and it must be clarified whether the arrhythmia leads to cardiomyopathy (there may be an underregistration) or vice versa. A patient with incessant right ventricular outflow tract tachycardia, with long evolution, hemodynamic repercussion, dilated cardiomyopathy and severe dysfunction of the left ventricle, refractory to antiarrhythmic drugs and with two failed ablations, pending endomyocardial biopsy and new ablation of his tachycardia is presented. Some clues to differentiate right ventricular outflow tract arrhythmias, in their benign (most frequent) and malignant variants, are discussed. Some clues to differentiate them are: the duration of the QRS complex, the coupling interval of premature contractions and the heart rate of the tachycardia.
Keywords: Tachycardiomyopathy, Malignant ventricular arrhythmias, Right ventricular outflow tract tachycardia

Taquicardia incesante del tracto de salida del ventrículo derecho - ¿Taquimiocardiopatía?: El enigma

RESUMEN

Las taquicardias ventriculares de larga duración o incesantes pueden causar insuficiencia cardíaca, disfunción del ventrículo izquierdo y cardiomiopatía, cuadros que revierten una vez resueltas las arritmias. Se trata de un diagnóstico de exclusión: puede existir una cardiopatía de base que empeora con la taquicardia y debe precisarse si la arritmia lleva a la cardiomiopatía (puede existir un subregistro) o viceversa. Se presenta un paciente con taquicardia incesante del tracto de salida del ventrículo derecho, de larga evolución, con repercusión hemodinámica, cardiomiopatía dilatada y disfunción grave del ventrículo izquierdo, rebelde a fármacos antiarrítmicos y con dos ablaciones fallidas, pendiente de biopsia endomiocárdica y nueva ablación de su taquicardia. Se discuten algunas pistas para diferenciar las arritmias del tracto de salida del ventrículo derecho, en sus variantes benignas (las más frecuentes) y malignas. Algunas pistas para diferenciarlas son: la duración del complejo QRS, el intervalo de acoplamiento de la extrasístole y la frecuencia de la taquicardia.
Palabras clave: Taquimiocardiopatía, Arritmias ventriculares malignas, Taquicardia del tracto de salida del ventrículo derecho

INTRODUCTION

Long-lasting tachycardia is a very well-recognized cause of heart failure, left ventricular (LV) dysfunction and induced cardiomyopathy and it is –generally– reversible if the cause of the tachycardia is effectively treated with drugs, ablation or surgery. It is a diagnosis of exclusion which actual incidence is difficult to precise, confirm or refute, and there may be an underregistration of the disease, which can be confirmed if recovery of LV function and normalization of the heart rate are achieved (in absence of other causes)[1,2].

More than 100 years after the first case was reported in 1913 (young patient with congestive heart failure and atrial fibrillation with rapid ventricular response), the understanding of its pathophysiology in humans is limited, despite numerous studies in animal models. There are other causes, in addition to tachycardias, that can cause it: conduction abnormalities, dyssynchrony, right ventricular pacing, left bundle branch block and ventricular preexcitation[1,2].

Tachycardia-induced cardiomyopathy (TIC) can take place in patients with LV dysfunction due to an underlying structural heart disease, with worsening of their myocardial dysfunction if the tachycardia is prolonged. There is a variety of chronic or incessant tachycardias involved in the pathogenesis of TIC: atrial fibrillation and flutter, supraventricular and ventricular tachycardias, and premature ventricular contractions. It has been observed that similar arrhythmias can be more or less prone to cause cardiomyopathy (CMP) and that they can be totally or partially responsible for LV dysfunction. Dilated CMP is the most common form in these cases[1,2] and it is important to make the diagnosis because it is a potentially reversible cause of heart failure.

In TIC, arrhythmia duration and heart rate, involving hemodynamic, structural (LV cavity dilatation, subendocardial fibrosis with normal or reduced LV wall thickness), cellular and neurohormonal changes, with reduced myocardial blood flow should be considered. The TIC due to sustained monomorphic ventricular tachycardia (VT) is less common and it is more frequent if associated with a structural heart disease. It is usually considered as idiopathic, related with the right ventricular outflow tract (RVOT) or LV, and with coronary cusps. Little has been published on the risk of sudden death in TIC and heart failure is related with the arrhythmic substrate due to electrical heterogeneity of the myopathic ventricle, repolarization abnormalities and other factors[1,2].

CASE REPORT

A 13-year-old male patient who was admitted to the *Cardiocentro Pediátrico William Soler* due to epigastric pain, sweating, pallor and vomiting is presented. A non-sustained RVOTT was then diagnosed. Positive data during physical examination: arrhythmic heart sounds, heart rate between 128-137 beats per minute, and systolic murmur II/VI in mitral focus, without irradiation.

Electrocardiogram: Multiple traces with right ventricular outflow tract tachycardia (**Figure 1** y **Figure 2**).

Telecardiogram: cardiomegaly with increased pul-

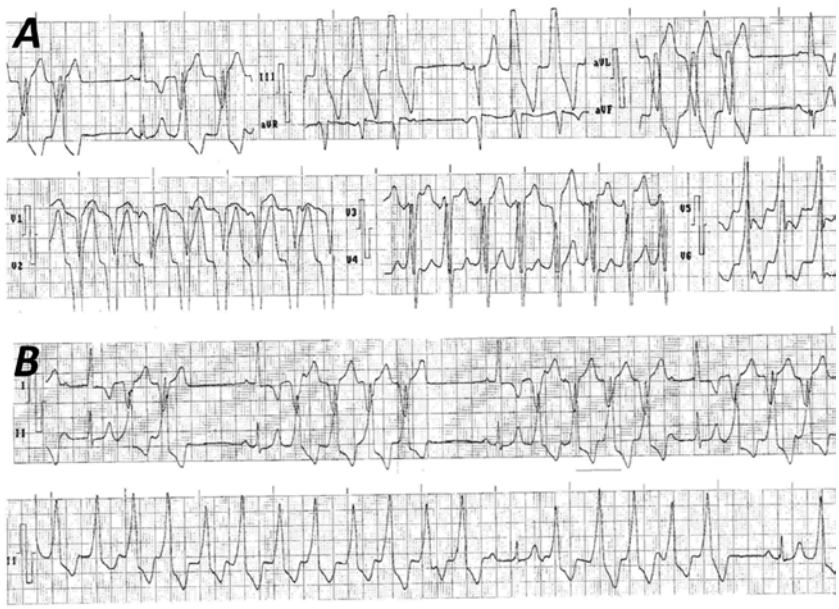

Figure 1. A. Right ventricular outflow tract tachycardia (predominant QRS complex negativity in V_1 and R in leads II, III and aVF), heart rate of 128 beats per minute, QRS complex duration 160 ms. Some occasional sinus complexes, T negative in I and aVL. **B**. Runs of right ventricular outflow tract tachycardia, the premature contraction that initiates bursts is observed after the T wave (intermediate coupling interval). Variable, normal and long PR intervals.

monary flow, and rectified main pulmonary artery.

Echocardiogram: marked LV remodeling, semispheroidal shape, global systolic dysfunction, ejection fraction between 17-29%, LV in diastole 70 mm and systole 63 mm. Mild mitral and tricuspid regurgitation. Bicuspid aortic valve with mild regurgitation. Clean atrial appendages, no intracardiac masses, no pleural or pericardial effusion, normal aortic arch and coronary pattern

Nuclear magnetic resonance imaging: non-ischemic cardiomyopathy with severe LV systolic dysfunction, without myocardial fibrosis areas, mild aortic valve regurgitation. Global and regional contractility: global LV hypokinesia with absence of apex closure and paradoxical motion of the interventricular septum. Left ventricle dilation.

Electrophysiological studies: incessant RVOT tachycardia. Radiofrequency was applied in the upper part of the right side of the interventricular septum, (**Figure 3**), without eliminating the arrhythmia (two procedures).

Diagnosis: dilated cardiomyopathy, incessant, refractory to antiarrhythmic drugs and with two failed ablations RVOT tachycardia.

After nine months of admission the state persists, without signs of low output or hemodynamic impairment. Several antiarrhythmic drugs (amiodarone, verapamil, propafenone, metoprolol) and other drugs such as spironolactone, enalapril, vitamins, L carnitine and acetylsalicylic acid have been administered. Endomyocardial biopsy and a new ablation attempt are pending.

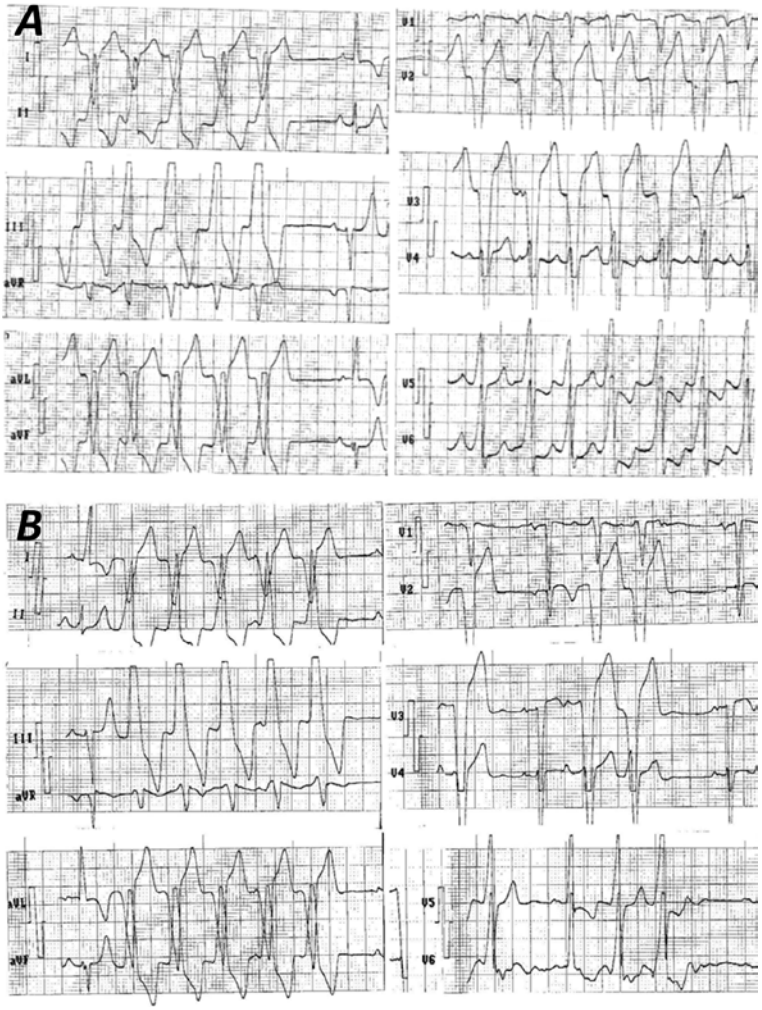

Figure 2. Tachycardia bursts. In both traces (**A** and **B**) the triggering premature contraction is inscribed after the T wave (intermediate coupling interval).

COMMENT

The TIC lead to structural and functional changes in the myocardium in which several factors are considered:

- The trigger: high heart rate.
- The mediator: calcium.
- The effect: myocytes fibrosis, electrical remodeling, contractile dysfunction, neurohormonal activation.
- Recovery: when the arrhythmia is suppressed through drugs or ablation, LV ejection fraction, ventricular dilation, diastolic dysfunction, reactive hypertrophy and persistent fibrosis are normalized.

After recovery, follow-up is necessary if there is an abnormal myocardial substrate, since histopathological abnormalities, diastolic dysfunction and ventricular enlargement with hypertrophic response may persist, even after LV ejection fraction is normalized[1,2].

The RVOT is a thin structure, complex from its embryology, with fusion of various structures, a mixture of structural and physiological properties, different from those of other regions. It has particular and complex characteristics in its embryology, histology, anatomy, physiology and pathophysiology.

Why is the RVOT arrhythmogenic? Some facts have been invoked: relatively high proportion of M cells (in relation to

late afterdepolarizations), thinnest surrounding myocardium (which decreases electrotonic effects that inhibit arrhythmia propagation), unique three-dimensional structure, and special architecture of ion channels[3]. Its role has been studied in the arrhythmias of idiopathic ventricular fibrillation, Brugada syndrome, catecholami-nergic polymorphic VT and *trorsade de pointes*. But why is the RVOT more arrhythmogenic if the disturbances are found in the whole ventricular wall? What is the significance of this fact? If ablation of the arrhythmia triggers and of some areas of this structure is performed, the events and electrical storms are solved. There are peculiar areas of depolarization and repolarization of the RVOT and the premature ventricular contractions in this area can cause benign arrhythmias in individuals without structural heart disease, but also malignant events[4].

The RVOT is a preferential site of origin for arrhythmias, in which its embryology plays a key role; the development of the heart is imbricated with the outflow tract tachycardias of Brugada syndrome and, in a lesser degree, of the arrhythmogenic right ventriclular cardiomyopathy. It is formed with a slow conduction phenotype and it does not express the genetic program of the working myocardium; therefore, its phenotypes differ from those of the free wall of the right and left ventricles. Adult RVOT ventricular arrhythmias develop with postnatal evolution and age plays its role in the disease progression. Arrhythmias are favored by slow conduction and spontaneous activity that are unmasked after birth and even increase; heart age uncovers the arrhythmic nature of a region with remnant of the embryonic phenotype in the adult myocardium. The heart grows, remodels, matures and acquires a place in arrhythmogenesis, with a relationship between RVOT development and arrhythmias. In the adult heart the RVOT myocardium with a working myocardial phenotype has lower expression than in the right and left ventricles, which favors slow conduction and low excitability. These facts are compounded by other factors such as fibrosis, patient age, wall stress, arrhythmic substrate and a possible modulatory mutation, all of which lead to arrhythmogenesis[3].

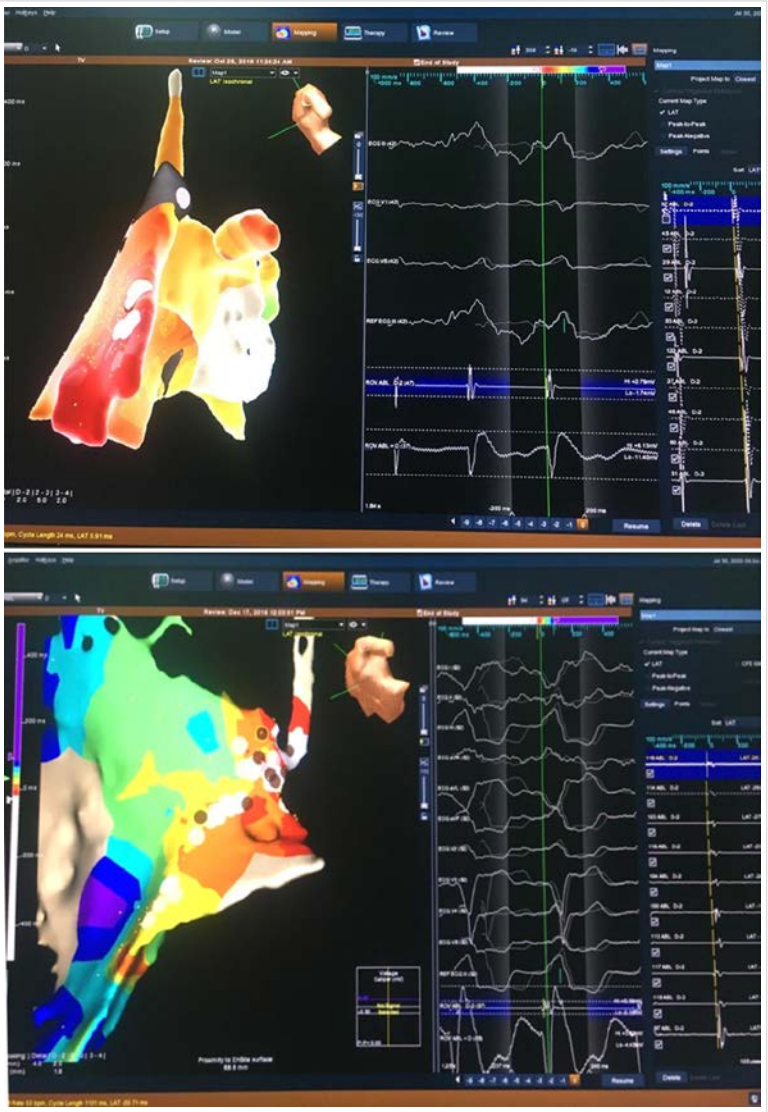

Figure 3. Images showing local activation time(LAT) maps of the right and left ventricular outflow tracts, with precocity in the posterior septal area of the first one. White and brown dots indicate the performed applications. Two radiofrequency sessions failed.

The RVOT is the site of origin of the most common type of VT in individuals without structural heart disease, it presents a left bundle branch block pattern (rS in lead V_1) and tall R wave in inferior leads (II, III and aVF), it is monomorphic, triggered, and from a clinical point of view, there is usually no hemodynamic decompensation. Thus, in a patient without heart disease who suffers palpitations and who presents RVOT premature contraction, a well-tolerated sustained VT related with this structure is thought to be present; however, it can also be the

site of origin of a ventricular fibrillation (like in Brugada syndrome and idiopathic ventricular fibrillation). There are polymorphic arrhythmias with syncope or cardiac arrest and premature ventricular contractions with short coupling interval (at the peak of the T wave); as well as the more common monomorphic VT, with palpitations and frequent premature ventricular contractions with long coupling interval. It is necessary to differentiate between benign monomorphic RVOTT and the malignant polymorphic one or ventricular fibrillation triggered by RVOT premature contractions; is it an idiopathic RVOTT or a malignant idiopathic VT?[4-6].

Viskin and Antzelevitch[5] speak of the worst nightmare when sudden death takes place in an individual with "benign" ventricular arrhythmias, with risk of stratifying a young person with a supposedly benign arrhythmia who then has a sudden death event. Neither the number of premature ventricular contractions nor their coupling interval allow absolute differentiation of polymorphic RVOTT from monomorphic RVOTT; however, there are some clues. The coupling interval of premature ventricular contractions, in the descending branch of the T-wave or earlier, points to malignancy, as opposed to the "intermediate" between the shortest interval of idiopathic ventricular fibrillation and the longest interval of RVOTT in benign monomorphic VT. A shorter interval points to a polymorphic arrhythmia as well as to malignancy, although its absence does not deny the possibility of a polymorphic RVOTT; this is usually faster than the monomorphic one and it is initiated by pre-mature ventricular contraction with short interval and it is named "short-coupled variant of RVOTT".

Other clues may be the QRS duration of the premature ventricular contractions (wider than in idiopathic ventricular fibrillation and in benign forms) and the shortest RR interval. The RVOT premature contractions have an intermediate coupling interval between the shortest in idiopathic ventricular fibrillation (ultrashort) and the longest in idiopathic monomorphic VT, idiopathic polymorphic VT and benign VT. There is a malignant variant due to RVOT premature contractions (polymorphic VT/ventricular fibrillation), but benign LV tachycardia also takes place in patients without structural heart disease, which may lead to polymorphic VT/ventricular fibrillation and sometimes even to sudden death. Both can undergo ablation through radiofrequency. Haissaguerre performed it in patients with idiopathic ventricular fibrillation triggered by stimuli from the distal Purkinje system and from the RVOT (in its origin or in the surrounding areas) and thus he managed to eliminate arrhythmias by acting on the polymorphic VT and ventricular fibrillation substrate, with implantation of a cardioverter-defibrillator, if necessary[4-11].

Premature ventricular contractions and RVOTT offer an image of left bundle branch block (predominance of QRS negativity in V_1 and inferior axis with QRS positivity in II, III and aVF) and short-coupling interval (not as much as in idiopathic ventricular fibrillation and *torsades de pointes*). Functional block and conduction delay by a rapid triggered start or by micro-reentry (single or multiple proximal focal spots) are presented, it may also be due to a chaotic fibrillatory conduction and there may be ventricular fibrillation or polymorphic VT without organic zone of delayed conduction[4,10].

In the patient that is presented, as in many others, we wonder: is it a CMP leading to RVOTT or is it an incessant RVOTT leading to CMP? This is a diagnosis of exclusion and it would be important to differentiate from other right ventricular diseases[1,2,8]. This is important because knowing this and solving it can reverse heart failure and LV dysfunction; there is also the possibility that the tachycardia may have worsened the evolution of some underlying disorder[1.2]. In our case, only time, or perhaps the result of the endomyocardial biopsy and above all the evolution after a successful ablation of the tachycardia, will have the last word; even when the tachycardia is solved if it is the tachycardia that leads to CMP, there may be sequelae that affect reality.

In our experience, dilated CMP arrhythmias appear in stages of severe hemodynamic impairment, pulmonary hypertension and congestive heart failure, which are not present in this patient.

Note that in this patient the premature ventricular contractions that trigger tachycardia events take place after the T wave, that is, with an intermediate coupling interval, between the shortest of the idiopathic ventricular fibrillation and the longest of the benign forms of RVOTT, these criteria are met here. In other cases, various coupling intervals of premature ventricular contractions have been seen in the same individual, which did not happen in this patient in whom the intervals were similar among them.

As discussed, RVOT plays an important role in arrhythmogenesis (malignant ventricular arrhythmias and sudden cardiac death), triggering and maintaining them (ventricular fibrillation and tachycardia,

polymorphic VT and malignant variant of RVOTT).

The RVOT premature contractions can cause idiopathic VT in individuals without structural heart disease, benign forms (successfully eliminated with radiofrequency in the 90% of cases), but sometimes they also can cause malignant ventricular arrhythmias (ventricular fibrillation, polymorphic VT, syncope and sudden death). It is worth to emphasize, because it was commented above, that RVOT premature contractions usually have an intermediate coupling interval between the ultrashort ones of idiopathic ventricular fibrillation, Brugada syndrome and *torsade de pointes* and the longest ones of benign idiopathic monomorphic VT. The shorter the interval, the greater the malignancy, although a longer interval does not guarantee that there is no risk. The aim is to eliminate the triggers as well as the ventricular fibrillation substrates and the polymorphic VT by radiofrequency ablation, either at the site of origin, its surroundings or in the RVOT epicardium, also to eliminate the premature contractions and subsequently to evaluate the implantation of an automatic cardioverter-defibrillator if necessary[4,5,7,9-11].

At the beginning, this patient showed symptomatology and hemodynamic impairment with RVOTT, during his admission he has remained with little symptomatology despite being in incessant tachycardia. Endomyocardial biopsy and a subsequent ablation attempt of his arrhythmia are pending. Idiopathic ventricular arrhythmias in an apparently normal heart represent a great conflict in their diagnosis and treatment, despite the contributions of genetic testing, imaging techniques, signal-averaged electrocardiogram and others; endomyocardial biopsy can significantly contribute to identify its causes, but it is not included as a routine study because of possible sample errors (focal or patch distribution); in this case, it is suggested that the use of three-dimensional electroanatomic mapping to guide the biopsy can increase the sensitivity of this study. Minor forms of arrhythmogenic right ventricular dysplasia/CMP may mimic an idiopathic RVOTT in which case electroanatomic mapping would be useful[12-16].

Idiopathic RVOTT in individuals without structural heart disease is usually benign, but sometimes this tachycardia and RVOT premature ventricular contractions can be seen to cause ventricular fibrillation and polymorphic VT (short-coupled variant) and it is necessary to differentiate the malignant form from the benign form[4,5,7,10,11].

This patient has had a malignant outcome, whether a structural heart disease leads to arrhythmia or, conversely, that the arrhythmia leads to dilated CMP. His arrhythmia can be categorized as a non-sustained repetitive RVOTT, but there are classic non-sustained VT in terms of duration and other very prolonged non-sustained VT or, like in this patient, actually an incessant arrhythmia. Some electrocardiographic characteristics (cycle length, coupling interval and QRS duration) suggest that this is a benign form but it is clearly not because of its incessant nature, its hemodynamic repercussions, its duration and its refractoriness to imposed therapies. A relatively short interval in the premature ventricular contraction that initiates the tachycardia (a sign of malignancy) is not observed, but an intermediate one between the shortest or ultrashort interval of idiopathic ventricular fibrillation and the longest interval of the truly benign forms (typical of the idiopathic RVOTT).

CONCLUSIONS

Long-lasting or incessant right ventricular outflow tract tachycardia is a reversible cause of dilated cardiomyopathy; it is of difficult diagnosis and of exclusion, so there is an underregistration; sometimes it worsens the condition of an underlying structural heart disease. Right ventricular outflow tract tachycardia, called idiopathic, has benign and malignant variants, with some clues to differentiate them. It is important to precise whether a cardiomiopathy gives origin to the arrhythmia or if it is the arrhythmia that leads to the cardiomiopathy.

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