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Case Report

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Changes in ventricular depolarization and repolarization in the clinical follow-up of a patient with Brugada syndrome

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ARTICLE INFORMATION

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Acronyms
BS: Brugada syndrome
ECG: electrocardiogram
ICD: implantable cardioverter-defibrillator
MVA: malignant ventricular arrhythmias
SCD: sudden cardiac death
VF: ventricular fibrillation

ABSTRACT
We present the case of a 55-year-old woman with syncopal episodes and a diagnosis of Brugada syndrome, who spontaneously presented the convex pattern. She received an implantable cardioverter-defibrillator and had a ventricular fibrillation event in the clinical follow-up (106 months). Over this time, 13 electrocardiograms were performed, all of them showing the convex pattern. Moreover, significant variability was observed in wave morphology and electrocardiographic measurements related to depolarization and ventricular repolarization.
Keywords: Brugada syndrome, Sudden cardiac death, Syncope, Ventricular fibrillation

Variación de la despolarización y repolarización ventriculares en el seguimiento clínico de una paciente con síndrome de Brugada

RESUMEN
Se presenta el caso de una mujer de 55 años, con cuadros sincopales y diagnóstico de síndrome de Brugada, al presentar el patrón convexo de manera espontánea. Se implantó un desfibrilador automático y en el seguimiento clínico (106 meses) presentó un episodio de fibrilación ventricular. Durante este tiempo se le realizaron 13 electrocardiogramas y presentó el patrón convexo en todos ellos, además se observó una significativa variabilidad morfológica y en las mediciones electrocardiográficas que reflejan la despolarización y repolarización ventriculares.
Palabras clave: Síndrome de Brugada, Muerte súbita cardíaca, Síncope, Fibrilación ventricular

INTRODUCTION

Brugada syndrome (BS) is a channelopathy that is part of the so-called J wave syndrome[1], associated with syncopal episodes or sudden cardiac death (SCD) due to malignant ventricular arrhythmias (MVA). It is diagnosed (class I recommendation, level of evidence C)[2] by the spontaneous appearance of the convex electrocardiographic pattern, or after a drug test with intravenous administration of sodium channel blockers, in one or more right precordial leads, with V_1 and V_2, or both, positioned in the sec-

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ond, third or fourth intercostal space[3].

Preventive therapeutic procedure in these patients includes lifestyle modifications, avoiding the use of drugs that induce ST-segment elevation in right precordial leads, alcohol abuse and excessive food intake; as well as early treatment of any febrile episode with antipyretics[2].

Sudden cardiac death prevention is based on the placement of an implantable cardioverter-defibrillator (ICD) in symptomatic patients. Asymptomatic patients are particularly challenging for medical personnel when deciding between conservative, drug treatment with quinidine or ICD implantation[2,4,5].

Measurements prolongation in some electrocardiographic patterns that reflect ventricular depolarization and repolarization, such as the QT interval or T_{PEAK}-T_{END} (T_{P-E}), have been associated with an increased risk of developing MVA at follow-up in patients with BS[6,7]. However, it is unknown to what extent these measurements may change from one electrocardiogram (ECG) to another, in these patients.

CASE REPORT

A 55-year-old woman with no family history of sudden death, who suffered a morning syncopal episode in 1993, presented 4 similar episodes in 1994, one of them with sphincter relaxation, all of them awake, some preceded by palpitations and others with weakness and general malaise. Because of this, she was assessed by Neurology and was commenced on a treatment of anticonvulsants for the diagnosis of epilepsy. In 1999 she underwent hysterectomy and in the postoperative period she had another syncope. In 2003 and 2004 she presented syncopal episodes with similar characteristics to those of the beginning. Despite having no symptoms over the last 4 years, she was referred in 2008 to the Department of Arrhythmia and Electrophysiology due to the convex pattern found in the ECG. An echocardiogram was performed and the presence of structural disease was ruled out. She was studied by programmed electrical stimulation according to the expert consensus statement[2,3,8,9], without inducing ventricular arrhythmias. However, due to her clinical symptoms, she received an ICD on May of that year.

On June 20, 2011 at 4:30 a.m. she had a syncopal episode with sphincter relaxation preceded by palpitations. The device detected a ventricular fibrillation (VF) and rescued her with electric shock.

That morning she presented two other similar syncopal episodes; however, the device did not record them, evidencing that these episodes had a different etiology.

From that last episode until March 2017, she has remained asymptomatic and there have been no ICD-recorded events of ventricular arrhythmias.

Thirteen ECGs have been performed during the 106-month follow-up, all of them showing the convex pattern (**Figure 1**). Moreover, a morphological variability of the electrocardiographic pattern is observed, as well as a quantitative change in some measurements that reflect ventricular depolarization and repolarization associated with MVA events in the follow-up of patients with BS[10-13]. The changes were between 80-140 ms for the T_{P-E}, between 20-80 ms for its dispersion (T_{P-E}d), from 400-480 ms for the QT interval and from 426 to 523 ms for the corrected QT interval (QTc).

COMMENT

Undoubtedly, risk stratification for ICD implantation is the cornerstone in the treatment of BS. In this patient, an ICD was implanted because of the spontaneous convex pattern as well as syncopal episodes, class IIa recommendation, level of evidence C[2]. This recommendation is based on the fact that the presence of the convex pattern spontaneously increases the risk of MVA, which does not change in relation to the number of derivations where the pattern appears or to the greatest increase in the J point elevation, nor to the record in the second, third or fourth intercostal space[6].

Nakano *et al*[14] demonstrated that the presence of the spontaneous convex pattern in the V_2 lead is associated with an increased risk of MVA episodes. On the other hand, Okamura *et al*[15], determined that this pattern significantly increases the risk of SCD or VF (HR 4.81, CI 95% [1.43-29.92], p=0.0079). The percentage of time in which a patient presents the convex pattern in a Holter registry has been found to be a predictor for MVA at follow-up[1]. However, there is no literature that indicates that a greater number of ECGs with this pattern in follow-up is associated with future events. This patient presented the convex pattern in all those that were performed (**Figure 1**), an interesting fact to point out.

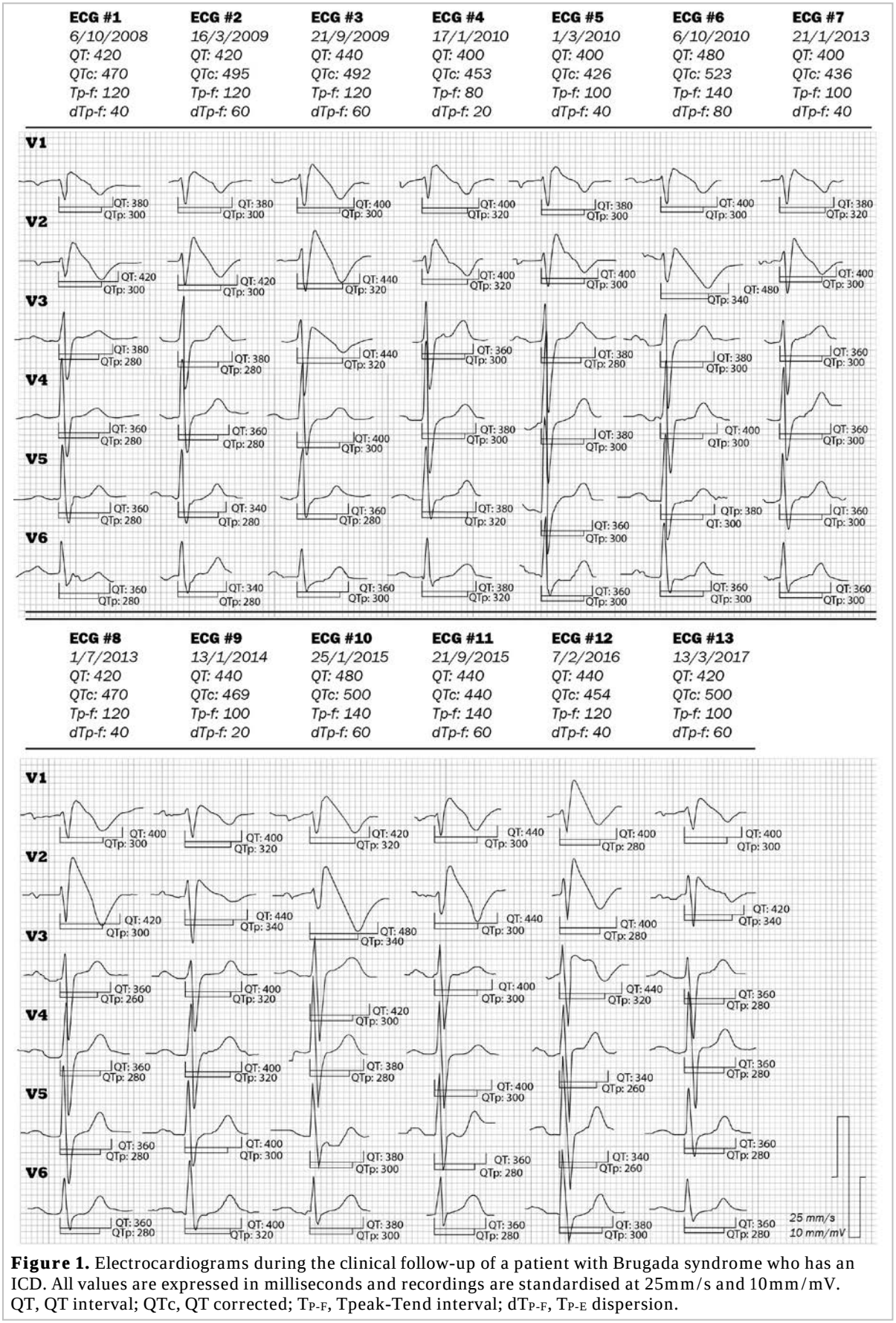

Figure 1. Electrocardiograms during the clinical follow-up of a patient with Brugada syndrome who has an ICD. All values are expressed in milliseconds and recordings are standardised at 25mm/s and 10mm/mV. QT, QT interval; QTc, QT corrected; T_{P-F}, Tpeak-Tend interval; dT_{P-F}, T_{P-E} dispersion.

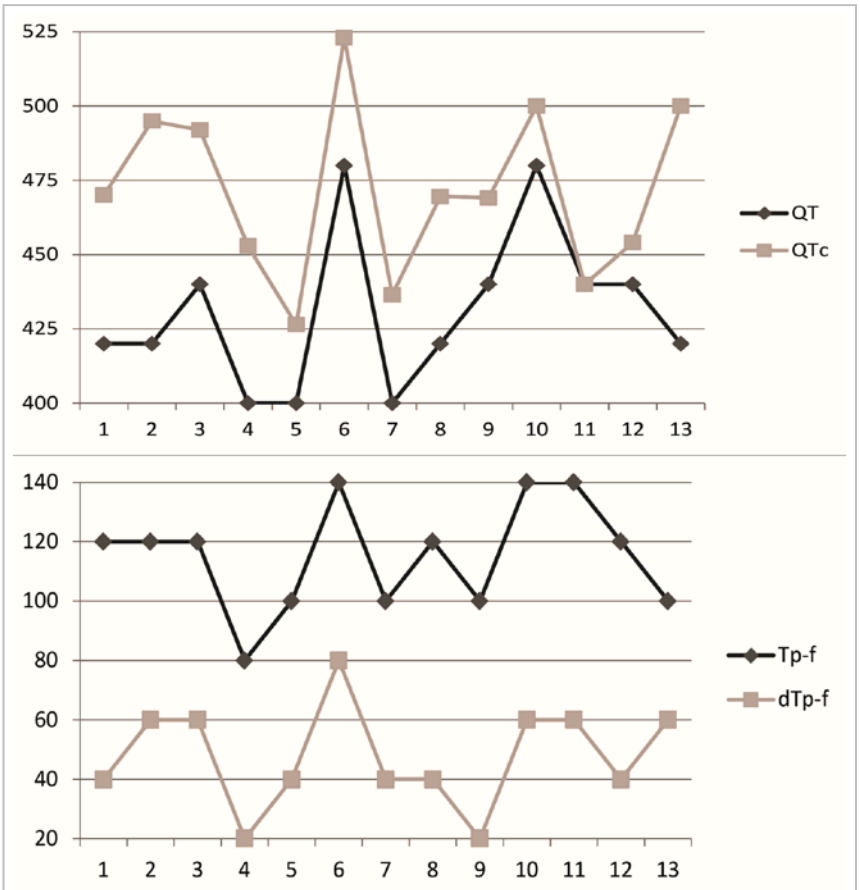

Figure 2. Variability of the electrocardiographic measurements in the 13 electrocardiograms performed in the clinical follow-up of a patient with Brugada syndrome who had an ICD. All values are expressed in milliseconds. QT, QT interval; QTc, QT corrected; T_{P-F}, Tpeak-Tend interval; dT_{P-F}, T_{P-E} dispersion.

In addition, syncope in these patients increases the risk of developing MVA, since in this group the annual frequency of sustained ventricular tachycardia or VF episodes is relatively high, between 1.9-8.8%. It is estimated that the risk is 4 times higher than that presented by asymptomatic patients and 4 times lower than patients with aborted cardiac arrest. The main difficulty lies in the clinical differentiation of syncope from cardiac and non-cardiac causes[6,7,15].

It has been shown that the presence of syncope clinically associated with ventricular arrhythmias significantly increases the risk of SCD or VF (HR 6.87, CI 95% [2.80-20.59], p<0.001)[15].

Prolongation of the different electrocardiographic measurements that reflect ventricular depolarization and repolarization do not change the procedure to be followed in a patient in whom secondary prevention is considered; however, these values have been recognized as MVA predictors and have been related to risk stratification in asymptomatic patients. Some of these predictors are the QT[10,11] and T_{P-E} intervals, as well as T_{P-E} dispersion[11,12].

The measurements made in this case were QT, QTc, T_{P-E} and T_{P-E}d. As shown in (**Figure 2**), there was a wide variability of these measurements over time, without a tendency to increase or decrease, but a true alternation between high and low values. This prolongation reflects an instability of the ventricular myocardium, predisposing the appearance of MVA; which evidences that these measurements are useful to predict arrhythmic episodes. There is no literature on this variability in patients with BS. Therefore, we believe that future studies should be carried out to determine the value of such electrocardiographic changes.

This case report clearly demonstrates that, by analyzing only a single ECG, we may underestimate the risk of MVA in a given patient.

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