

ST alternans induced by propafenone. Use-dependence of heart rate phenomenon demonstrated in clinical practice

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ARTICLE INFORMATION

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Acronyms

AF: atrial fibrillation

ABSTRACT

ST alternans reflects changes in action potential duration with increased electrical heterogeneity proportional to the alternation intensity. Although the mechanisms of ST and T alternans are still largely unknown, four mechanisms have been proposed: a) calcium overload, b) effect of chemicals from sustained ischemia, c) stimulation of the 5-HTreceptor and d) inhomogeneous blockade of sodium channels. Propafenone is a class IC sodium channel blocker, frequently used in the pharmacological cardioversion of atrial fibrillation, and has a use-dependence of heart rate phenomenon that can induce a Brugada pattern and electrical alternans. In this article, a clinical case demonstrating these two phenomena is presented.

Key words: Electrical alternans, ST alternans, Propafenone, Brugada pattern

Alternancia del ST inducido por propafenona. Fenómeno uso-dependencia de frecuencia demostrado en la práctica clínica

RESUMEN

La alternancia del ST refleja alteraciones en la duración del potencial de acción con aumento de la heterogeneidad eléctrica proporcional al grado de alternancia. A pesar de que los mecanismos de la alternancia del ST y la T son aún desconocidos en gran parte, se han planteado 4 mecanismos: a) una sobrecarga de calcio, b) efecto de productos químicos derivados de isquemia mantenida, c) estimulación del receptor 5-HT y d) bloqueo no homogéneo de los canales de sodio. La propafenona es un bloqueador de canales de sodio Clase IC, usado frecuentemente en la cardioversión farmacológica de la fibrilación auricular, y presenta un fenómeno uso-dependencia de frecuencia, que puede inducir a un patrón de Brugada y alternancia eléctrica. En este artículo se presenta un caso clínico demostrativo de estos dos fenómenos.

Palabras clave: Alternancia eléctrica, Alternancia del ST, Propafenona, Patrón Brugada

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INTRODUCTION

Electrical alternans of electrocardiographic waves was first described by Hering¹, more than a century ago, and even today it is an intriguing issue as to

its mechanism and electrophysiological impact. This situation reflects changes in the action potential duration with increased electrical heterogeneity proportional to the degree of alternans².

A case of electrical alternans and Brugada pattern is presented, both induced by propafenone.

CASE REPORT

A 59-year-old female patient with a history of good health comes to the emergency medical services because of an episode of "intense palpitations" of 3 hours duration. Physical examination shows an anxious patient with arrhythmic and tachycardic heart sounds, variable first sound and II/VI mitral systolic murmur. She presents neither rales nor signs of peripheral hypoperfusion; blood pressure 130/80 mm Hg and heart rate of 121 beats per minute.

An electrocardiogram is performed where atrial fibrillation (AF) is observed with rapid ventricular response alternating with 2:1 atrial flutter (**Figure 1**). Echocardiogram is performed which shows normal diameters of the cavities, good systolic function, without disruption of regional wall motion at rest, and mild mitral insufficiency.

The patient refuses to undergo electrical cardioversion and pharmacological cardioversion with propafenone (600 mg, orally) is administered, plus pro-

phylaxis with heparin and 50 mg of atenolol to prevent conversion to a flutter with rapid atrioventricular conduction (with 1:1 conduction). After 25 minutes of propafenone administration, conversion at 2:1 atrial flutter is observed, and the emergence of a Brugada pattern with ST segment alternans, more obvious in V₂ (**Figure 2**) is noteworthy.

Subsequently, return to sinus rhythm and progressive disappearance of Brugada pattern and ST alternans (**Figure 3**) are observed.

The patient did not present recurrence of AF or other arrhythmias. Within three months after the episode, she remains asymptomatic without recurrence of AF.

COMMENT

Although the mechanisms of ST and T alternans are still largely unknown, four mechanisms have been proposed:

- Calcium overload: hypothesis supported by the fact that calcium antagonists reduce alternans³. Transient calcium currents are an important mechanism of electrical alternans during ischemia due to intracellular properties of calcium for regulating transmembrane currents and the changes on the beat-to-beat action potential duration^{4,5}.
- Effect of chemicals from sustained ischemia: it has been demonstrated that administration of an acid perfusion increases ST alternans⁶.
- Stimulation of 5-HT receptor: the nexopamil, a calcium and 5-HT₂ channel blocker attenuates T-wave alternans, more than diltiazem, during and after coronary occlusion⁷.
- Inhomogeneous blockade of sodium channels. Tachibana *et al.*⁸ showed that flecainide (sodium channel blocker) induces ST elevation with alternans and can trigger ventricular fibrillation in the canine healthy heart. They also demonstrated that verapamil did not suppress the alternans, but 4-aminopyridine (I_{to} blocker) did it, and concluded that, in their cases, the sodium and po-

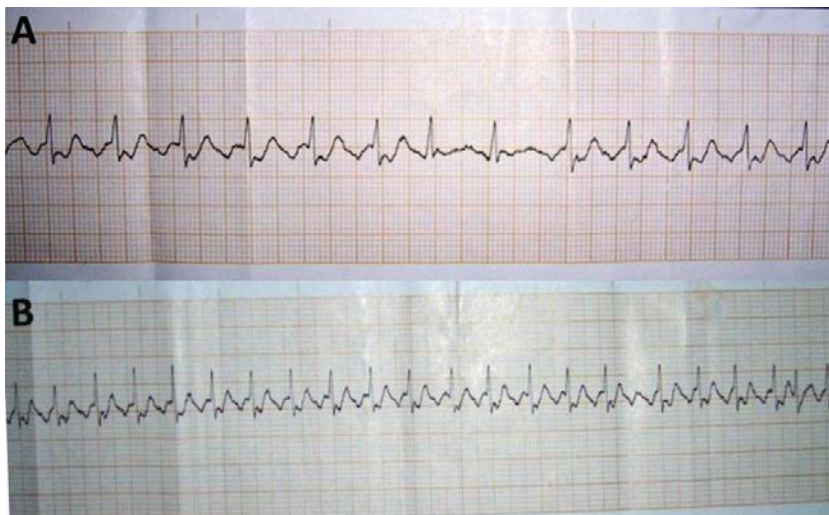


Figure 1. Electrocardiogram where AF is observed with rapid ventricular response (**A**) alternating with 2:1 atrial flutter (**B**).

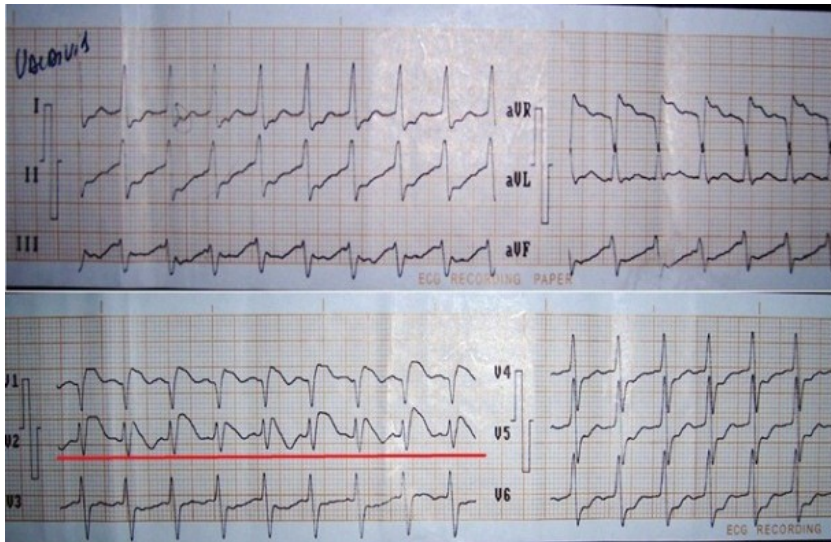


Figure 2. Brugada pattern with ST segment alternans more obvious in V2 (line).

tassium currents are more important in the ST alternans. These results are supported by other authors⁹.

Blockade of sodium channels, either by a channelopathy as in the Brugada Syndrome or drug-induced, may exacerbate I_{to} currents, which lead to a loss of the action potential dome. When this phenomenon is not homogeneous in the myocardium (it is generally more intense in the right ventricular epicardium) it produces an exacerbation of existing electrical heterogeneity and creates the substrate for the development of ventricular arrhythmias by functional reentry (phase 2 reentry)¹⁰⁻¹⁴. This exacerbation of heterogeneity is expressed as a ST elevation in electrocardiogram.

Propafenone is a class IC sodium channel blocker that presents the use-dependence of heart rate phenomenon¹⁵. As discussed in other cases¹⁶, the degree of blockade of sodium channels du-

ring a heartbeat is determined by the preceding diastolic interval; and in specific frequencies, the blockage leading to a loss of action potential dome in the epicardium of the right ventricle may cause prolongation of the diastolic interval which is sufficient to reduce blockade of sodium channels in the next heartbeat, in some sites of the epicardium of the right ventricle, so it will cause a less prominent elevation. Subsequently, the shortest diastolic interval, resulted in these sites, can generate a more potent blockade of sodium channels that will be expressed as a more noticeable elevation¹⁶. So, ST alternans and Brugada pattern induced by propafenone can be explained this way.

The diagnosis of Brugada syndrome is determined by what is stated in the report of the Second Consensus Conference¹⁷, which is based on the presence of a type 1 spontaneous (or induced by one of the sodium channel blockers) electrocardiogram suggested for this purpose, plus the presence of one of the following clinical findings¹⁴:

- Demonstrated ventricular fibrillation
- Polymorphic ventricular tachycardia
- Family history of sudden cardiac death in persons <45 years
- Type 1 electrocardiogram in family members
- Ventricular tachycardia induced by programmed

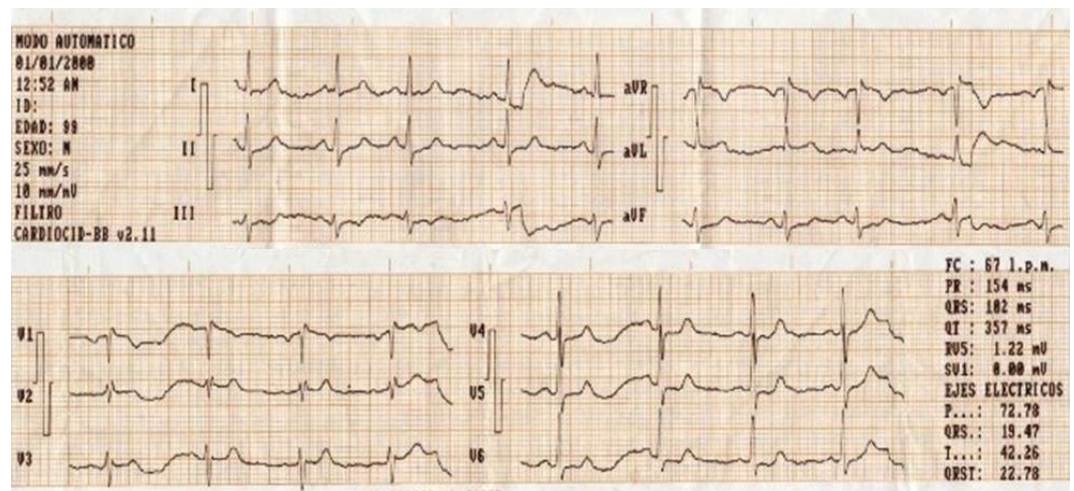


Figure 3. Disappearance of Brugada pattern and ST segment alternans.

electrical stimulation

- f) Syncope
- g) Nocturnal agonal respiration

Our patient had no clinical features of this syndrome, and her return from type 1 pattern associated to a follow-up without new evidence of the pattern suggests a normal variant, which means that the patient is a carrier of a genetic variant (possibly H558R polymorphism) which is found in the general population and would not cause the disease. It is likely that this polymorphism, combined with other genetic variants, drugs, or certain pathologic disorders, may predispose to the development of the disease^{18,19}.

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