Induced Brugada-Type Electrocardiogram, a Sign for Imminent Malignant Arrhythmias

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Case presentation: A previously healthy 20-year-old man arrives at the emergency department for a consultation for mild fever. During his initial interview, he complains of palpitations to the triage nurse and therefore he undergoes an ECG, which is placed in the chart. A few minutes later, while awaiting his turn to be seen, he goes into cardiac arrest. The patient does not respond to resuscitation and dies in the emergency department. The autopsy reveals no cardiac structural abnormalities or evidence of myocarditis. The cause of death is determined as sudden unexplained cardiac death. The ECG from the emergency department revealed ST-segment elevation in the right precordial leads consistent with a Brugada ECG pattern.

Introduction and Cases
The Brugada syndrome is a heterogeneous genetic disease that predisposes to life-threatening ventricular tachyarrhythmias and sudden cardiac death (SCD). The syndrome is usually identified by a characteristic Brugada-type ECG that consists of ST elevation of a coved type in the precordial leads V1 to V3, although affected individuals may have a normal ECG.1,2 Because patients with Brugada syndrome usually become symptomatic at a relatively young age, early diagnosis is crucial to prevent SCD in those with a higher risk of developing an arrhythmic event.3

Approximately one fourth of the cases of Brugada syndrome are caused by loss of function mutations in the cardiac sodium channel SCN5A. Several nongenetic factors have been mentioned in the literature as possible inducers of the ECG pattern resembling Brugada syndrome.2 As such, a Brugada-type ECG may appear in some patients during febrile states and in those who are under the influence of cocaine and pharmaceutical drugs that have a sodium channel–blocking effect, such as antiarrhythmics, anesthetics, and tricyclic antidepressants, among others.4–9 The role of propofol in the appearance of a pattern of Brugada syndrome has also been described,5 but its pathophysiological mechanism remains unclear.

In summary, there are several medications, electrolyte abnormalities, and disease states that may elicit the pattern of ST-segment elevation in leads V1 to V3. The clinical meaning and the risk of arrhythmias induced by this pattern are unknown.

In our set of patients with Brugada syndrome, we therefore reviewed those individuals who developed the Brugada-type ECG under inducers. Our patients were hospitalized with a characteristic ECG pattern elicited not only by some of the aforementioned drugs but also by fever. After a short time, some patients developed cardiac arrhythmias, which progressed in some cases to SCD. The purpose of this Clinician Update is to describe the risk of cardiac arrhythmias and sudden death in patients who present with a Brugada-type ECG in their ECGs obtained during acute medical situations.

We collected data on 47 patients (69% male; mean age, 48±16.2 years)
who presented during an acute medical event with a typical Brugada-type ECG, which meets the criteria of the European Society of Cardiology consensus report task force (Table).2 We used the clinical histories, follow-up visit reports, and blood samples of those who agreed to participate in the genetic screening. The cases were obtained either through direct contact from the patients themselves or from their attending physicians for further clinical management and genetic advice.

**Clinical Characteristics**

In 16 patients, a Brugada-type ECG was developed during a febrile episode. In 26 patients, the ECG abnormality was induced because of a drug or medication (eg, cocaine, anesthetics, antiarrhythmics, antidepressants, antihistamines) (Figure), and 5 were due to electrolyte imbalances. Of the 47 patients with an acute Brugada-type ECG, 24 (51%) had malignant arrhythmias, 18 patients developed SCD (or aborted SCD), 3 subjects had ventricular tachycardia (VT) episodes, and 3 had syncope. Of the 18 patients who developed SCD, 6 were associated with febrile episodes, 8 with anesthetics, 1 with electrolyte imbalance, 1 with methadone, 1 with procainamide, and 1 with an antihistamine.

Nine patients treated with antiarrhythmic drugs (eg, propafenone, flecainide, procainamide) developed a Brugada-type ECG. These medications were prescribed to all of the patients to prevent atrial fibrillation episodes. Shortly after the appearance of the Brugada-type ECG pattern, 2 patients had life-threatening arrhythmias: 1 had documented VT, and the other had SCD. Genetic analysis was performed in 26 study subjects, and 4 of them had a mutation in the SCN5A gene.

**Discussion**

This Clinician Update provides data on 47 patients with a Brugada-type ECG induced by several factors known to unmask the Brugada syndrome. From our 47 subjects, 24 developed symp-
toms related to the Brugada syndrome during the acute event, including 18 patients with SCD, 3 with VT, and 3 with syncope. On the basis of our results, the presence of the Brugada ECG pattern in patients during an acute event such as fever, treatment with sodium channel–affecting medication, drug overdose, or electrolyte imbalances should be considered a risk factor for the development of life-threatening cardiac arrhythmias.

Several fever-induced Brugada-type ECG cases have been described previously in the literature. Studies have reported mutant sodium channels that exhibit temperature-dependent gating changes consistent with more evident ECG abnormalities at increased temperature. Regardless of the existence of a predisposing genetic base, most of our patients with fever and a Brugada-type ECG developed malignant arrhythmias shortly after the onset of the fever.

A number of substances facilitate the elevation of the ST segment by either reducing the inward sodium current or increasing the outward potassium current. Sodium channel blockers, cocaine, antidepressants, and antihistamines are known to facilitate the Brugada-type ECG by reducing the inward current. Hyperkalemia, vagotonic agents, and I(KAtp) activators augment the outward current, which is also transduced in the ECG as the typical Brugada pattern. In our study, a total of 19 patients were on substances known to reduce the cardiac sodium current. All patients were prescribed antiarrhythmic medication to prevent atrial fibrillation, and 2 of these patients had life-threatening arrhythmias (VT and SCD) while taking the medication. Therefore, we conclude that patients who are treated with Class Ic medication and who present with a Brugada-type ECG are at high risk of ventricular arrhythmias.

Anesthetics such as bupivacaine, lidocaine, and propofol are known sodium blockers. The mechanism by which propofol unmasks this ECG pattern is not yet clear.

Conclusions
Patients who are in an acute situation and who present with a Brugada-type ECG are at a considerably higher risk of SCD and should be considered a medical emergency. In our series, 51% of the patients had symptoms related to Brugada syndrome, including 38% who developed cardiac arrest during the episode. A therapeutic intervention with antipyretics or by termination of the culprit medication is warranted. These data also indicate that individuals with Brugada syndrome and their family members who are genetic carriers of a sodium channelopathy should be aware that some medications and disease states may increase their risk of arrhythmias.

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Disclosures
None.

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