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The Brugada syndrome

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The Brugada syndrome

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Key words

ST segment elevation

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Brugada syndrome describes the syndrome of sudden cardiac death in the setting of the following electrocardiographic findings: right bundle branch block pattern with

ST-segment elevation in the right precordial leads. The right bundle branch block may be incomplete while the ST segment elevation is minimal. The electrocardiographic findings are not constant. Patients suspected of having Brugada syndrome should be promptly referred for electrophysiological testing and treatment. Rapid referral and placement of an implantable cardioverter defibrillator (ICD) is associated with an excellent prognosis, whereas failure to diagnose this condition is associated with a high risk for sudden death. Therefore, it is imperative that all emergency physicians be familiar with the typical ECG manifestations of Brugada syndrome. Three illustrative cases are presented with a review of the syndrome. (Am J Emerg Med 2003;21:146-151. Copyright 2003, Elsevier Science (USA). All rights reserved.)

In 1992, Pedro and Josep Brugada described a new syndrome that was associated with sudden death in individuals with a structurally normal heart and no evidence of atherosclerotic coronary disease.^[1] Patients with this syndrome were noted to have a distinct set of electrocardiographic abnormalities, characterized by a right bundle branch block (RBBB) pattern with sinus tachycardia (ST)-segment elevation in the right precordial leads. This syndrome is known in the medical literature as “Brugada syndrome.”^[2] Since its first formal description in the medical literature, this entity has been increasingly diagnosed.^[3] Although originally thought to be primarily a disease in men of Southeast Asian descent, more recent reports have noted the presence of this deadly syndrome in women, children, and in non-Asian ethnic groups.^{[2] [4] [6]} In fact, the syndrome has been reported throughout the world.^[2] Brugada syndrome is now suspected to be responsible for 40% to 60% of what had previously been referred to as “idiopathic ventricular fibrillation.”^[3]

Patients with Brugada syndrome have unpredictable episodes of ventricular tachycardia (most commonly polymorphic^[2]). If this dysrhythmia is persistent, it eventually degenerates into ventricular fibrillation and results in sudden death (unless promptly treated by medical personnel). On the other hand, if the dysrhythmia is self-terminating, it usually results in syncope or near-syncope, depending on its duration. Patients with self-terminating episodes of ventricular tachycardia will often present to physicians for evaluation. When the diagnosis is suspected based on electrocardiogram (ECG) findings, patients should be referred for prompt electrophysiological testing for confirmation of the diagnosis. If the electrophysiological testing is confirmatory, patients must be treated by placement of an internal cardioverter defibrillator (ICD). No antidysrhythmics have been shown to be effective in treating this syndrome and preventing mortality.

All emergency physicians should be familiar with the electrocardiographic (ECG) manifestations of Brugada syndrome to ensure early diagnosis and prompt referral. Failure to diagnose and refer these patients for ICD placement is associated with a high rate of mortality (approximately 30% at 2 years^[2]). Three cases are presented which demonstrate some of the typical ECG manifestations of Brugada syndrome, as well as the consequences of a missed diagnosis.

Case presentations

Case no. 1

A 54-year-old black woman presented to the ED after a witnessed syncopal episode. The duration of unconsciousness was less than 1 minute. The patient did not have any preceding chest pain, shortness of breath, or palpitations. Her medical history was notable for hypertension, but she did not have a history of coronary artery disease, dysrhythmias, or syncope. She did not have a known family history of cardiac disease, syncope, or sudden death. On arrival to the ED she was asymptomatic. Her vital signs and physical examination were normal. An ECG was obtained (Fig 1) and interpreted by the emergency physician (EP) as showing a nonspecific T-wave abnormality; the cardiology interpretation showed a normal sinus rhythm, left atrial enlargement, and incomplete right bundle branch block (IRBBB).

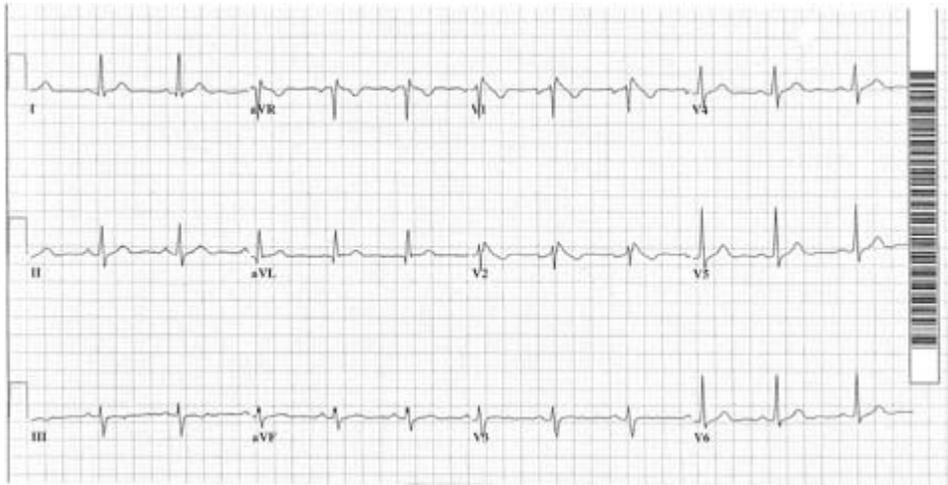


Fig. 1. (Case No. 1) Normal sinus rhythm with left atrial enlargement and incomplete RBBB. ST-segment elevation is seen in leads V1 and V2 with the “coved” morphology.

No previous ECGs were available for comparison.

The patient was admitted to the hospital for evaluation of syncope. Serial cardiac enzyme testing was normal and the patient demonstrated no dysrhythmias during 24-hour cardiac monitoring. The patient was discharged, still asymptomatic, with recommendations for outpatient follow-up at an unspecified date. Twelve hours after discharge, the patient had a witnessed collapse. Paramedics were called immediately. When they arrived, the patient was unconscious, pulseless, and apneic. Her cardiac rhythm on the monitor was polymorphic ventricular tachycardia (Fig 2).



Fig. 2. (Case no. 1) Wide QRS complex tachycardia with multiple QRS complex morphologies, consistent with polymorphic ventricular tachycardia.

Standard advanced life support measures used by the paramedics and subsequently by ED staff was unsuccessful, and the patient died. At autopsy, no cardiac abnormalities were discovered.

Case no. 2

A 40-year-old black man presented to the ED after experiencing three brief episodes of chest tightness and palpitations during the previous 2 days. The episodes were associated with severe lightheadedness. The episodes lasted less than 1 minute, and he could not identify any precipitating factors. He did not have a medical history or family history of cardiac disease. He did admit, however, to frequent alcohol consumption, including vodka the previous day. On arrival to the ED, he was asymptomatic. His vital signs and physical examination were normal. The patient showed no signs of intoxication. An ECG was obtained (Fig 3) and interpreted by the EP as normal; the cardiology interpretation was borderline left ventricular hypertrophy, IRBBB, and benign early repolarization.

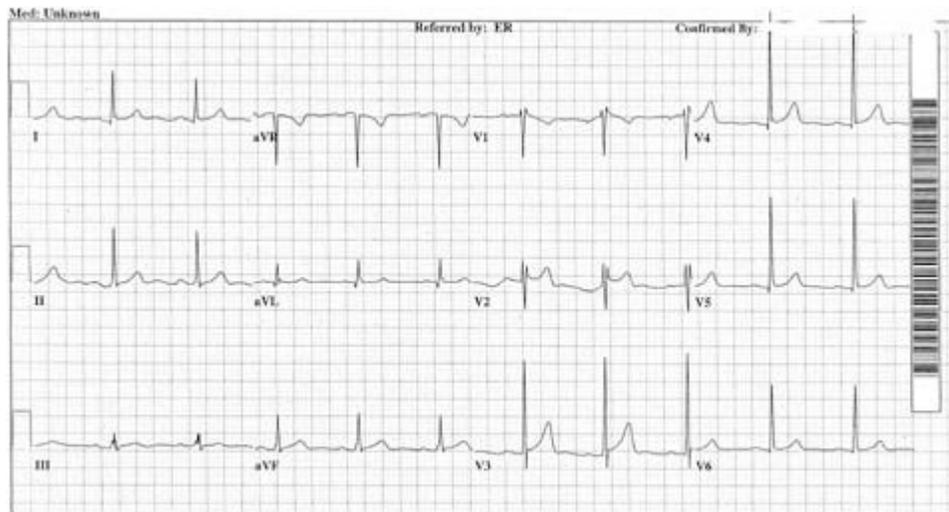


Fig. 3. (Case no. 2) Borderline left ventricular hypertrophy with incomplete RBBB. ST segment elevation was also seen in leads V1-V4 typical of the saddle-type morphology.

An old ECG from the previous year (Fig 4) was obtained but not judged to be significantly different.

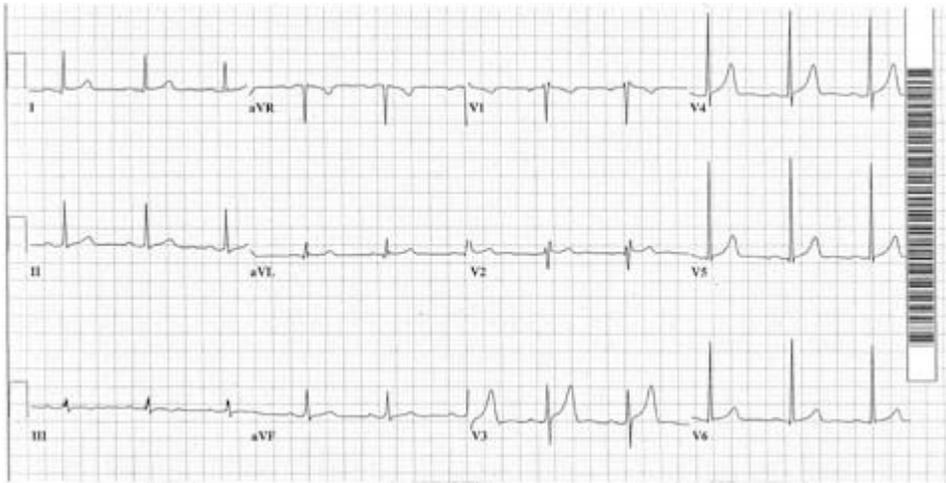


Fig. 4. (Case no. 2) Previous ECG from case no. 2 with incomplete RBBB and no significant change in the ST-segment elevation.

The patient's symptoms were thought to be noncardiac in origin, possibly related to alcohol consumption, and he was discharged from the ED. One week later, the patient had a witnessed collapse. When paramedics arrived, the patient's cardiac rhythm was polymorphic ventricular tachycardia. Despite standard advanced life support measures, his rhythm degenerated into ventricular fibrillation by the time he arrived in the ED (Fig 5) and he eventually was pronounced dead in the ED. Autopsy studies failed to reveal any evidence of underlying cardiac abnormalities.

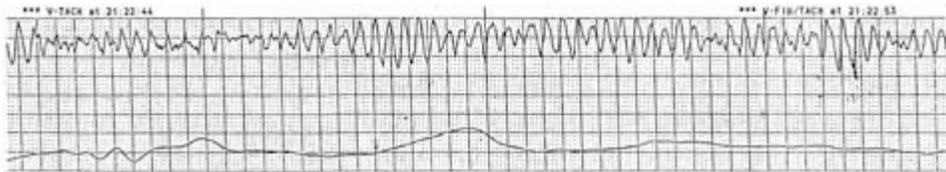


Fig. 5. (Case no. 2) Coarse ventricular fibrillation.

Case no. 3

A 30-year-old black woman presented to the ED after experiencing an episode of chest tightness, palpitations, and near-syncope prior to arrival. The symptoms lasted approximately 3 minutes and occurred while she was walking up a hill. She did not have a history of chest pain, but she did report a history of several syncopal episodes during the previous 10 years. The episodes would occur at rest. She had never been fully evaluated for the cause of these syncopal episodes beyond her ED visits. She did not have a known family history of cardiac disease, syncope, or sudden death. At the time of arrival in the ED, she was asymptomatic. Her vital signs were normal and her physical examination, including cardiac examination, was unremarkable.

An ECG was obtained (Fig 6) and interpreted as showing normal sinus rhythm with an IRBBB and J-point elevation in leads V1 and V2.

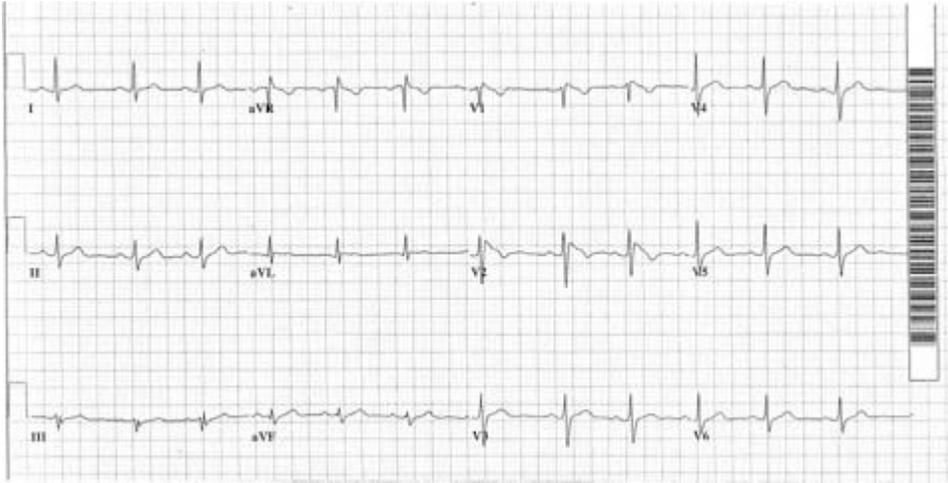


Fig. 6. (Case no. 3) Normal sinus rhythm with incomplete RBBB and ST-segment elevation in leads V1 and V2. The ST-segment elevation demonstrates the “coved” morphology.

A previous ECG from 9 years earlier was obtained (Fig 7) and did not show this same pattern.

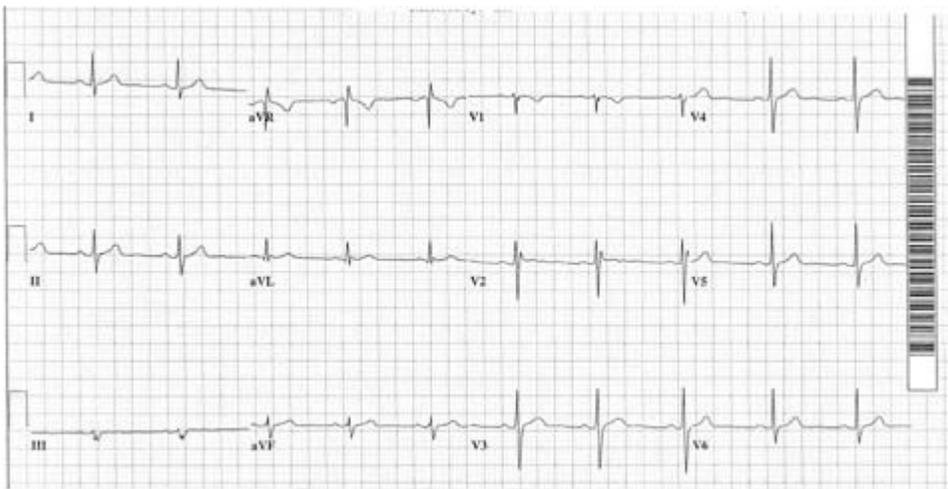


Fig. 7. (Case no. 3) A previous ECG from case no. 3 obtained 9 years earlier did not show the pattern as noted in Figure 6.

The emergency physician evaluating the patient consulted a cardiologist, who recommended admission for acute coronary syndrome based on the abnormal ECG.

Serial cardiac enzyme testing was normal. A stress thallium study performed the next morning was negative for cardiac ischemia, and plans were made for discharge in the

afternoon. Before her discharge, another emergency physician at the same hospital discovered the admission ECG still in the ED and recognized the abnormalities as suggestive of Brugada syndrome. The medical team caring for her was contacted and informed about this diagnosis. A repeat ECG was performed (Fig 8) and showed persistence of the IRBBB pattern with ST-segment elevation in the right precordial leads.

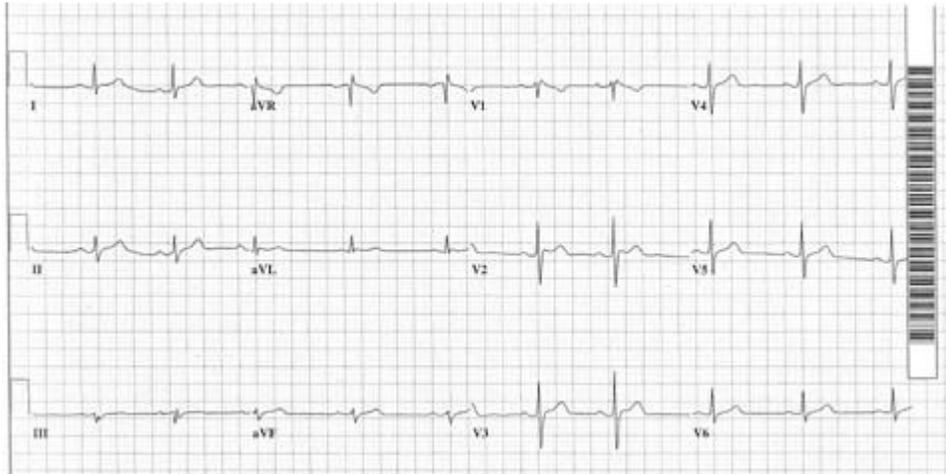


Fig. 8. (Case no. 3) Normal sinus rhythm with incomplete RBBB and ST-segment elevation in leads V1 and V2 without significant change from Figure 6.

The patient was promptly referred for EP testing, where the diagnosis of Brugada syndrome was confirmed. The patient received an ICD and is now doing well.

Discussion

Background

Sudden death from life-threatening dysrhythmias occurs in 250,000 to 350,000 adults in the United States each year,^[7] and ventricular fibrillation is perhaps the most common dysrhythmia encountered in patients experiencing cardiac arrest.^[8] Although most cases of dysrhythmic sudden death are caused by acute cardiac ischemia, it is estimated that 10% to 20% of patients dying suddenly or resuscitated from ventricular fibrillation do not have identifiable atherosclerotic lesions or structural abnormalities.^{[9] [10]} These cases have traditionally been referred to as “idiopathic ventricular fibrillation.” In 1992, Brugada and Brugada reported a series of eight patients with recurrent episodes of aborted sudden death not attributable to atherosclerotic disease or structural abnormalities.^[1] These patients had common clinical and ECG features that distinguished them from other known diseases. It is now thought that the Brugada syndrome is responsible for 40% to 60% of these cases of idiopathic ventricular fibrillation.^[3]

Interestingly, patients with aborted sudden death with the typical “Brugada-type” ECG pattern had previously been described in the late 1980s by Martini et al.,^[11] but Brugada and Brugada were the first to suggest a functional cardiac disorder.^[3] Southeast Asians

have also known about this condition for many decades, and it is known by various regional terms. In the Philippines it is known as “Bangungot” (scream followed by sudden death during sleep); in Japan it is known as “Pokkuri” (unexpected sudden death at night); and in Thailand it is known as “Lai Tai” (death during sleep).^[12] It is the leading cause of natural death in South Asian males younger than 50 years, with annual incidences as high as one death per 1000 inhabitants in Laos.^[2] The increased prevalence in Southeast Asia is attributed to genetic transmission.^[12]

Pathophysiology

A familial occurrence was noted to be present in approximately half of patients with Brugada syndrome, suggesting a genetic component to the disease. Also suggestive of a genetically determined disease is the clustering of first onset of symptoms in the fourth and fifth decades of life.^{[2] [12]} Recent studies confirmed a genetic association: mutations in the gene *SCN5A* that encodes for the human cardiac sodium channel have been identified that essentially produce a “channelopathy.”^{[2] [13] [15]} The result is a loss of proper function of the sodium channel and a predisposition to development of ventricular fibrillation^[2] (a more detailed description of the cellular mechanisms underlying Brugada syndrome is beyond the scope of this review but may be found in ^[3]). The sodium channel dysfunction can be effected by temperature, worsening at higher body temperatures. Medications, including type I antidysrhythmics and other drugs that affect the cardiac sodium channels, can precipitate ventricular fibrillation.^[16] Autonomic disturbances can also play a role in Brugada syndrome.^[17] A circadian pattern has been noted in the development of ventricular fibrillation, with more episodes occurring at night when there is decreased sympathetic activity.^[18]

Diagnosis and treatment

ECG abnormalities that suggest the diagnosis were first described by Brugada and Brugada,^[1] when it was noted that patients with sudden death or aborted sudden death had ECGs with RBBB and ST-segment elevation in leads V_1 - V_3 . However, some authors have stated that many of the published cases as well as subsequent patients diagnosed with Brugada syndrome do not have a true RBBB.^{[3] [4] [19]} Our review of the published cases has found that many patients have an IRBBB pattern, and that the ST-segment elevation is often isolated to leads V_1 and V_2 only.

Two types of ST-segment elevation morphologies have been described in the right precordial leads: convex upward (“coved”) and concave upward (“saddle-type”)^{[3] [4] [20]} ; Figure 9 shows the 2 types of ST-segment elevation associated with Brugada syndrome.

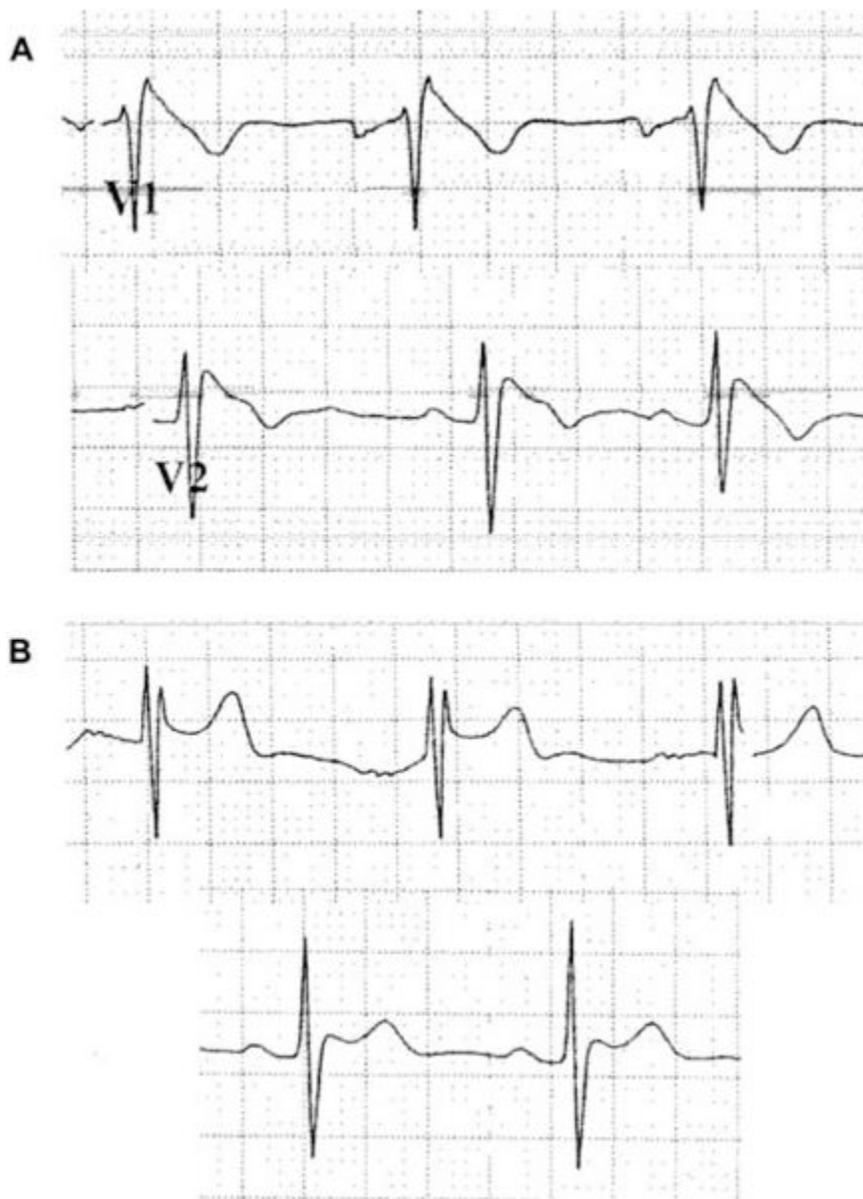


Fig. 9. (A) The “coved”-type ST-segment elevation; note the convex morphology. (B) The “saddle”-type ST-segment elevation; note the concave morphology.

Figures 1 and 6 demonstrate the coved pattern; Figure 3 (lead V_2) shows the saddle-type pattern. Physicians should be aware that these ECG abnormalities are not static; they can change with time. The ECG morphologies can transform from one type to the other or may normalize completely.^{[3] [20]}

A presumptive diagnosis of Brugada syndrome is often made when patients with the typical Brugada-type ECG pattern develop sudden death. Patients with this ECG pattern who have aborted sudden death (self-terminating or medically treated ventricular tachycardia/ventricular fibrillation), syncope, or other symptoms that suggest the

presence of dysrhythmias should be referred for EP testing for confirmation of the diagnosis. Patients with a family history of sudden death who have the ECG pattern should also be referred for EP testing. There is debate regarding the proper workup of asymptomatic individuals with no family history of sudden death who have the ECG pattern.^{[2] [5]} However, malignant dysrhythmias reportedly occur in one third of initially asymptomatic patients within a 2-year period if they have the typical ECG pattern.^[12] This strongly argues in favor of referring even asymptomatic patients with the Brugada-type ECG pattern for EP testing.

During EP testing, patients with Brugada syndrome will have inducible polymorphic ventricular tachycardia during programmed electrical stimulation. The induced dysrhythmia is sustained in almost all cases and results in hemodynamic collapse, requiring electrical cardioversion for termination.^[12] Electrophysiologists can further confirm the diagnosis by administering class I medications (ajmaline, flecainide, procainamide), which will increase the ST-segment elevation in patients with Brugada syndrome. Once the diagnosis is confirmed, patients must be treated with placement of an ICD. When provided with an ICD, mortality at 10-year follow-up has been 0%.^[12] The use of antidysrhythmics, including beta-adrenergic blocking agents and amiodarone, has not been demonstrated to confer any benefit.^[2]

Brugada syndrome and children

It is important to note that in Brugada's first description of this syndrome, ^[1] three of the eight patients reported were children. Other authors have also suggested Brugada syndrome as a possible cause of sudden cardiac death in children, even in the first months of life in which it can be misdiagnosed as sudden infant death syndrome.^[6] Brugada has recommended that an ECG should be a routine examination of each newborn to search for this syndrome (as well as long QT syndrome).^[2] The sensitivity, specificity, and cost-effectiveness of this recommendation is unknown. However, physicians should include Brugada syndrome in the differential diagnosis of infants and children with aborted sudden death or syncope.

Conclusion

Brugada syndrome was first reported 10 years ago. Since that time, it has been diagnosed with increasing frequency. The diagnosis should be suspected in patients who have the typical findings in the right precordial leads of the ECG: an RBBB or IRBBB pattern with ST-segment elevation. Patients suspected of having Brugada syndrome should be promptly referred for EP testing and treatment. Rapid referral and placement of an ICD is associated with an excellent prognosis, whereas failure to diagnose this condition is associated with a high risk for sudden death. Therefore, it is imperative that all emergency physicians be familiar with the typical ECG manifestations of Brugada syndrome.

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