Diagnosis of Brugada Syndrome, a Rare Inherited Arrhythmogenic Disorder

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Keywords

Brugada syndrome · Genetic disorder · Ajmaline test · Electrophysiology study · Sudden cardiac death

Abstract

Brugada syndrome (BrS) is a rare, autosomal dominant genetic disorder with mutation in the *SCN5A* gene. It is associated with an increased risk of arrhythmias and sudden cardiac death. BrS can be diagnosed by characteristic electrocardiogram (ECG) findings and significant events, such as syncope, palpitations, nocturnal respiratory apnea, and family history of sudden cardiac death below the age of 45 years. Special investigations, such as electrophysiology study, ajmaline provocation test, and genetic testing, play an important role in its diagnosis. This case report describes a patient who presented with chest pain and dizziness along with a positive family history of sudden cardiac deaths below the age of 45 years. He was discovered to have type 2 Brugada pattern on ECG, and by ajmaline provocation test, the type 1 pattern was unmasked, which established a definitive diagnosis of BrS. The patient was then advised for an implantable cardioverter-defibrillator. This case highlights the need for physicians to be competent in identifying patients with BrS in order to provide the necessary management and prevent fatal outcomes.

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Introduction

Brugada syndrome (BrS) is named by the Spanish cardiologists Pedro Brugada and Josep Brugada who reported it as a distinct clinical syndrome in 1992 [1]. The worldwide prevalence of BrS was estimated at 0.01% and is highly prevalent in Southeast Asia [2]. BrS is an autosomal dominant genetic disorder. Incomplete penetrance is frequent in families, and the disease can be sporadic in up to 60% of patients. *SCN5A*, which was identified as the first BrS-associated gene, has emerged as the most common gene associated with this condition. BrS is also characterized by abnormal findings on the surface electrocardiogram (ECG) in conjunction with an increased risk of ventricular tachyarrhythmias and sudden cardiac death [3]. BrS is associated with other conduction abnormalities, including first-degree atrioventricular block, intra-ventricular conduction delay, and sick sinus syndrome. There is an increased risk of atrial arrhythmias, most notably atrial fibrillation, which in turn has been associated with increased disease severity and a higher risk of ventricular fibrillation. Given its potential consequences, physicians must be familiar with the electrocardiographic features of BrS. The following case report describes the importance of taking a detailed history and performing the necessary workup in order to diagnose BrS in a young male.

Fig. 1. Type 2 Brugada pattern during first encounter.

Case Report

A 24-year-old Indian male, a known case of hypertension, with no compliance to medication, presented to the Emergency Department with chest pain and dizziness. He presented early in the morning with sharp pricking, moderate-intensity, left-sided chest pain which started gradually and had been progressively increasing in intensity with radiation to the upper back and associated dizziness. The pain exacerbated on exercise but was present even at rest. He had no complaints of palpitations, dyspnea, syncope, leg swelling, or vomiting. He had been having intermittent episodes of chest pain for the past 3 years, which used to settle within a few minutes. Dizziness had been present on and off for a year as well, occurring twice a week and lasting for a few minutes. It occurred more frequently when he was stressed and was associated with headaches, darkening of vision, and chest pain. Headache was generalized but more at the occipital region and pressing in nature. It often occurred following an episode of dizziness without any radiation. There was no history of vomiting, tinnitus, and loss of weight or appetite.

Three-generation family history was looked into and showed that his brothers died at an early age. One died at 3 days of age due to an unknown cause and the other died at 14 years of age due to heart failure. His paternal aunt died at 40 years of age due to cardiac arrest.

He was a known case of hypertension for 3 years with baseline blood pressure of 160/90 mm Hg and not compliant with medicines due to financial reasons. He underwent an eardrum repair surgery and appendectomy in 2014 and 2017, respectively. He did not take any medicines and had no known allergies. He was unmarried, worked as a cleaner, and was a nonsmoker and occasional drinker. On clinical examination, the patient was lying comfortably on the bed, oriented, alert, and not in distress. He had a temperature of 36.4 °C, respiratory rate of 21/min, pulse rate of 90/min, and blood pressure of 162/101 mm Hg. His pulse was of reg-

ular rhythm, character, and volume. He had no evidence of jugular venous distention, visible precordial pulsations, hepatomegaly, or pedal edema. Auscultation of his chest revealed normal S1, S2, and no other added sounds. Other system examinations were unremarkable.

Investigation and Management

A 12-lead ECG on arrival showed normal sinus rhythm with the presence of saddle back ST-T wave configuration in V2, which was consistent with type 2 BrS pattern as well as incomplete right bundle branch block (Fig. 1). Complete blood count revealed microcytic hypochromic red blood cells with hemoglobin of 14.9 g/dL, white blood cell count of $7.9 \times 10^3/\mu\text{L}$, and platelets of $209 \times 10^3/\mu\text{L}$. Electrolytes, thyroid function tests, random blood glucose, HbA1c, urea, creatinine, creatine kinase isoenzyme MB, NT-pro-BNP, and troponin T values were within normal limits. HIV 1 and 2 antigen and antibody and hepatitis B surface antigens were non-reactive. His lipid profile revealed elevated triglycerides of 225 mg/dL and a low high-density lipoprotein of 40 mg/dL. Chest X-ray was unremarkable. Computed tomography of the brain was normal with no evidence of infarct or intracerebral/extracerebral bleed. Transthoracic echocardiogram was done to rule out structural causes. It showed normal cardiac anatomy and function.

Lisinopril 5 mg was administered in the Emergency Department, and the patient was admitted to the Cardiology Ward to further evaluate the suspicion for BrS. Ajmaline provocation test was conducted by infusing ajmaline at a rate of 1 mg/min. The resuscitation equipment and defibrillator were kept ready to be used in the event of a cardiac arrest. ECG was monitored and 12-lead ECG was printed every 1 min. At 5 min, ECG showed classical type 1 Brugada pattern (Fig. 2), and the test was terminated. He was closely monitored for another 90 min for the occurrence of any life-threatening arrhythmias. However, he remained asymptomatic and hemodynamically stable, and the ECG gradually settled back to type 2 pattern.

Fig. 2. Conversion of type 2 Brugada pattern to type 1 after ajmaline test.

An implantable cardioverter-defibrillator along with a follow-up in the clinic was planned for the management; however, the patient refused due to financial reasons.

He was then counselled about avoiding the conditions that can trigger arrhythmias. He was advised to avoid hot showers and steam bath, to treat fever promptly with antipyretics, avoid excessive alcohol intake, and was also provided with the list of medications that should be avoided.

Discussion

Individuals with BrS may experience ventricular arrhythmias, syncope, and nocturnal agonal respiration or may be asymptomatic. The severity of symptoms varies from person to person. There are some known triggers for BrS like fever, cocaine, and sodium-blocking drugs. Another specific presentation seen in BrS is sudden unexpected nocturnal death syndrome and sudden infant death syndrome, which is the death of a child within the first year of life without an identifiable cause [1].

Patients with typical ECG features who are asymptomatic and have no other clinical criteria are said to have the Brugada pattern. Patients with typical ECG features who have experienced sustained ventricular tachyarrhythmia, or who have one or more of the other associated clinical criteria, are said to have BrS [4].

Three ECG patterns of ST segment elevation have been associated with BrS. Type 1 displays ≥ 2 mm of downsloping or cove-shaped ST segment elevation followed by a negative T wave in the right precordial leads. Type 2 has ≥ 2 mm of ST elevation at the terminal por-

tion of the ST segment, with a positive T wave that creates a saddleback appearance, and type 3 may have either cove-shaped or saddleback ST segment elevation with < 1 mm magnitude of elevation at the terminal portion.

Definitive diagnosis of BrS requires the presence of a type 1 ECG pattern or conversion of a type 2 or type 3 pattern to type 1 following provocation testing with a sodium channel blocker, plus one of the following: documented ventricular fibrillation, self-terminating polymorphic ventricular tachycardia, family history of sudden cardiac death at age < 45 years, type 1 ECG pattern in a family member, electrophysiological induction of ventricular tachycardia, unexplained syncope felt consistent with a tachyarrhythmia, or nocturnal agonal respirations [5].

In our case, the patient complained of chest pain associated with dizziness, and ECG showed type 2 Brugada pattern in V2 with associated incomplete right bundle branch block. Upon ajmaline provocation test, the type 2 pattern was converted to a type 1 Brugada pattern. This characteristic conversion of the ECG pattern along with the positive family history of sudden cardiac death below the age of 45 years indicated a definitive diagnosis of BrS in this patient. An implantable cardioverter-defibrillator would be the best management for this patient.

Screening his family members with ECG and genetic testing is recommended to identify the positive cases, and even if they are asymptomatic, this would help in determining who would require counselling on the precautionary methods and would require close follow-up.

Conclusion

BrS has specific clinical characteristics and can be diagnosed with a thorough history, ECG, and relevant investigations. This case highlights the need for physicians to be competent in identifying high-risk patients with BrS to prevent the risk of sudden cardiac death and life-threatening arrhythmias.

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Statement of Ethics

Patient consent for publication was obtained from the patient.

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Disclosure Statement

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