SHORT COMMUNICATION

Brugada Syndrome with atypical characteristics: Case report

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Abstract The Brugada Syndrome (BrS) is a heterogeneous genetic disease characterized by persistent or transient ST-segment elevation in the right precordial electrocardiography (ECG) leads and a high incidence of sudden death and life-threatening ventricular tachyarrhythmias in patients with structurally normal hearts. The syndrome generally manifests in men during adulthood. The ECG manifestations can be overt or concealed. We report a case of BrS whose type 1 ECG pattern during febrile state converted to type 2 ECG after alleviation of fever with atypical characteristics (78-year-old woman with monomorphic ventricular tachycardia on holter monitoring, a history of the sudden infant death of her child, and without inducible ventricular arrhythmia by programed ventricular stimulation [PVS]).

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1. Introduction

The Brugada Syndrome (BrS) is a heterogeneous genetic disease characterized by persistent or transient ST-segment elevation in the right precordial ECG leads and a high incidence of sudden death and life-threatening ventricular tachyarrhythmias in patients with structurally normal hearts. It is estimated to cause 4–12% of all sudden cardiac deaths and up to 20% among patients without structural heart abnormalities in some regions of the world.1 The syndrome is inherited as an autosomal dominant trait. Since it was linked to mutations in the SCN5A gene that encodes the α subunit of the cardiac sodium channel protein, more than 80 mutations have been linked to the syndrome in the SCN5A gene.2 Although the genetic mutation is equally distributed between the sexes, the clinical phenotype is 8–10 times more prevalent in males than in females.3 The ECG manifestations can be overt or concealed that can be unmasked by sodium channel blockers, during a febrile state, or with vagotonic agents.2

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We report a case of BrS whose type 1 ECG pattern during febrile state converted to type 2 ECG after alleviation of fever with atypical characteristics (78-year-old woman with monomorphic ventricular tachycardia on holter monitoring, a history of sudden infant death of her child and without inducible ventricular arrhythmia by programed ventricular stimulation [PVS]).

2. Case report

A previously healthy 78-year-old woman was admitted to the emergency department following recurrent syncopal episodes with fever, weakness, shortness of breath, and cough symptoms. Her son reported that the patient had two episodes of loss of consciousness. The first episode lasted about 1–2 min and the patient regained consciousness without confusion soon afterward. The second episode occurred 5 min after the first episode while the patient was sitting on the bed. The son denied that she had any accompanying seizure activity. Her past medical history was normal and she denied taking any drugs or having chest pain.

During the initial physical examination, she was alert, blood pressure was 105/70 mmHg, heart rate was 80 beats/min, and body temperature was 39.0 °C. Cardiac auscultation showed normal heart sounds with no murmur or friction rub. Chest auscultation revealed bilateral rhonchi and inspiratory crackles in the right lower lung. The neurological examination was normal. Initial laboratory data showed leukocytosis (14,400/mm³), elevated C-reactive protein (189 mg/l), and normal blood chemistry, including potassium (4.3 mEq/L), cal-

Figure 1  (A) A 12-lead ECG, recorded while the patient was febrile, showing downsloping ST-segment elevation in leads V1–V2, consistent with a type-I (coved) Brugada ECG pattern. (B) ECG, taken several hours after the alleviation of fever, converted to a type-2 (saddle-back) Brugada ECG pattern.
cium, magnesium, and serial cardiac markers (troponin I, and CK-MB). The chest X-ray showed hazy infiltrates in the right lower lung. A cranial computed tomography was unremarkable, except for cerebral atrophy. A 12-lead ECG (Fig. 1A), recorded while the patient was febrile (temperature 39.0 °C), showed downsloping ST-segment elevation in leads V1–V2, consistent with a type-I (coved) Brugada ECG pattern.

She was transferred to the cardiac intensive care unit for continuous ECG monitoring and was treated with intravenous paracetamol. A second ECG (Fig. 1B) taken several hours after the alleviation of fever, converted to a type-2 (saddleback) Brugada ECG pattern. An echocardiogram showed normal systolic function and the absence of segmental wall motion abnormalities. Her family history was significant for the sudden unexplained infant death (9 months of age) of her son. Ambulatory ECG monitoring showed monomorphic short-run ventricular tachycardia. Pneumonia was healed with an antibiotic (Ceftriaxone) and an antipyretic (Paracetamol) for 10 days. The patient was diagnosed with BrS and as the patient had syncope and a positive family history of sudden cardiac death, an implantable cardioverter defibrillator (ICD) implantation was suggested. Because of these factors, together with her age and her request that an ICD not be implanted, a subsequent electrophysiological study (EPS) was performed for risk stratification and no ventricular arrhythmias were induced. Quinidine was administered and the patient was recommended to receive urgent antipyretic treatment for fever that might induce Brugada-like ECG changes. Electrocardiogram screenings were negative for consenting family members. One year after her discharge, the patient remained alive and free of cardiac events and syncope.

3. Discussion

BrS is definitively diagnosed when a type 1 ST-segment elevation is observed in >1 right precordial lead (V1–V3) in the presence or absence of a sodium channel-blocking agent and one of the following: documented ventricular fibrillation (VF), polymorphic ventricular tachycardia (VT), a family history of sudden cardiac death at <45 years old, coved-type ECGs in family members, inducibility of VT with programmed electrical stimulation, syncope, or nocturnal agonal respiration. A new consensus document defines only two ECG patterns to be considered. Type 1 is identical to the classic type 1 described in the previous consensus, although the new type 2 pattern combines patterns 2 and 3 of the previous consensus. The syndrome predisposed to malignant ventricular arrhythmias generally manifests in men and during adulthood. It is reported that the youngest patient with the BrS was two days old and the oldest was 84. Infants with an unidentified cause after a postmortem investigation are labeled as having suffered from sudden infant death syndrome (age <1 year) (SIDS), and it has been reported that an estimated 10% of SIDS stems from mutations in channelopathy-susceptibility genes that cause potentially lethal syndromes such as long QT syndrome, catecholaminergic polymorphic ventricular tachycardia, and BrS. Our patient and her dead son are at both ends of this range and confirm the association of BrS and SIDS. Unfortunately, genetic testing was not performed for our patient.

Fever-induced Brugada cases have been previously reported in the literature. Mutant sodium channels exhibiting temperature-dependent gating changes have been reported to give rise to fever-induced ventricular arrhythmias in BrS by significantly reducing the sodium currents in the hyperthermic state. Junttila et al. reported that regardless of the existence of a predisposing genetic base, most of their patients with fever and a Brugada-type ECG developed malignant arrhythmias shortly after the onset of the fever. Thus, fever that can unmask BrS and precipitate symptoms associated with malignant arrhythmias, as it did in our patient, should be treated rapidly with antipyretics in these patients.

A polymorphic VT is most commonly associated with the BrS. Monomorphic VT is rarely observed and is more prevalent in children. In contrast, our patient displayed short-run monomorphic VT during a 24-h Holter ECG monitoring.

Symptomatic patients displaying the type 1 Brugada ECG (spontaneously or after a drug challenge) who present with aborted sudden death are at a high risk for recurrence and they should receive an ICD without an additional need for EPS. The guidelines also recommend that patients with a clinical picture of arrhythmia-mediated syncope or nocturnal agonal respiration and a type 1 ST-segment elevation should receive the protection of an ICD after noncardiac causes of these symptoms have been carefully ruled out. The patient was recommended for an ICD implantation according to the current guidelines. Because of these factors, together with her age and the request of the patient that an ICD not be implanted, a subsequent EPS was performed for risk stratification, although the role of PVS in BrS is controversial and no ventricular arrhythmias were induced. In our case, fever-induced BrS cases undergoing EPS, which failed to induce ventricular arrhythmia despite the presence of the symptoms, have been described in the literature and the role of PVS remains a challenge in this population.

Our patient did not receive an ICD and so low-dose quinidine (550 mg) was administered orally. Quinidine’s effectiveness has been demonstrated to prevent VT/VF induction by PVS and concluded as a therapeutic option, though its long-term efficacy in the prevention of SCD has not been studied. One year after discharge, our patient remained alive and free of cardiac events and syncope.

In conclusion, BrS should be kept in mind not only in young male patients, but also in women and older patients who present with fever and symptoms associated with malignant arrhythmias and ST elevations. The fever should be treated rapidly with antipyretics as it can precipitate VT/VF. Risk stratification remains a challenge and the role of PVS needs to be evaluated in fever-induced BrS. Further clinical evaluations are needed to establish the effectiveness of quinidine in BrS as an alternative to an ICD.

References
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