CASE REPORT

Brugada syndrome with elevated cardiac biomarkers

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SUMMARY

A 45-year-old man presented to our hospital with a history of palpitations, presyncope and chest pain. Vital signs and physical examination were unremarkable. Initial ECG revealed sinus rhythm with non-specific ST changes. Subsequent ECGs showed rsr' in V1 and saddle-back pattern of ST elevation in lead V2, indicative of type 2 Brugada ECG pattern. Telemetry monitoring revealed multiple runs of asymptomatic non-sustained polymorphic ventricular tachycardia. Ajmaline challenge test confirmed the diagnosis of Brugada syndrome. The subsequent rise and fall of cardiac biomarkers was suggestive of acute myocardial infarction which was refuted by having normal coronaries by cardiac catheterisation. Echocardiogram showed normal cardiac structures and function without any evidence of myopericarditis. Automated intracardiac defibrillator was recommended which the patient declined.

BACKGROUND

First described in 1992, Brugada syndrome (BS) is characterised by abnormal ECG patterns and increased risk of sudden cardiac death (SCD). For the diagnostic criteria of BS, the patient needs to have type 1 ECG pattern (coved ST-segment elevation) in V1–V3 either spontaneously or after sodium channel blocker test in conjunction with one of the following: documented ventricular arrhythmia, positive family history of SCD before 45 years and arrhythmia-related symptoms such as syncope, seizures or nocturnal agonal respiration.¹

This syndrome was recognised as sudden unexpected nocturnal death syndrome in healthy men younger than 50 years. It is considered to be endemic in Southeast Asian countries like Japan (12/10 000),² Thailand and Philippines. The incidence of BS is not well established in the Middle East. The clinical presentation of patients with BS can vary from being asymptomatic, to having syncope, atrial fibrillation, ventricular arrhythmias or even sudden death. BS may be precipitated by different medications and conditions like fever and electrolytes abnormalities. Conditions leading to elevated troponin have not been implicated as precipitants of BS. We describe the first reported case of BS associated with high cardiac enzymes, angiographically normal coronary arteries and without evidence of myopericarditis.

CASE PRESENTATION

A 45-year-old previously healthy man presented to our hospital with first episode of palpitations associated with dizziness. These symptoms were followed by severe central chest pain which prompted his visit to the emergency room. The patient denied any recent constitutional symptoms. He does not take

any prescribed or over the counter medications. Review of systems, medical, surgical and family history was unremarkable. He was physically active, and works in a local grocery store. There is no history of tobacco, alcohol or illicit drug use. Physical examination in the emergency room revealed a well built man, in mild distress. Core body temperature was 38°C and respiratory rate 18 breaths/min. His blood pressure was 150/90 mm Hg and heart rate 90 bpm. His general physical, cardiac and rest of the clinical examination were normal.

INVESTIGATIONS

Baseline laboratory investigations including serum electrolytes, lipid profile, complete blood count, liver and kidney function tests were normal. His chest X-ray was unremarkable. Echocardiogram showed chambers with normal size and function. The pericardium, the valves and other cardiac structures were normal.

Cardiac biomarkers followed a typical myocardial infarction pattern with rapid rise and fall of troponin I and creatine kinase (figure 1). Presentation troponin I and CK-MB of 0.72 and 12.2 mg/dL peaked at 9.3 and 50.6 mg/dL, respectively within 24 h prior to declining. Cardiac catheterisation showed angiographically normal coronaries.

Initial ECG showed normal sinus rhythm, normal intervals and non-specific ST changes. Subsequent ECG performed a couple of hours later revealed rsr' in V1 and V2 and saddle-back pattern of ST elevation in V2, suggestive of type 2 Brugada ECG pattern (figure 2).

His hospital course was complicated by telemetry monitor showing multiple episodes of asymptomatic non-sustained polymorphic ventricular tachycardia (VT), 110–120 bpm.

The diagnosis of BS was confirmed by ajmaline challenge test.

Type 1 Brugada ECG pattern either spontaneously or after sodium channel blocker test is necessary for the diagnosis of BS and characterised by the presence of pseudo right bundle branch block and coved ST-segment elevation >2 mm in V1–V3 leads (figure 3). Type 2 BS ECG pattern consist of saddle-back ST elevation >1 mm in V1–V3 leads as compared with type 3 ECG pattern in which saddle-back ST elevation <1 mm in the same leads.¹ The ECG findings typically fluctuate over time between the three BS ECG patterns or even becoming normal.^{3 4} The yield and sensitivity of ECG to detect those findings can be increased by placing the right precordial chest leads up to the second or third intercostal spaces.⁵ The role of ST elevations in more than one right pericardial leads including V3 for the diagnosis

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Figure 1 Rise and fall of cardiac biomarkers.

of BS has been studied by Richter *et al.* Type 1 BS ECG patterns of 186 patients were studied, the ST elevation in V3 did not yield any additional diagnostic information and ST elevation in one pericardial lead (V1 or V2) provided the same clinical outcome when compared with ST elevation in more than one lead.⁶

Patients with Brugada type 2 or type 3 ECG patterns need to have sodium channel blocker test to unmask the diagnostic type 1 ECG pattern. Sodium channel blockers like flecainide, ajmaline, procainamide and pilsicainide can be used and current data indicate that ajmaline is probably the best drug of choice.⁷

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of BS with elevated cardiac enzymes include

- ▶ Pulmonary embolism
- ▶ Acute right ventricular (RV) myocardial infarction
- ▶ Acute pericarditis/myopericarditis
- ▶ Arrhythmogenic RV cardiomyopathy
- ▶ Sepsis
- ▶ Acute pulmonary embolism
- ▶ Acute and chronic heart failure

Figure 2 The rsr' pattern in V1 and saddle-back shaped ST-segment elevation in V2 (type 2 Brugada ECG pattern).

Figure 3 After sodium channel blocker, ECG showed coved ST-segment elevation in V2, rs' pattern in V1 and V2 (type 1 Brugada ECG pattern).

TREATMENT

The patient refused further electrophysiological studies and implantation of automated intracardiac defibrillator (AICD). He was counselled and educated about different management options and informed about the risk of sudden death precipitated by different medications and conditions. Moreover, he was instructed to search the website (<http://www.brugadadrugs.org/avoid/>) prior to taking any medication.

The patient was informed about the availability of genetic testing, ECG screening for family members and avoidance of provoking factors.^{8 9}

The only proven treatment that decreases the risk of SCD in patients with BS is an AICD.^{1 10} Studies are ongoing to explore the effectiveness of quinidine¹¹ and other pharmacological agents that might decrease arrhythmic risk in patients with BS. Isoproterenol (which increases the L-type calcium (ICaL) current), might be useful for treating electrical storm in BS.¹⁰

OUTCOME AND FOLLOW-UP

At 2 months follow-up the patient is doing well. He denied any episode of palpitation or syncope. The patient was recounselled about the need of AICD and screening the other family members.

DISCUSSION

BS is an autosomal dominant inherited disorder, accounting for 4% of all causes of SCD. It has variable penetrance, predominantly affecting men (80% of patients) more than women, with a ratio 9:1¹² and mean age at diagnosis is between 40 and 45 years.¹ Although there are reported cases of BS in childhood (mean age 8 ± 5 years), affecting both gender equally and the symptoms (syncope, VT, supraventricular tachycardia and sudden death) triggered mainly by febrile illness.¹³ The effects of sex hormones (testosterone) on the cardiac ionic currents and predominant of BS in adult males is yet under investigation.^{14 15} The recent molecular and genetic research has revealed many genetic defects associated with BS. These include ionic imbalance during phase 1 of cardiac action potential, mutation involving the SCN5A, KCNE3, KCNE5¹⁶ and KCND3¹⁷ genes.

The clinical manifestations of BS are more common at night,¹⁸ during rest, postprandial and during recovery from

exercise,¹⁹ as a result of increased parasympathetic tone. The clinical signs and symptoms are unmasked with fever,²⁰ electrolyte imbalances like hyperkalaemia or hypercalcaemia, as well as metabolic derangements due to cocaine²¹ and alcohol intoxication. Medications like antiarrhythmic drugs, antidepressant and other psychotropic drugs, etc, may precipitate a clinical event.²² In this case, the patient had symptoms of palpitation at rest, after a heavy meal, but without other known precipitating factors. Initially the cardiac biomarkers were mildly elevated which is unusual in BS. Investigation to rule out the common causes of such troponin rise and fall were excluded by having normal coronary arteries with no evidence of myopericarditis. Arrhythmia causing this amount of troponin leak is improbable. Whether another clinical variant of BS causing troponin leak exists, needs further investigation.

BS patients with syncope, SCD, ventricular arrhythmia or spontaneous ST-segment elevation are at higher risks for subsequent arrhythmic events.^{23–25} Family history of SCD has not been found to increase the risk of arrhythmia in patients with BS.²⁶ Asymptomatic BS patients with drug-induced type 1 ECG are at lower risk of arrhythmic events, with estimated annual risk 0.5% per year.^{26 27} The risk stratification for asymptomatic BS patients is considered one of the challenges for the current studies. The Second Consensus on BS (2005) recommends that patients who are asymptomatic but with spontaneous type 1 ECG pattern need to have electrophysiology study (EPS) in order to determine the inducibility of ventricular arrhythmia and implantation of implantable cardioverter-defibrillator (class IIa).¹ On the other hand, in 2006 the American Heart Association/American College of Cardiology/European Society of Cardiology (AHA/ACC/ESC) guidelines for prevention of SCD, indicated that the evidence is limited to support the use of EPS in patients who are asymptomatic but with spontaneous type 1 BS ECG pattern (class IIb).¹⁰ The PRogrammed ELectrical stimulation preDICTive value (PRELUDE) study showed that around 40% of 308 patients with BS have positive electrophysiology studies and during the 34 months follow-up, 14 arrhythmic events occurred. Interestingly, 9 of 14 arrhythmic events occurred in patients with negative EPS results.²³

Our patient is considered at high risk for arrhythmic events because he was symptomatic and had documented paroxysmal VT and would benefit from an AICD.

Learning points

- ▶ The diagnosis of Brugada syndrome can be challenging, the typical Brugada ECG patterns may fluctuate over time.
- ▶ Patients with Brugada syndrome and elevated cardiac biomarkers need further investigations to determine the aetiology of myocardial injury.
- ▶ Implantation of implantable cardioverter-defibrillator is the only proven and effective treatment for patients with Brugada syndrome.
- ▶ The prognostic significance of elevated cardiac markers with normal coronary angiogram in patients with Brugada syndrome is unclear.

Contributors All the authors contributed to editing and research, approved the final version of the manuscript and were involved in patient interview and care.

Competing interests None.

Patient consent Obtained.

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