CASE REPORT

Antiarrhythmic Induced Electrical Storm in Brugada Syndrome: A Case Report

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Brugada syndrome (BS) may be "unmasked" by several pharmacological and/or physiological agents in an otherwise normal electrocardiogram. Once diagnosed the possibility of persistent ventricular tachycardia/fibrillation exists. Although this is treated with various antiarrhythmic agents, there remains a cohort of patients who fail to respond to conventional antiarrhythmic therapy therefore, amplifying the electrical storm. We report a case of a BS diagnosed via procainamide challenge, the resultant near fatal electrical storm aggravated by amiodarone and the eventual resolution with isoproterenol.

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antiarrhythmic agents; Brugada syndrome; ventricular tachycardia; ventricular fibrillation; electrical storm

INTRODUCTION

The Brugada syndrome (BS) was first described in 1992 as a distinct arrhythmogenic entity that may lead to sudden cardiac death (SCD) in patients without overt structural heart disease.¹ This syndrome exhibits specific ECG characteristics: a widened QRS complex with a right bundle branch block pattern and ST segment elevation and T-wave inversion in the right precordial leads.² The distinctive ECG appearance may be transient, making the identification of patients at risk for SCD difficult. BS is a direct result of a genetic defect of the SCN5A gene coding for the sodium ion channel. A reduction in sodium channel current can generate heterogeneity of repolarization and increase the risk of intramyocardial re-entry.¹⁻³

When the ECG is normal, BS may be "unmasked" by various stimuli including potent sodium channel blockers. Various pharmacological provocative agents can be utilized in this manner to support the diagnosis of BS.⁴

In this report we describe BS diagnosed only after pharmacological provocation, the subsequent near fatal electrical storm and the resolution of the electrical storm with isoproterenol, a beta-adrenergic agonist.

CASE REPORT

A 45-year-old female with no known cardiac disease and a history of two episodes of syncope over a 5-year period presented to the emergency room following another syncopal event. The patient did not report any family history of syncope or premature/sudden death. The initial ECG revealed sinus rhythm (SR) with normal QRS and QT intervals. There were no ST segment, T wave or conduction abnormalities present (Fig. 1). Electrolytes and cardiac markers were within normal limits.

Continuous telemetry monitoring over the course of the first 12 hours revealed occasional short episodes of nonsustained polymorphic ventricular tachycardia (VT). Diagnostic studies included

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Figure 1. Baseline ECG.

two-dimensional echocardiography and an exercise treadmill test. There was no evidence of left or right ventricular pathology on two-dimensional echocardiogram, and the exercise test provided normal results. Due to the presence of nonsustained polymorphic VT, an electrophysiology study (EPS) was performed. With routine programmed stimulation, there was no inducible VT. Procainamide 750 mg intravenously (IV) was then administered and immediately produced marked right precordial ST segment elevations of 2–3 mm resembling a "saddleback type" pattern, accompanied by monomorphic premature ventricular contractions (Fig. 2).

The diagnosis of BS was established and therapeutic options were discussed with the patient.

The patient was returned to the telemetry unit after the conclusion of the EPS study. About 30 minutes later, the patient experienced a syncopal event with repeated episodes of polymorphic VT, which then degenerated into ventricular fibrillation (VF) requiring external defibrillation. Polymorphic VT recurred repeatedly and IV amiodarone 150 mg, was administered by the emergency response team and then via infusion. Minutes later VT/VF recurred and was terminated promptly with defibrillation. Additional amiodarone boluses were

Figure 2. ECG consistent with Brugada syndrome following procainamide administration.

Figure 3. VT/VF electrical storm.

given. The surface ECG recurrently demonstrated VT and VF (Fig. 3) and many defibrillations were required. Amiodarone was discontinued. Isoproterenol 1 mcg/min IV was started. After a few hours the 12 lead ECG normalized to the baseline level with resolution of all ECG changes suggestive of BS (Fig. 4). After 3 days of arrhythmic stability, an implantable cardiac defibrillator (ICD) was inserted without complication. Isoproterenol was continued for an additional 24 hours and then discontinued. The patient was monitored for another 48 hours without any subsequent arrhythmic events. She was discharged from the hospital. One week following hospital discharge ambulatory monitoring via a Holter monitor revealed an episode of nonsustained VT lasting 17 seconds, which spontaneously terminated prior to ICD shock.

DISCUSSION

BS may be responsible for up to 45% of all SCD in patients with structurally normal hearts.¹ A family history of SCD is a common finding among patients with BS. It has been linked to a genetic mutation located on the SCN5A gene, which may involve either a complete loss of function of sodium ion channel or an acceleration of recovery from the sodium channel activation.^{1,2} The subsequent transmural voltage gradient can produce the pathognomonic precordial lead ST segment elevation on ECG.⁵ This "Brugada sign" has been reported to have a prevalence of 0.07–0.16%^{6,7} among epidemiological surveys and has been suggested to serve as a useful tool for screening patients at high risk for malignant ventricular arrhythmias and SCD. However,

Figure 4. ECG after isoproterenol administration.

a normal ECG may also be present and under these circumstances pharmacological agents and/or physiological conditions may provoke or "unmask" the ECG pattern, which is transient and returns to baseline once the provocative agent is withdrawn. Such agents include class I antiarrhythmic agents, tricyclic antidepressants, antihistamines, anticholinergics, and/or metabolic/electrolytic abnormalities such as hyperthermia and hypokalemia.⁸⁻¹² Of note, ST segment elevation may occur in a number of settings such as myocardial infarction and acute pericarditis, thereby making the diagnosis a challenge.

The presentation of BS is varied, ranging between asymptomatic states and cardiac arrest. Patients may present with a constellation of vague symptoms such as lightheadedness, syncope, and palpitations or may present with resuscitated SCD. An important point is that BS must be considered in the differential diagnosis when young patients present with recurrent syncope or palpitations or with a family history of SCD.¹³

In this case report, procainamide successfully "unmasked" the ECG pattern consistent with that of BS followed by VT/VF storm. Precipitating agents utilized for "unmasking" the ECG pattern have been implicated in provoking electrical storm.¹⁴ Pharmacological blockade by procainamide, a class IA agent, produced a proarrhythmic state by inten-

sified sodium channel blockade with subsequent recurrent VT/VF, probably aggravated by amiodarone administration. Agents such as amiodarone and beta-blockers, which are often used for the treatment of electrical storm in ischemic patients, may in addition, aggravate the arrhythmic state. In contrast, isoproterenol, a beta-adrenergic agonist, has been suggested to be effective in the terminating VT/VF electrical storm among patients with BS. Isoproterenol boosts the L-type calcium current, and has been shown to effectively normalize ST-segment elevations and control electrical storms in patients with BS.¹⁵ The mechanism of ventricular arrhythmia in BS is suggested to be phase 2 re-entry,¹⁶ which occurs due to increased outward current or decreased inward current, inducing changes in the epicardial action potential. Isoproterenol, via its beta-adrenergic stimulatory effect, increases inward calcium current and attenuates the excess of outward current, resulting in normalization of the action potential.¹⁷⁻²¹ Brugada syndrome is a specific arrhythmia in which the beta-adrenergic stimulation provided by isoproterenol has a therapeutic effect. Other arrhythmogenic states such as catecholaminergic polymorphic VT will be exacerbated by beta-stimulation in general and isoproterenol in particular.²² Isoproterenol is also used in treatment of carotid sinus syncope, atrioventricular heart block, and complete heart block.

Several important clinical lessons can be drawn from this case of a patient. This patient's presentation of unexplained syncope mediated by a potentially fatal condition was only hinted at by the observation of polymorphic nonsustained VT. Successful diagnosis via pharmacological challenge, procainamide in this case, was associated with VT/VF electrical storm, thus underscoring the need for careful observation and monitoring of patients diagnosed with BS in this manner. Finally, the treatment of malignant VT/VF with amiodarone can lead to an incomplete resolution or an aggravation of proarrhythmia. Isoproterenol hastened resolution of the unstable arrhythmic substrate in this case.

REFERENCES

1. Antzelevitch C, Brugada P, Brugada J, et al. Brugada syndrome: 1992–2002: A historical perspective. *J Am Coll Cardiol* 2003;41:1665–1671.
2. Brugada J, Brugada R, Brugada P. Right bundle branch and ST-segment elevation in leads V1 through V3. *Circulation* 1998;97:457–460.
3. Brugada J, Brugada R, Brugada P. Determinants of sudden cardiac death in individuals with the electrocardiographic pattern of Brugada syndrome and no previous cardiac arrest. *Circulation* 2003;108: 3092–3096.
4. Morita H, Morita ST, Nagese S, et al. Ventricular arrhythmia induced by sodium channel blocker in patients with Brugada syndrome. *J Am Coll Cardiol* 2003;42:1624–1631.
5. Shimizu W, Antzelevitch C, Suyama K, et al. Effect of sodium channel blockers on ST segment, QRS duration, and corrected QT interval in patients with Brugada syndrome. *J Cardiovasc Electrophysiol* 2000;11:1320–1329.
6. Hermida JS, Jandaud S, Lemoine J, et al. Prevalence of drug-induced electrocardiographic pattern of the Brugada syndrome in a healthy population. *Am J Cardiol* 2004;94:230–233.
7. Junttila MJ, Raatikainen MJP, Karjalainen J, et al. Prevalence and prognosis of subjects with brugada-type ecg pattern in a young and middle-aged Finnish population. *Eur Heart J* 2004;25:874–878.
8. Kurita T, Shimizu W, Inagaki M, et al. The electrophysiologic mechanism of ST-segment elevation in Brugada syndrome. *J Am Coll Cardiol* 2002;40:330–334.
9. Roleau F, Asfar P, Boulet S, et al. Transient ST segment elevation in right precordial leads induced by psychotropic drugs: Relationship to the Brugada syndrome. *J Cardiovasc Electrophysiol* 2001;12:61–65.
10. Babaliaros V, Hurst WJ. Tricyclic antidepressants and the Brugada syndrome: An example of Brugada waves appearing after the administration of desipramine. *Clin Cardiol* 2002;25:395–398.
11. Kovacic JC, Kuchar DL. Brugada pattern electrocardiographic changes associated with profound electrolyte disturbance. *Pacing Clin Electrophysiol* 2004;27: 1020–1023.
12. Nakazawa K, Sakurai T, Takagi A, et al. Autonomic imbalance as a property of symptomatic Brugada syndrome. *Circ J* 2003;67: 511–514.
13. Brugada P, Brugada R, Mont L, et al. Natural history of Brugada syndrome: The prognostic value of programmed electrical stimulation of the heart. *J Cardiovasc Electrophysiol* 2003;14: 455–457.
14. Gasparini M, Priori SG, Mantica M, et al. Flecainide test in Brugada syndrome: A reproducible but risky tool. *Pacing Clin Electrophysiol* 2003;26: 338–341.
15. Antzelevitch C, Brugada P, Borggreffe M, et al. Brugada syndrome: Report of the second consensus conference. *Heart Rhythm* 2005;2: 429–440. Review. Erratum in: *Heart Rhythm* 2005;2: 905.
16. Yan GX, Antzelevitch C. Cellular basis for the Brugada syndrome and other mechanisms of arrhythmogenesis associated with ST-segment elevation. *Circulation* 1999;100: 1660–1666.
17. Credner S, Klingenhoben T, Mauss O, et al. Electrical storm in patients with transvenous implantable cardioverter-defibrillators. incidence, management and prognostic implications. *J Am Coll Cardiol* 1998;32:1909–1915.
18. Tanaka H, Kinoshita O, Uchikawa S, et al. Successful prevention of recurrent ventricular fibrillation by intravenous isoproterenol in a patient with Brugada syndrome. *PACE* 2001;24:1293–1294.
19. Izumida N, Asano Y, Doi S, et al. Changes in body surface potential distributions induced by isoproterenol and Na channel blockers in patients with the Brugada syndrome. *Int J Cardiol* 2004;95(2-3):261–268.
20. Belhassen B, Viskin S, Antzelevitch. The Brugada syndrome: Is the implantable cardioverter defibrillator the only therapeutic option? *PACE* 2002;25: 1634–1639.
21. Bordachar P, Reuter S, Garrigue S, et al. Incidence, clinical implications and prognosis of atrial arrhythmias in Brugada syndrome. *Eur Heart J* 2004;25: 879–884.
22. Francis J, Sankar V, Nair VK, et al. Catecholaminergic polymorphic ventricular tachycardia. *Heart Rhythm* 2005;2: 550–554. Review.