Case Report

Brugada Syndrome Caused by Autonomic Dysfunction in Multiple Sclerosis

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Only one case report has previously described a patient with multiple sclerosis and a type I Brugada pattern on the electrocardiogram. Patients with multiple sclerosis have several neurological deficits including sensory symptoms, acute or subacute motor weakness, gait disturbance, and balance problems that may lead to an increased risk of falls. Concurrent autonomic dysfunction and neurologic consequences of multiple sclerosis may precipitate both mechanical falls and falls with loss of consciousness. While mechanistically different, the type I Brugada pattern presents similarly with syncope due to an insufficient cardiac output during dysrhythmia. In such patients, intracardiac defibrillators have shown to prevent sudden cardiac death in patients with the Brugada syndrome. In light of these similarly presenting but unique clinical entities, MS patients who develop a syncopal event in the setting of a spontaneous type I Brugada pattern pose a diagnostic and therapeutic dilemma. This case illustrates an approach to the risks and benefits of an ICD placement in an MS patient with the type I Brugada pattern.

1. Introduction

The Brugada syndrome (BruS) is an autosomal dominant genetic disorder with variable expression characterized by typical electrocardiogram (ECG) findings with an increased risk of ventricular arrhythmias and sudden cardiac death [1]. It is essential to distinguish BruS and Brugada sign (BrS) which are two terms distinguishable by the presence or absence of symptoms. Patients with BrS are asymptomatic and have no other clinical criteria. This distinction aids in decision-making for appropriate management.

Multiple sclerosis (MS) is a chronic disease that leads to the diffuse destruction of the nervous tissue [2]. Its associations with cardiac complications have been extensively described [3]: these lesions may ultimately affect regulation of the cardiac autonomic nervous system (ANS), thus causing orthostatic signs and symptoms. MS can also present with gait instability, neuropathic pain, ataxia, and weakness, which all may increase the risk for falls.

We describe a case of a patient with multiple sclerosis presenting to the hospital after experiencing an episode of questionable syncope and ST segment elevation on the ECG that was found to have BrS.

2. Brugada Syndrome Diagnosis Criteria

BruS is diagnosed in symptomatic patients with a pseudo right bundle branch block and ST segment abnormality characteristic of type 1 morphology with a 2 mm or more elevation in the leads V1 and V2 on the ECG (Figure 1). This may occur either spontaneously or in patients with type 2 or 3 patterns during a provocative drug test with intravenous administration of class I antiarrhythmic drugs. Documented ventricular fibrillation or polymorphic VT, syncope of a probable arrhythmic cause, or a family history of sudden cardiac death [4, 5] together with a spontaneous or induced type I Brugada pattern make the diagnosis of BruS.

3. Autonomic Dysfunction in Multiple Sclerosis

Dysfunction of the autonomic nervous system can cause light-headedness, dizziness, orthostatic intolerance, tachycardia or
bradycardia, blood pressure fluctuations, and bowel or bladder dysfunction. In MS, cardiovascular dysfunction is mainly due to ANS dysfunction from overall demyelinating plaque burden in the medulla disrupting reflex pathways from higher cortical centers. Alternatively, there may be interference as the descending autonomic pathways course through the brainstem and spinal cord [6]. ANS dysfunction explains the orthostatic symptoms including syncope, near syncope, and orthostatic hypotension that have previously been reported in MS patients [7, 8]. Cardiovascular abnormalities may be clinical or subclinical and can also lead to sudden death in some cases [7].

4. Brugada Pattern and Multiple Sclerosis

In our literature search, there has been only one previously reported case of the type 1 Brugada pattern on the ECG in an asymptomatic patient with multiple sclerosis [9]. The authors stipulated that the only abnormality that could be linked to such an ECG finding is the dysfunction of the autonomic nervous system (ANS), due to lesions in the brain and spine. There is evidence that an imbalance between the sympathetic and parasympathetic nervous systems contributes significantly to the pathophysiology of the Brugada syndrome [10].

5. Case Presentation

This is a 60-year-old right-handed man with past medical history of relapsing-remitting multiple sclerosis diagnosed 20 years ago with prior beta interferon treatment for 8 years and with chronic left residual hemiparesis who presented to the emergency room after experiencing generalized weakness followed by a fall to the ground with apparent loss of consciousness. While the patient reported no loss of consciousness, he did not have memory of the events surrounding the fall. EMS was called and patient was airlifted to the nearest percutaneous intervention-capable center after the ECG showed a ST segment elevation in the leads V1 to V3, so the ST segment elevation myocardial infarction (STEMI) alert was activated. In the emergency department, the patient was without chest pain. Upon further questioning, he denied any family history of heart disease including no cardiomyopathy, heart failure, arrhythmias, or premature or sudden cardiac death. Vitals demonstrated mild tachycardia to 105 beats per minute and a temperature of 38 degrees Celsius, and labs revealed a negative troponin level. Ultimately, the ST segment elevation myocardial infarction (STEMI) alert was cancelled due to the high clinical suspicion of the type 1 Brugada pattern in a syncopal patient with anteroseptal ST elevations without chest pain. Workup for the febrile episode revealed positive serology for influenza B. Oseltamivir was started and the patient completed 5 days of treatment. The patient was no longer febrile and his tachycardia had resolved, but he continued to show a persistent type 1 Brugada pattern on the ECG during the entire hospitalization course as seen below (Figure 2). The patient subsequently went for a transthoracic echocardiogram which demonstrated a normal left and right ventricular function and no structural abnormalities. He also underwent coronary angiography, which revealed nonobstructive coronary artery disease.

Ultimately, the primary concern was to elucidate, whether the patient’s initial clinical presentation represented an episode of arrhythmogenic syncope induced by the underlying Brugada syndrome, as this would lead to a recommendation for implantation of a cardiac defibrillator. Electrophysiology service was consulted and felt that the mechanism of his fall was mechanical and not related to a true syncopal event. They recommended an outpatient follow-up for consideration of an event monitor or loop recorder.

6. Discussion

The differential diagnosis for BrS includes several conditions that can lead to Brugada-like ECG abnormalities including acute myocardial ischemia or infarction, various central and autonomic nervous system abnormalities, and viral and febrile states among others [3, 11]. Defective myocardial sodium channels reduce sodium inflow currents, thereby reducing the duration of normal action potentials [12]. Febrile states have been reported to unmask a Brugada-like ST segment elevation secondary to reduced sodium influx at a high temperature [13]. Acute myocardial infarction or ischemia in the right ventricular outflow tract produces a ST segment elevation mimicking the Brugada syndrome probably due to the depression of I_{Ca-L} and the activation of I_{KATP} during ischemia [14]. Also, a sympathetic and parasympathetic tone imbalance may unmask the Brugada pattern on the ECG [15, 16] which may support our theory that autonomic nervous dysfunction is a possible culprit.
Our patient has several different conditions that could cause him to have a ST segment elevation in V1 to V3. One of the first important ones is an acute coronary syndrome which was ruled out initially with negative serial troponin levels and definitively with a normal coronary angiogram. The patient was febrile, but he continued to have evidence of the type 1 Brugada pattern on the ECG despite improvement in his temperature and treatment for influenza. Patient’s history was somewhat unclear due to loss of consciousness from arrhythmogenic syncope. Consideration can be made for an electrophysiology study; if an arrhythmia was induced, ICD implantation would be a class IIB recommendation [2]. Had the patient consciousness been secondary to an arrhythmia in the setting of the Brugada pattern on the ECG, ICD would be a class IIA recommendation [2] (Figure 3. ICD in the Brugada syndrome algorithm). Thus, it is important to be able to distinguish arrhythmogenic causes of syncope from other causes, particularly in the setting of multiple sclerosis as management and prognosis of such a patient will highly depend on this determination.

Although this patient’s fever and influenza had been resolved, the classic Brugada pattern on the ECG has not been resolved. In our review, the abnormality that could be linked to the stated ECG finding is the dysfunction of the autonomic nervous system related to multiple sclerosis. Our patient did not yet have genetic testing for BruS and had no family history of sudden cardiac death. Additionally, our patient did not receive drugs with sodium channel blocking effects. In the setting of the asymptomatic Brugada syndrome, no ICD placement is recommended [17]. It is important to note that an AICD placement does not come free of risks and the patient was spared an unnecessary procedure.

Further investigation is needed in cases where the diagnostic criteria of BruS fall short, especially in patients with a

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**Table: ICD in the Brugada Syndrome Algorithm**

| Condition                          | Recommendation |
|------------------------------------|----------------|
| Prior cardiac arrest or Sustained VT? | **Class I: ICD recommended** |
| No                                 | **Class IIA: ICD can be useful** |
| Spontaneous type 1 ECG and history of syncope judged to be caused by ventricular arrhythmias? | No |
| No                                 | **Class IIB: ICD may be considered** |
| Inducible VF on EP study?           | No or No EP study |
| Asymptomatic with drug induced type 1 ECG and family history of SCD | **Class III: ICD may be considered**

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**Figure 2: ECG: Brugada pattern. Right bundle branch block and ST segment elevation in V1 and V2.**

**Figure 3: ICD in the Brugada syndrome algorithm. Consensus recommendations for ICDs in patients diagnosed with the Brugada syndrome [8].**
typical type 1 BrS but the mechanism of syncpe is in ques-
tion. In our case, the patient was advised to follow closely with
the electrophysiology service. But there are other modalities
who have shown to be useful in such cases. In one study, the
intracardiac loop recorder has shown to contribute to the ex-
clusion of ventricular arrhythmia as a mechanism of atypical syncpe in patients with electrocardiographic evi-
dence of the type 1 Brugada pattern [18]. Continuous car-
diac monitoring assists in risk stratification in patients with
suspected BrS and may help to inform the possible decision for ICD implantation.

7. Conclusion
In summary, there is evidence that anatomical and/or func-
tional abnormalities of the ANS can provoke ECG changes
like BrS; however, the clinical significance for these patients
needs further clarification. Due to the significant autonomic
dysfunction that accompanies patients with multiple sclero-
sis, the formal diagnosis of the Brugada syndrome may
prove more difficult. The prognostic significance of isolated
BrS in multiple sclerosis patients remains a matter of con-
siderable debate. In a patient like ours where the etiology of
syncpe is an unclear manifestation of BrS type 1, the ECG
must be carefully investigated with a close follow-up, and
more recently developed modalities of arrhythmia detection
such as implantable loop recorders may prove to be useful
towards confirming a diagnosis of the Brugada syndrome.

Disclosure
The authors have confirmed that this article is unique and not
under consideration or published in any other publications.

Conflicts of Interest
We have no actual or potential conflict of interest in relation
to this manuscript.

Authors’ Contributions
MI and RC conceived and designed the experiments. MI and
GS analyzed the data. MI wrote the first draft of the manu-
script. MI, RC, and GS contributed to the writing of the manu-
script. MI and RC agree with the manuscript results and
conclusions. MI, GS, and RC jointly developed the structure
and arguments for the paper. RC made critical revisions
and approved the final version. All authors reviewed and
approved the final manuscript.

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References
[1] A. Sarkozy, A. Sorgente, T. Boussy et al., “The value of a family
history of sudden death in patients with diagnostic type I
Brugada ECG pattern,” European Heart Journal, vol. 32,
no. 17, pp. 2153–2160, 2011.
[2] B. Hemmer, M. Kerschensteiner, and T. Korn, “Role of the
innate and adaptive immune responses in the course of multi-
ple sclerosis,” Lancet Neurology, vol. 14, no. 4, pp. 406–419,
2015.
[3] W. Shimizu, “Acquired forms of the Brugada syndrome,” Jour-
nal of Electrocardiology, vol. 38, no. 4, pp. 22–25, 2005.
[4] S. G. Priori, A. A. Wilde, M. Horie et al., “HRS/EHRA/APHRS
expert consensus statement on the diagnosis and management
of patients with inherited primary arrhythmia syndromes:
document endorsed by HRS, EHRA, and APHRS in May
2013 and by ACCF, AHA, PACES, and AEPC in June 2013,”
Heart Rhythm, vol. 10, no. 12, pp. 1932–1963, 2013.
[5] S. G. Priori, C. Blomstrom-Lundqvist, A. Mazzanti et al., “2015
ESC Guidelines for the management of patients with ventricu-
lar arrhythmias and the prevention of sudden cardiac death:
the Task Force for the management of patients with ventricu-
lar arrhythmias and the prevention of sudden cardiac death of
the European Society of Cardiology (ESC) endorsed by: Asso-
ciation for European Paediatric and Congenital Cardiology
(AEPC),” European Heart Journal, vol. 36, no. 41, pp. 2793–
2867, 2015.
[6] J. Seze, T. Stojkovic, J. Y. Gaurvrit et al., “Cardiac repolarization
abnormalities in multiple sclerosis: spinal cord mri correlates,”
Muscle & Nerve, vol. 23, no. 8, pp. 1284–1286, 2000.
[7] K. Kanjwal, B. Karabin, Y. Kanjwal, and B. P. Grubb, “Auto-
nomic dysfunction presenting as postural orthostatic tachycar-
dia syndrome in patients with multiple sclerosis,” Interna-
tional Journal of Medical Sciences, vol. 7, pp. 62–67,
2010.
[8] R. A. Marrie, N. Reider, J. Cohen et al., “A systematic review
of the incidence and prevalence of cardiac, cerebrovascular,
and peripheral vascular disease in multiple sclerosis,” Multi-
ple Sclerosis, vol. 21, no. 3, pp. 318–331, 2015.
[9] M. A. Babaei Bigi, A. Aslani, and A. Aslani, “Significance of
cardiac autonomic neuropathy in risk stratification of Brugada
syndrome,” Europace, vol. 10, no. 7, pp. 821–824, 2008.
[10] E. Gialafos, E. Andreoudou, P. Kokotis et al., “Brugada sign in a
multiple sclerosis patient: relation to autonomic nervous sys-
tem dysfunction and therapeutic dilemmas,” Interna-
tional Journal of Cardiology, vol. 202, pp. 652–653, 2016.
[11] C. Antzelevitch, P. Brugada, M. Borggreve et al., “Brugada syn-
drome: report of the second consensus conference,” Heart
Rhythm, vol. 2, no. 4, pp. 429–440, 2005.
[12] G. X. Yan and C. Antzelevitch, “Cellular basis for the Brugada
syndrome and other mechanisms of arrhythmogenesis associ-
ated with ST-segment elevation,” Circulation, vol. 100, no. 15,
pp. 1660–1666, 1999.
[13] C. Antzelevitch and R. Brugada, “Fever and Brugada syn-
drome,” Pacing and Clinical Electrophysiology, vol. 25, no. 11,
pp. 1537–1539, 2002.
[14] H. Kataoka, “Electrocardiographic patterns of the Brugada
syndrome in right ventricular infarction/ischemia,” The Amer-
ican Journal of Cardiology, vol. 86, no. 9, article 1056, 2000.
[15] K. Mizumaki, A. Fujiki, T. Tsuneda et al., “Vagal activity mod-
ulates spontaneous augmentation of ST elevation in the daily
life of patients with Brugada syndrome,” Journal of Cardiovas-
cular Electrophysiology, vol. 15, no. 6, pp. 667–673, 2004.
Brugada syndrome,” *European Heart Journal*, vol. 20, no. 6, pp. 465–470, 1999.

[17] S. G. Priori, A. A. Wilde, M. Horie et al., “Executive summary: HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes,” *EP Europace*, vol. 15, no. 10, pp. 1389–1406, 2013.

[18] M. Kubala, L. Aïssou, S. Traullé, A.-L. Gugenheim, and J.-S. Hermida, “Use of implantable loop recorders in patients with Brugada syndrome and suspected risk of ventricular arrhythmia,” *EP Europace*, vol. 14, no. 6, pp. 898–902, 2012.