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Transcranial Magnetic Stimulation as an Antidepressant Alternative in a Patient With Brugada Syndrome and Recurrent Syncope

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Abstract

Brugada syndrome (BrS) is a common occult cause of sudden cardiac arrest in otherwise healthy-appearing adults. The pathognomonic electrocardiographic pattern may be unmasked only by certain medications, many of which are unknown. We report a case of a depressed but otherwise healthy man with an asymptomatic right bundle branch block on electrocardiography who experienced antidepressant-induced BrS and ultimately recovered with transcranial magnetic stimulation (TMS). After an initial trial of nortriptyline, the patient's depressive symptoms improved; however, he experienced a syncopal event and was subsequently diagnosed as having BrS. Cross titration to bupropion, which had not previously been known to exacerbate BrS, was followed by another cardiac event. As a result, the patient was referred for TMS as a substitute for pharmacotherapy. After 31 TMS sessions over 8 weeks, the patient demonstrated significant improvement by subjective report and objective reduction in his Patient Health Questionnaire-9 scores from 10 (moderate) to 1 (minimal). Transcranial magnetic stimulation is a Food and Drug Administration–approved nonpharmacologic treatment for depression. Given the potential lethality of BrS with known and unknown psychopharmacologic agents, providers should consider TMS as first-line therapy in this patient population. Bupropion should be added to the list of agents known to exacerbate this disease.

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Brugada syndrome (BrS) is a common cause of sudden cardiac arrest (SCA) in otherwise healthy-appearing adults. Although it is marked by pathognomonic electrocardiographic (ECG) patterns, these findings are often concealed at baseline only to be unmasked by medications.[1] Further complicating detection, patients susceptible to SCA from BrS may not manifest signs or symptoms of illness and can have normal physical and cardiac examination findings without a history of syncope.[2] Although various psychotropic medications have been documented to induce or exacerbate the BrS pattern, the potential for syncope, arrhythmia, and SCA in otherwise healthy patients is an important but underappreciated concern in behavioral health. We report repeated arrhythmic events in a patient with previously undiagnosed BrS who was successfully treated with subsequent transcranial magnetic stimulation (TMS).

Definitive diagnosis of BrS consists of a pathognomonic type 1 pattern—coved ST-segment elevation of at least 2 mm (0.2 mV) followed by a negative T wave—in at least 2 of the right precordial leads (V1-V3) combined with at least 1 of the following: documented ventricular fibrillation, polymorphic ventricular tachycardia, a family history of SCA at younger than 45 years, coved-type ECGs in family members, inducibility of ventricular tachycardia with programmed electrical stimulation, syncope, or nocturnal agonal respiration.[3] In addition to the type 1 pattern, patients may demonstrate a type 2 or type 3 pattern. These patterns are not diagnostic of BrS but may convert into type 1 under a sodium channel blocker challenge.

Although clearly a heterogeneous disease, one established mechanism of BrS arrhythmias is a mismatch between transient outward currents I_{to} vs the fast sodium inward current (I_{Na}) and L-type I_{Ca} channels, leading to electrical dispersion in the heart and reentry through a vulnerable window of cardiac tissue.[2] The I_{Na}-blocking effect of medications is thought to increase this mismatch, leading to the unmasking of a previously concealed proclivity toward a—or exacerbating an existing—BrS pattern.

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Epidemiologically, BrS has been linked to multiple genes, with a mutation in *SCN5A* composing most known cases. The male to female ratio is estimated to be 8:1 as a result of a preponderance of I_{to} channels in males. It is notably prominent in Japanese and Southeast Asian populations, with a prevalence of BrS-like patterns as high as 14.6 per 10,000.[4] Patients who experience an aborted sudden death have the highest rate of repeat events (69%), and those who experience syncope and an unprovoked pattern on ECG also have a significant risk of repeat events (29%). Asymptomatic patients also have an increased risk of cardiac events (8%).[5] Overall, the mean ± SD age of sudden death from BrS is 41±15 years. It is estimated to be responsible for 4% of all sudden deaths and at least 20% of those occurring in structurally normal hearts.[2]

Placement of an implantable cardioverter defibrillator is the most effective treatment for BrS, although the high complication rate in BrS and the uncertainty about risk stratification significantly mitigates enthusiasm for this treatment in younger patients.[6] Despite placement of implantable cardioverter defibrillators, patients remain susceptible to shocks and electric storms, suggesting that resumption of offending agents after implantation may not be appropriate.

CASE REPORT

The subject of this case is a 35-year-old man with a medical history of asymptomatic right bundle branch block and first-degree atrioventricular block. This patient was diagnosed as having major depressive disorder based on symptoms of increasing sadness, anxiety, hopelessness, low energy, poor appetite, and impaired concentration. Although the severity had noticeably affected his work performance and he had endorsed suicidal ideations, he denied having intent or plans for self-harm. He had no history of psychosis, mania, panic attacks, or obsessive compulsive symptoms.

The patient was initially administered nortriptyline based on an extensive family history of depression refractory to first-line agents. One month after initiating pharmacotherapy, he experienced a 12-minute syncopal event while jogging. His nortriptyline level was 190 ng/mL (therapeutic range, 50-150 ng/mL). An ECG taken 48 hours later demonstrated a QRS duration of 150 milliseconds and manifested a characteristic type 2 BrS pattern (Figure 1). During an exercise test, the type 2 pattern converted to type 1 as the heart rate exceeded 100 bpm.

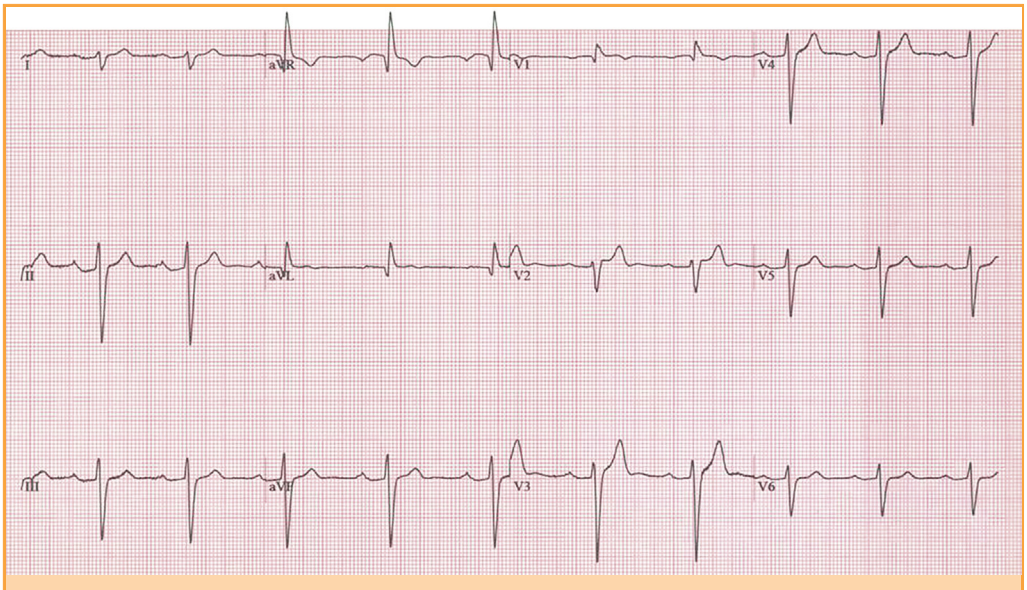

FIGURE 1. Electrocardiogram 48 hours after exercise-induced syncope (while taking nortriptyline) showing a QRS duration of 150 milliseconds, right bundle branch block, first-degree atrioventricular block, and an apparent type 2 Brugada syndrome pattern.