Brugada Syndrome: A Primer for Nurse Practitioners

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ABSTRACT

Brugada syndrome (BrS) is a less known cardiac condition which falls into the category of a channelopathies. BrS has been diagnosed for more than 2 decades. Currently BrS remains a major cause of sudden cardiac death in young adults who have no known abnormal heart structure. Nurse practitioners' awareness of the clinical presentation, diagnosis, treatment, and ongoing care is essential for maximizing patient outcomes.

Keywords: Brugada syndrome, channelopathies, electrocardiogram, sudden cardiac death

INTRODUCTION

Brugada syndrome (BrS) is a lesser known cardiac condition that falls into the category of a channelopathy. The term "channelopathies" broadly refers to a category of disorders in which there is a disturbance in the channels that regulate the movement of ions such as sodium and potassium into and out of the cell. Although BrS has been described in the literature for more than 2 decades, it is not well understood and is often underrecognized by clinicians. To date, BrS remains a major cause of sudden cardiac death (SCD) in young adults who have no previous history of an abnormal heart structure.[1]

PATHOPHYSIOLOGY

Even though the pathophysiology of BrS remains controversial, many recent researches have linked BrS to genetic mutations. Thirty percent of the population with BrS has a mutation in the sodium voltage-gated channel alpha subunit 5 (*SCN5A*) gene.[2] The *SCN5A* gene belongs to a gene family that is responsible for providing instructions for sodium channel production.[2] These sodium channels play an important role in generating and transmitting electrical signals in the cell.[2] One of the main functions for these channels is to help move sodium ions across the cell membrane.[2] Large numbers of these channels are found in cardiac muscle and are crucial in initiating cardiac impulses, coordinating atrial and ventricular contractions, and maintaining a normal cardiac rhythm.[2]

When *SCN5A* genes mutate, they alter the ion channel structure and disturb sodium ion flow into muscle cells of the heart.[2] This leads to the abnormal electrocardiogram (ECG) pattern that is a classic sign of BrS. The *SCN5A* gene is also responsible for the cardiac action potential alteration in phase 0 postulated to be caused by a premature inactivation of the sodium channel.[2]

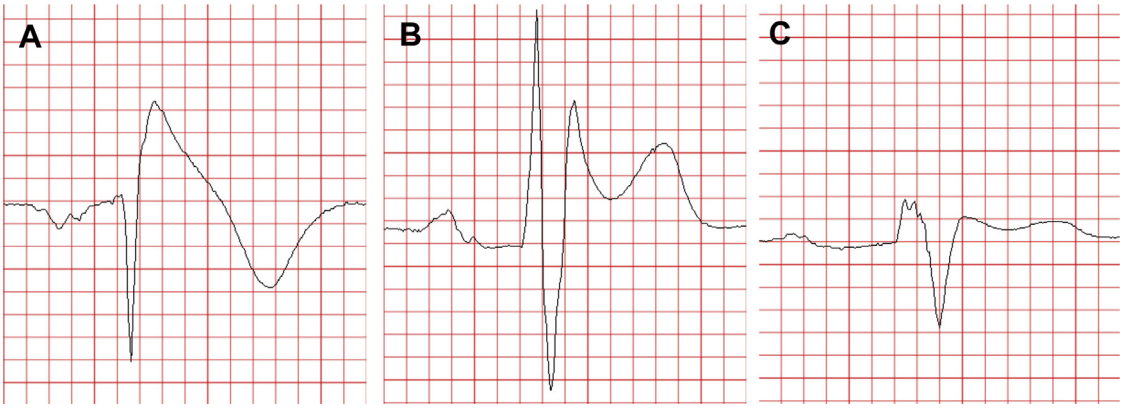
Mutated *SCN5A* genes in males increase the risk of developing a spontaneous type 1 Brugada ECG (Figure 1).[3] A recent systematic review of individuals with existing BrS reported that a family history of sudden cardiac death (SCD), type 1 Brugada ECG, inducible ventricular arrhythmia, syncope, and male sex were associated with an increased risk of future cardiac events such as ventricular fibrillation.[4] Therefore, most health care practitioners emphasize the importance of genetic tests for determining BrS risk stratification.

RISK AND PREVALENCE

Because BrS occurs infrequently, it makes risk stratification of this syndrome clinically challenging. Familial and genetic backgrounds are the most significant risk factor for this syndrome.[3]

Juang and Horie[5] found that the prevalence of BrS with an unknown etiology varies geographically. To illustrate, it has been reported that BrS type 1 pattern appears more frequently in Asian and European individuals than Americans, whereas type 2 and type 3 appear less in Europeans and Americans

Figure 1. Brugada-type electrocardiogram patterns. (A) Brugada type 1; (B) Brugada type 2; (C) Brugada type 3; Presented at 25 mm/s, 1 cm/mV. Used with permission from Liam O'Neil, publication director at Radcliffe Cardiology (https://www.radcliffecardiology.com/articles/brugada-syndrome-diagnosis-clinical-implications-and-risk-stratification).



but more in Asians.[5] Surprisingly, this condition is rare in children despite the presence of genetic mutations from birth.[3] The first occurrence of arrhythmias peaks at age 30–39 years of age, which in part explains the relationship between BrS and sudden death in individuals previously thought to be healthy.[3]

RECOGNIZING THE PROBLEM

Although most patients with BrS are asymptomatic, discussion about cardiac dysrhythmic events as well as sudden cardiac death (SCD) occurrence must not be neglected. To minimize the occurrence of BrS complications later in life, patient history and physical examination must be completed at the earliest for those who are at high risk of having BrS.

Increased Risk

Determining who is at increased risk for developing this condition is crucial to prevent SCD and dysrhythmias from occurring. Because BrS is a genetic disorder, obtaining a family history is an important diagnostic tool. Research reports a 50% chance of inheriting the genetic mutation; however, penetrance or actual development of the condition is $< 30\%$ in individuals with genetic mutatation.[6] The importance of a familial history was illustrated in a recent case report that reported a BrS diagnosis was made in a 32-year-old after 5 of his family members died secondary to SCD.[7]

Syncope is considered to be not only an early sign of BrS, but also a common sign.[3] It has been reported that a work-up for a syncopal episode assisted in diagnosing one-third of patients with BrS.[3] Although the reason behind the syncope in BrS patients is controversial, it has been postulated to be caused by the proarrhythmic effects of vagal stimulation and resulting decreased cardiac output.[3] Because of the association with SCD, it should also be considered that syncope may be a result of an arrhythmia with a resulting disruption of oxygen and nutrients to the brain.[8] Therefore, an extensive clinical history should be obtained at the time of syncope to assist in diagnosing its origins.

Few studies assert that there is an association between BrS and epilepsy.[9] It has been reported that an individual with a gene mutation in *SCN5A* has susceptibility for seizure activity.[9] However, there is no definitive evidence to support this claim; therefore, a thorough assessment, including an ECG, is needed when a patient presents with epilepsy.

Recent studies reported that fever could trigger a BrS arrhythmia.[10] One report estimated that 18% of cardiac arrhythmia cases in BrS patients were triggered by fever.[10] Additionally, patients with fever-induced BrS have a high risk of developing type 1 BrS.[10] Although the exact mechanism is unclear, it has been posited that when the cardiac sodium channels mutated, it