REVIEW ARTICLE

BRUGADA SYNDROME

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ABSTRACT

Brugada syndrome is a genetic disease that is characterized by abnormal electrocardiographic findings and an increased risk of sudden cardiac death.[1] it is named by the Spanish cardiologists Pedro Brugada and Joseph Brugada. It is the major cause of sudden unexplained death syndrome (SUDS), and is the most common cause of sudden death in young men without known underlying cardiac disease in Thailand and Laos.

KEY WORDS: Electrocardiogram, Brugada Syndrome, Sudden cardiac death.

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INTRODUCTION

The Brugada syndrome is a genetic disease that is characterized by abnormal electrocardiogram (ECG) findings and an increased risk of sudden cardiac death.[1] It is named by the Spanish cardiologists Pedro Brugada and Joseph Brugada. It is the major cause of sudden unexplained death syndrome (SUDS), and is the most common cause of sudden death in young men without known underlying cardiac disease in Thailand and Laos.[2,4]

The ECG findings of Brugada syndrome were first reported among survivors of cardiac arrest in 1989. In 1992 that the Brugada brothers recognized it as a distinct clinical entity, causing sudden death by causing ventricular fibrillation in the heart.[3]

In 1998, a hereditary (autosomal dominant) gene defect was found, involved in the coding of protein components in the sodium channels in heart cells.[4] The channel defect causes abnormal electrical conduction in the heart with resultant ventricular arrhythmias, including full-blown ventricular fibrillation leading to death. Many patients presented with unexplained fainting spells (Syncope).

Brugada syndrome is a potentially life-threatening heart rhythm disorder.[1] It's characterized by a specific abnormal heartbeat called a Brugada sign, which is detected by an electrocardiogram. Brugada syndrome is frequently an inherited condition.[5] Approximately 20% of the cases of Brugada syndrome have been shown to be associated with mutation(s) in the gene that encodes for the sodium ion channel in the cell membranes of the muscle cells of the heart (the myocytes).[6] The gene, named SCN5A, is located on the short arm of the third chromosome (3p21. Over 160 mutations in the SCN5A gene have been discovered to date, each having varying mechanisms and effects on function, thereby explaining the varying degrees of penetration and expression of this disorder.[7]

Loss of function of the sodium channel is a mutation in the gene that disrupts the sodium channel's ability to bind properly to ankyrin-G.[8] This condition is inherited in an autosomal dominant pattern and is more common in males.[9] In addition it has a higher prevalence in most Asian populations.

In Japan, it is found in less than 1% of the population; and in the U.S., in less than 0.5%. Of these, most will not have any problems. But the EKG pattern, coupled with a history of unexplained fainting, a history of a relative dying young raises a red-flag risk of sudden death.[10]

In the Philippines, a cross-sectional study done in 2003 to measure the prevalence of Brugada type EKG pattern reported finding the Brugada type 1 (coved) ECG pattern in 0.2% of the population and in 0.3% among males. The prevalence of any type Brugada ECG pattern was 2%.[11] The risk of sudden death among individuals with this marker remains to be determined.

The syndrome has been linked to SUDS, causing sudden death in apparently healthy young people over the age 30. A study of patients with SUNDS and their families, screened for genetic mutations in SCN5A, the gene known to cause the Brugada syndrome, suggested that SUNDS and the Brugada syndrome are phenotypically, genetically, and functionally the same disorder.[12] In Thailand,

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where the estimated prevalence of SUDS is 26-38 per 100,000 populations, a study on patients with the Brugada syndrome showed low heart rate variability at night that may predispose to the occurrence of ventricular fibrillation episodes.[13]

A study done to evaluate the significance of cardiac autonomic neuropathy (CAN) in the Brugada Syndrome concluded that CAN is an important risk factor in BS, and that men are susceptible to the development of cardiac events.[10]

DISCUSSION

The Brugada Syndrome was first described in 1986. Initially it was thought to affect primarily males of Asian descent but recent studies have shown that the disease affects people of both sexes from all over the world. This syndrome is genetically determined. Approximately 60% of patients with (aborted) sudden death with the typical electrocardiogram have a family history of sudden death, or have family members with the same electrocardiographic abnormalities.[14] The pattern of transmission is autosomal dominant. There is a predominance of affected males. The disease is responsible for 4 to 12% of unexpected sudden deaths, and for up to 50% of all sudden death in patients with an apparently normal heart.[15]

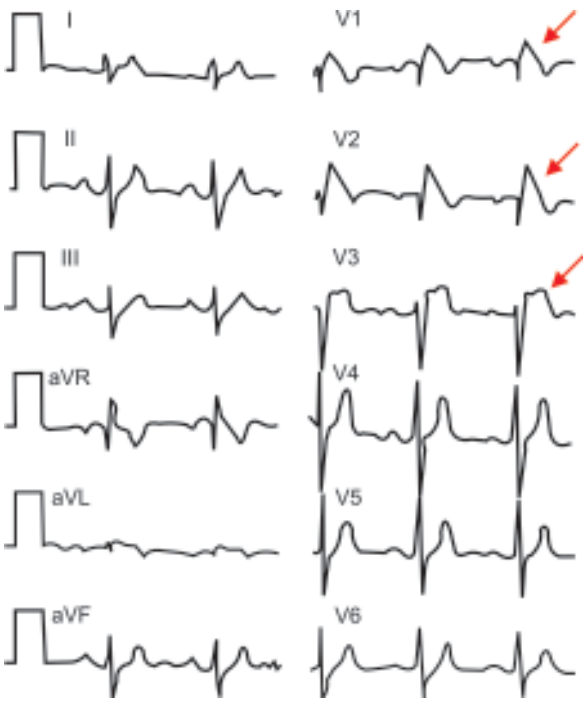

Fig 1: ECG showing Brugada syndrome. (Reproduced from Braunwald Textbook of Cardiology 9th edition with thanks).

The syndrome of right bundle branch block, ST segment elevation in V1 to V3 and sudden death is a clinical-electrocardiographic diagnosis based on syncopal or sudden death episodes in patients with a structurally normal heart with a characteristic electrocardiographic pattern. The ECG shows ST segment elevation in the precordial leads V1 to V3, with morphology of the QRS complex resembling a right bundle branch block. This pattern of right bundle branch block has also been called J point elevation.[8]

The episodes of syncope and sudden death are caused by fast polymorphic ventricular tachycardia or ventricular fibrillation. The complete syndrome is characterized by episodes of fast polymorphic VT in patients with an electrocardiogram showing a pattern of right bundle branch block and ST segment elevation in leads V1 to V3.[5] When the episodes terminate spontaneously the patient develops syncopal attacks. When the episodes are sustained, full blown cardiac arrest and sudden death occur.[16,17] Thus, these manifestations can range widely; at the one end of the spectrum we have asymptomatic individuals and at the other end those who die suddenly. Many people who have Brugada syndrome don't have any symptoms, and so they're unaware of their condition. Brugada syndrome is much more common in men than in women.

Brugada syndrome has 3 different ECG patterns. Type 1, has a coved type ST elevation with at least 2 mm (0.2 mV) J-point elevation a gradually descending ST segment followed by a negative T-wave. Type 2, has a saddle back pattern with a least 2 mm J-point elevation and at least 1 mm ST elevation with a positive or biphasic T-wave. Type 2 pattern can occasionally be seen in healthy subjects. Type 3, has either a coved (type 1 like) or a saddle back (type 2 like) pattern with less than 2 mm J-point elevation and less than 1 mm ST elevation. Type 3 pattern is not uncommon in healthy subjects.

The classic (type 1) Brugada syndrome presents with the coved-type ST elevation in more than 1 right precordial lead, V1 through V3, with or without a sodium channel blocker, with one of the following criteria: syncope, documented ventricular fibrillation, electrophysiological inducibility of ventricular tachycardia, positive family history of cardiac death younger than age 45, nocturnal agonal respiration, self-terminating polymorphic ventricular tachycardia, and type 1 ST elevation in family members.[5,8]

The pattern seen on the ECG is persistent ST elevations in the electrocardiographic leads V_1-V_3 with a right bundle branch block (RBBB) appearance with or without the terminal S waves in the lat-

eral leads that are associated with a typical RBBB. A prolongation of the PR is also frequently seen. Adrenergic stimulation decreases the ST segment elevation, while vagal stimulation worsens it. (There is a case report of a patient who died while shaving, presumed due to the vagal stimulation of the carotid sinus massage) The administration of class Ia, Ic and III drugs increases the ST segment elevation, and also fever. An exercise decrease ST segment elevation in some patients but increases it in others (after exercise when the body temperature has risen). The changes in heart rate induced by atrial pacing are accompanied by changes in the degree of ST segment elevation. When the heart rate decreases, the ST segment elevation increases and when the heart rate increases the ST segment elevation decreases. However, the contrary can also be observed.

Many people who have Brugada syndrome are undiagnosed because the condition often doesn't cause any noticeable symptoms. The most important sign or symptom of Brugada syndrome is an abnormal pattern on an electrocardiogram (ECG) called a Brugada sign. A Brugada sign is only detected on an ECG. Clinical manifestation of brugada syndrome include: Fainting (syncope), irregular heartbeats or palpitations and sudden cardiac arrest.[21,23] In diagnosed cases of Brugada syndrome, genetic testing is required for work up and evaluation of disease.[20]

Risk factors include family history of Brugada syndrome, male sex, Asian origin and fever. While having a fever doesn't bring on Brugada syndrome itself, fever can increase the risk of fainting or other complications of Brugada syndrome, especially in children.[33,34]

Complications of Brugada syndrome require emergency medical care.[35] These include sudden cardiac arrest and fainting. If not treated immediately, this sudden loss of heart function, breathing and consciousness, which often occurs while sleeping, is fatal. With fast, appropriate medical care, survival is possible. Immediate Cardiopulmonary resuscitation (CPR) can improve the chances of survival.[24] If subjects suffering from Brugada syndrome experiences faint attack, seek emergency medical attention and consult cardiologist.

Diagnosis is made by the typical ECG findings described above. It is important to note that not everyone with the syndrome will have the typical ECG findings. In fact, the ECG can vary day by day in affected individuals. In individuals in whom the ECG is normal, the characteristic findings can be elicited by the administration of procainamide, flecanide, or ajmaline, a sodium channel blocker. This is not without risk, however; in one European study looking at ajmaline two patients developed symptomatic VT. This test is therefore most appropriately performed by the electro physiologist.[26,27]

Those considered at high risk have: A family history of sudden cardiac death,[32] personal history of serious heart rhythm problems or fainting spells. Medications alone usually can't be used to treat Brugada syndrome — only a medical device called an implantable cardioverter-defibrillator (ICD) can be life saving in drying situations. Implanting the device is usually recommended for people at high risk of sudden cardiac death or other complications of Brugada syndrome.[28] For high-risk individuals, treatment may include an ICD. This small device continuously monitors heart rhythm and delivers electrical shocks when needed to control abnormal heartbeats. The procedure to implant an ICD requires hospitalization for a day or two.

ICDs may cause complications, some life-threatening, so it's important to weigh the benefits and the risks.[31] People who have an ICD implanted as a treatment for Brugada syndrome have reported receiving shocks from their ICD even when their heartbeat was regular. This may be because many people who receive an ICD as a treatment for Brugada syndrome are young, and they may receive shocks when their heart rates increase during normal stresses, such as exercise. Under such circumstances ICD is programmed accordingly to reduce this risk to avoid inappropriate shocks. The cause of death in Brugada syndrome is ventricular fibrillation. The episodes of syncope (fainting) and sudden death (aborted or not) are caused by fast polymorphic ventricular tachycardia or ventricular fibrillation. These arrhythmias appear with no warning. While there is no exact treatment modality that reliably and totally prevents ventricular fibrillation from occurring in this syndrome, treatment lies in termination of this lethal arrhythmia before it causes death. This is done via implantation of an ICD, which continuously monitors the heart rhythm and will defibrillate an individual when ventricular fibrillation occurs. Some recently performed studies had evaluated the role of quanidine, a Class Ia anti arrhythmic drug, for decreasing VF episodes occurring in this syndrome.[36] Quinidine was found to decrease number of VF episodes. Some drugs have been reported to induce the type-1 ECG and/or (fatal) arrhythmias in Brugada syndrome patients.[37] Patients with Brugada syndrome can prevent arrhythmias by avoiding these offending drugs.[38]

CONCLUSION

The Brugada syndrome may be responsible for a significant proportion of patients presenting with syncope or sudden cardiac death in patients with otherwise healthy hearts. There is a genetic component, so a positive family history of early sud-

den cardiac death should heighten your suspicion for this syndrome. Prompt consultation with a cardiologist is recommended (even in asymptomatic patients) as electrophysiological studies can also be diagnostic in many of these patients.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
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None declared.