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Review Article

Brugada syndrome; diagnosis, risk stratification and management: A review

Jefrin Daniel E*, Subash Chandran.M.P, Sree Lekshmi.R.S and Prasobh G R

Department of Pharmacy, Sree Krishna College of Pharmacy and Research Centre, Thiruvananthapuram, India.

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Brugada syndrome is an unprecedented inherited arrhythmia syndrome which may lead to an increased risk of unexpected cardiac loss of life, in spite of a structurally regular heart. Symptoms include palpitations, syncope, nocturnal agonal respiration, ventricular fibrillation. Diagnosis is primarily based totally on a specific electrocardiogram pattern, determined both spontaneously and in the course of a sodium channel blocker test. Some pathogenic genes are identified as the causative agents of the disease. Among those SCN5A is the most prevalent one among affected sufferers Key stratification stays a venture, in spite of latest insights from big population cohorts. Implantable cardiac defibrillators are the primary remedy in management of Brugada syndrome which is related to excessive complications in the population. This review explains the genetic basis, diagnosis, risk stratification, management and steps for enhancing good health care team outcomes.

Key words: Brugada syndrome, syncope, risk stratification, genetic disorder, ST-segment elevation, sudden cardiac death.

INTRODUCTION

Brugada syndrome was known after Joseph and Pedro Brugada who first defined it in 1992. The first case was identified in 1986. Brugada syndrome is a genetic disorder associated with disruption of hearts normal rhythm characterised by means of the ECG findings such as ST-segment elevations with inside the proper precordial leads (V1-V3). Brugada syndrome mainly affects patients of middle age (Probst et al., 2010).

Epidemiology

The occurrence of Brugada syndrome is about three to five consistent with 10,000 people. Brugada syndrome is about eight to ten instances greater risk in adult males than females. This gender difference isn't discovered in pediatric patients. This has been hypothesized to be because of better testosterone stages after puberty and special proportions of ionic currents primarily based totally on sex. Brugada syndrome is likewise greater regularly occurring in those who are of Southeast Asian descent. The suggested affected age is 41 years. Brugada syndrome owed for 4% of all surprising cardiac deaths (Sarquella et al., 2016).

*Corresponding author. Jefrin Daniel E, E-mail: ejefrindaniel@gmail.com.

Etiology

The first genetic affiliation with Brugada syndrome discovered a loss-of-function mutation withinside the cardiac voltage-gated sodium channel gene SCN5A. It is thought to be located in 15%-30% of Brugada Syndrome cases (Kapplinger et al., 2010). Mutations in calcium and potassium channels, related channel proteins, and desmosomal proteins have additionally been related with the disease. Brugada syndrome is inherited in an autosomal dominant pattern; however, affected people can also additionally exhibit variable expressivity and decreased penetrance. Additionally, many environmental and genetic factors can also additionally impact the phenotype, inclusive of temperature, medications, electrolyte abnormalities, and cocaine.

PATHOPHYSIOLOGY

Molecular mechanism

The right precordial ST-segment elevation with inside the ECG isn't clearly understood. Currently there are mechanisms that can provide an explanation for the ECG alteration; neither mechanism has been conclusively confirmed, nor they are at the same time exclusive (Wilde, 2010). The first hypothesis, repolarization, specializes in the presence of transmural voltage

gradients because of heterogeneity in action potential duration among the RV epicardium and endocardium (disequilibrium among INa and Ito). This generates transmural dispersion of repolarization and causes the ST-segment elevation (Yan, 1999). The second hypothesis, depolarization, includes preferential conduction slowing with inside the RV outflow tract, main to ST-segment elevation withinside the right precordial leads (Tukkie, 2004). Regional variations in conduction velocity with inside the RV epicardium could be irritated with the aid of using INa reduction and cause the incidence of epicardial reentrant excitation waves. Additionally, in 2009, Boukens et al. advised that the embryological development of the right ventricle ought to provide an explanation for the electrophysiological heterogeneity with inside the ventricular myocardium, which include the RV outflow tract that could provide the arrhythmogenic substrate (Boukens, 2009).

Genetics

Brugada syndrome is a disorder with an autosomal dominant sample of transmission. Incomplete penetrance is common in families, and the disorder may be sporadic in as much as 60% of sufferers (Campuzano, 2010). In 1998, the primary pathogenic mutation withinside the SCN5A gene has been identified (Chen et al., 1998). This gene encodes the alpha subunit of the cardiac sodium channel (Nav1.5). There are greater than 350 pathogenic mutations in numerous genes were published (SCN5A, GPD1L, SCN1B, SCN2B, SCN3B, RANGRF, SLMAP, KCNE3, KCNJ8, HCN4, KCNE5, KCND3, CACNA1C, CACNB2B, CACNA2D1, and TRPM4). These genes encode subunits of cardiac sodium, potassium, and calcium channels in addition to genes which are further involved in trafficking or law of those channels. Despite the excessive quantity of gene mutations, approximately about 35% of Brugada syndrome patients were decided to have a genetic cause. Of them, almost 30% carry a pathogenic mutation with inside the SCN5A gene (Webster, 2013). All different genes collectively are accountable for approximately 5% of all brugada syndrome instances. Therefore, 65% of instances don't have a genetic origin.

Phenotype modulators

Several modulating elements that play a key position with inside the ECG dynamic nature were published with bradycardia and vagal tone thought to make a contribution to ST-phase elevation and arrhythmia initiation (Giudicessi, 2013). This fact explains that more ST-segment elevation documented in vagal situations, inclusive of arrhythmias and sudden cardiac death at night. The importance of hormones is likewise debated, in that a regression of the everyday ECG capabilities has been determined in castrated men, and the degrees of testosterone appear to be better in male Brugada syndrome sufferers. In addition, temperature is likewise a primary modulator in Brugada Syndrome. Febrile states might also additionally unmask sure Brugada syndrome sufferers and quickly increases the chance of arrhythmias. It appears that fever could be a special essential cause aspect a number of the pediatric population that constrained records exists so far of Brugada syndrome in children.

RISK STRATIFICATION

It is nicely conventional that the etiology of Brugada syndrome is multifactorial, regarding genetic, environmental, and hormonal components that make contributions to its phenotype manifestation. In addition, a few clinical features had been recognized as high-threat markers in Brugada syndrome. It is found that the symptomatic patients with recurrent syncope, agonal breathing all through sleep, or unknown seizures are prone to sudden loss of life and need ICD. However, a debate remains ongoing on the value of risk stratification parameters, together with an electrophysiological inducibility, in asymptomatic patients Some will argue that it has no cost, at the same time as others will declare that the electrophysiology study (EPS) allows the identity of a subgroup of asymptomatic patients at better threat who will benefit from ICD implantation. Other modulating elements additionally had been investigated. For example, genetic research have mentioned that compound pathogenic mutations in Brugada syndrome sufferers motive greater excessive phenotype (Cordeiro et al., 2006) and that polymorphisms which are common might also additionally modulate the impact due to pathogenic mutations (Lizotte et al., 2009). In addition, it has been posted recently that pathogenic mutations when combines with common single nucleotide polymorphisms might increase the risk of arrhythmias in patients with brugada syndrome though at present genetics are not beneficial in risk stratification. At this moment genetic screening is only recommended as a diagnostic tool (Somva et al., 2013).

CLINICAL MANIFESTATION

Signs and symptoms

One third of Brugada syndrome patients are identified as symptomatic and the symptoms include palpitations, syncope, nocturnal agonal respiration, ventricular fibrillation and it may further lead to cardiac arrest. Two third of the Brugada syndrome patients do not experience any symptoms.

Diagnosis of brugada syndrome

BrS is identified in sufferers with Type 2 or Type 3 ST-segment elevation in 1 lead a few of the proper precordial leads V1, V2 placed with inside the second, third, or fourth intercostal area.

Diagnostic criteria

ST-phase elevation is associated with a huge type of benign in addition to malignant pathophysiologic conditions. A differential prognosis is tough at times, especially while the degree of ST-segment elevation is fantastically small and the specificity of sodium channel blockers (e.g. flecainide, ajmaline, procainamide, disopyramide, propafenone, pilsicainide) to become aware of patients at threat is uncertain (Brugada, Mizu et al., 2000). A consensus report recently posted with the aid of using the Arrhythmia Working Group of the European Society of Cardiology addresses those and other ambiguities regarding the diagnostic standards for Brugada syndrome (Prio et al., 2000, Antzelevitch et al., 2002).

Expert Consensus statement ‘‘Diagnosis and control of patients with inherited number one arrhythmic syndromes 2013”. BrS is identified in patients with ST-segment elevation with type I morphology mm in 1 lead a few of the proper precordial leads V1,V2 placed with inside the second, third, or fourth intercostal area taking place both spontaneously or after provocative drug check with intravenous administration of Class I antiarrhythmic capsules

Other E.C.G. findings in brugada syndrome

ECG in BrS patients may additionally display different adjustments. The PRc programming language is regularly extended (200ms) and displays the presence of an extended HV c programming language. Also defined are: P wave abnormalities (extended or biphasic P waves), past due potentials detected via way of means of signal-averaged ECG and QRS widening and fragmented QRS. Augmentation of ST section elevation via way of means of 0.5mV in V1 to V3 one to 4 mins put up exercise has been reported by Makimoto et al. in 37% of Brugada syndrome patients and became a sizable unbiased predictor of cardiac events. Atrial traumatic inflammation takes place in approximately 10 to 20% of Brugada syndrome patients and is related to extended threat of syncope and sudden cardiac death Sick sinus syndrome and atrial stand nevertheless have additionally been defined. Conduction delays in the RVOT have additionally been reported.

Misdiagnosis of brugada syndrome

Brugada syndrome kind ECG adjustments may be visible in patients following cardioversion and remains for some hours and can lead to a wrong analysis of Brugada syndrome. Misdiagnosis of Brugada syndrome can occur with ECG changes of early repolarisation, athlete’s heart, right bundle branch block, acute pericarditis, myocardial infarction, prinzmetal angina, arrhythmogenic right ventricular cardiomyopathy (ARVC), myocarditis, Duchenne muscular dystrophy, electrolyte disturbances and hypothermia.

Management of brugada syndrome

Each affected person have to first be cited a specialized centre for inherited arrhythmia. For all sufferers, step one of control is focused on counseling in everyday life: this consists of keeping off excessive alcohol intake, treating fever aggressively and decreasing exercise activity progressively. A listing of remedies that can increase the arrhythmia threat is given to the affected person. A familial screening has to continually be accomplished to acquire early identification of affected loved ones who will be prone to sudden cardiac death (Priori et al., 2003). After this primary step, which applies to all sufferers, the discussion begins off evolved approximately which healing technique to propose until now.

The simplest verified green remedy is ICD implantation, however different opportunities will simply emerge with inside the following few years, including catheter ablation, which is constrained to sufferers with common arrhythmia recurrences. Asymptomatic sufferers with a drug-brought on ECG pattern gift with a completely low threat of arrhythmia that does not suggest ICD implantation. The main query still pertains to ICD implantation in patients with intermediate threat.

A spontaneous ECG pattern in an asymptomatic affected person defines a cumulative threat of VF accomplishing 12% at 10 years (Sacher et al., 2013).This threat seems higher than in symptomatic sufferers with vasovagal syncope, and argues for an early discussion with the affected person approximately an ICD implantation (Olde et al., 2015). In those cases, man or woman assessment of related risk factors has to be accomplished to increase stratification accuracy. However, physicians need to recognize that, for now, although there is a especially clean picture of the threat at a population level Pharmacist were nevertheless not able to properly stratify affected person threat at an man or woman level. Thus, it’s far crucial to offer the affected person with complete facts approximately the boundaries of our knowledge. More importantly, the affected person needs to be concerned with the therapeutic choice which will have a greater psychological impact on healing.

Enhancing health care team outcomes

Brugada syndrome isn’t very common, however due to the fact its far related to unexpected loss of life, its far critical for healthcare employees to be aware about the ECG presentation. The ailment is excellent controlled through an interprofessional group that consists of a cardiologist, electrophysiologist and a genetic counselor. The key to analysis is a complete scientific record of syncopal attacks, chest pain or dizziness. Once the analysis is made, sufferers want to be knowledgeable approximately the capability for cardiac arrest. While an ICD is robotically implanted in those sufferers, it additionally predisposes them to device-associated headaches and irrelevant shocks. The real prevalence of loss of life from Brugada syndrome isn’t recognized however may also account for 3%-20% of all unexpected deaths in sufferers with structurally regular hearts. Sudden deaths have a tendency to arise early after the fourth decade of life. The patient, family, and coworkers ought to be knowledgeable approximately the fundamentals of CPR. Once the analysis of Brugada syndrome is made genetic counseling have to be provided to the family (Louis et al., 2018, Mizusawa, 2016).

DISCUSSION

The common age of presentation of Brugada syndrome is 41 years, and men were mostly affected than women. The occurrence of Brugada syndrome is about three to five consistent with 10,000 people. Patients are predisposed to ventricular tachycardia, ventricular fibrillation, and sudden cardiac death. Moreover, patients are affected by concurrent cardiac abnormalities like right bundle branch block, first degree AV block and sick sinus syndrome. Several mechanisms have been implicated with inside the pathophysiology of Brugada syndrome. In the inherited, autosomal dominant form of the syndrome, a gene mutation alters the shape and characteristics of sodium ion channels found in the heart. Impaired ion channels do not allow the flow of sodium into the cardiac cell, which adversely influences the heart rhythm. Another mechanism is through mutation of the SCN5A gene, which is responsible for the production of cardiac sodium channels. SCN5A gene is mostly observed in 30% of affected individuals. Implicated electrolyte abnormalities encompass hypercalcemia, in addition to hyperkalemia and hypokalemia.

Diagnosis of Brugada syndrome is primarily based on ECG findings that encompass ST-segment elevations in leads V1 to V3 and right bundle branch block patterns on ECG together with one of the following: records of ventricular tachycardia or fibrillation, family history of sudden cardiac death or agonal breathing while sleeping. Brugada syndrome predisposes a affected person to an entire life danger of unexpected cardiac demise, and there are presently no pharmacologic remedies to lessen this danger. Thus, ICD is frequently encouraged as it has greater efficacy in reducing unexpected cardiac death, however the selection of this device relies upon at the affected person's capacity to tolerate it. If a affected person cannot tolerate an ICD, pharmacologic remedy then serves as a second-line treatment. The drugs such as quinidine, disopyramide, quinine sulphate, beta agonists and phosphodiesterase inhibitors.

There are some reports that under hypothyroid conditions SCN5A gene mutation variants can induce brugada syndrome. Future studies to determine the relationship between brugada syndrome and hypothyroidism are needed.

CONCLUSION

The diagnosis of brugada syndrome must be performed in patients lacking personal or family history of this syndrome. Furthermore, patients should be counseled regarding the usage of anesthetics, antihistamines, cocaine, antiarrhythmics, and psychotropic drugs as they have been observed to initiate Brugada syndrome. Brugada syndrome's sudden symptoms, excessive mortality rate, and ability to present atypically make this a tough ailment to manage. Brugada syndrome is life threatening and emergency physicians must be relied upon to diagnose and manage.

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