BRUGADA SYNDROME AND SUDDEN CARDIAC DEATH

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ABSTRACT

A recently discovered cause of sudden cardiac death, Brugada syndrome is a conductivity disorder in structurally normal hearts. We present here a case of an incidental Brugada sign, outlining the clinical and pathophysiological findings in Brugada syndrome. We also give an account of the published guidelines regarding implantable cardioverter-defibrillators and highlight the importance of educating clinicians and the public alike in the management of Brugada syndrome.

CASE PRESENTATION

A 49 year old gentleman, with no relevant medical history, presented with epigastric discomfort associated with sweating but no nausea or vomiting. He was haemodynamically stable and clinical examination proved unremarkable. The electrocardiogram (ECG) showed ST segment elevation in the right chest leads whilst serial troponin levels were within normal range. Coronary angiogram showed normal contractility and no significant coronary artery disease. The working diagnosis was of epigastric discomfort secondary to dyspepsia, with the Brugada sign being an incidental ECG finding. The plan was for this patient to be managed expectantly and with regular ECGs.

HISTORY OF BRUGADA SYNDROME

The first paper on Brugada syndrome described eight cases and was published in 1992. It describes the first documented case which occurred in a three year old Polish boy who in 1986 presented with multiple episodes of loss of consciousness; he was resuscitated repeatedly by his father. The child's sister had died suddenly at two years of age. The ECGs of the both siblings were very similar and abnormal.

In recent years there has been an exponential increase in the number of cases reported[1]. Recent genetic profiling seems to indicate that Brugada syndrome is a primary conduction disorder[2].

BRUGADA SYNDROME

This channelopathy is characterised by sudden death associated with one or more of several ECG patterns i.e. incomplete right bundle branch block (RBBB); ST elevation; and J-point elevation in the anterior precordial leads (V_1-V_3). Three different types have been described, classified according to their characteristic ST segment abnormalities in leads V_1-V_3[3]. It is debatable whether the RBBB is real or reflecting early repolarisation of the right ventricular epicardium. In some but not all cases this resolves after normalisation of the ST segment. In addition, the PR interval is usually increased, reflecting a prolongation in the H-V interval.

There is a propensity for life-threatening ventricular arrhythmias, with the complete syndrome being characterised by episodes of fast polymorphic ventricular tachycardias (VT). These may range from self-limiting runs causing syncopal attacks to ongoing arrhythmias causing a full blown cardiac arrest and sudden cardiac death.

The above mentioned abnormalities occur in the setting of a structurally normal heart.

PATHOPHYSIOLOGY

Recent research has implied a loss-of-function mutation of the SCN5A gene in about 10-30% of patients with Brugada syndrome. This affects the cardiac voltage-gated sodium channel ($Na_{v1.5}$) leading to a reduction in the sodium current (I_{Na}) available during the phases 0 (upstroke) and 1 (early repolarisation) of the cardiac action potential.

One of the hypotheses which have been put forward to explain the underlying mechanism is the 'Repolarisation-defect theory'. It proposes that there is an increased contribution of the transient outward current (I_{to}) to the action potential waveform in right ventricular epicardial cells compared to endocardial cells (giving a more prominent notch in the action potential of the former). This difference is accentuated by a decrease in I_{Na}, creating a voltage gradient during repolarisation and the characteristic morphology of ST elevation[2]. Another hypothesis explains the ECG findings as a reflection of disordered conduction (delayed activation and slow conduction) in the right ventricle, mainly the outflow tract. This is known as the depolarisation hypothesis.

DIAGNOSIS

A patient may be completely asymptomatic and said to have the Brugada sign. Those suffering from Brugada syndrome typically present with syncope but sudden cardiac death may also occur, commonly during sleep. Physical examination is unremarkable whilst there is usually a strong family history of sudden cardiac death.

INVESTIGATIONS:

1. ECG Changes: ST elevation $\geq$ 2mm in $\geq$ 1 lead from V1-V3 with typical morphology, with an associated RBBB pattern.
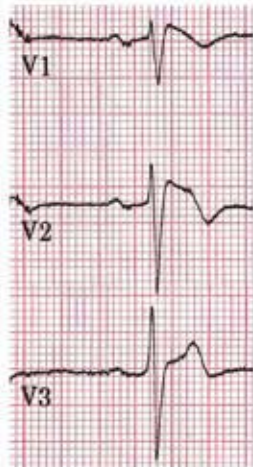2. Imaging, including angiography shows no underlying structural or coronary disease.

Figure 1: ECG from our patient showing typical Brugada pattern

3. Stress tests: Symptoms and ECG findings are not usually reproducible with exercise; interestingly, ST elevation normalises with increase in heart rate on exertion[4].

CRITERIA FOR THE DIAGNOSIS OF BRUGADA SYNDROME HAVE BEEN ESTABLISHED AS FOLLOWS[5]:

Major criteria
- Presence of ECG marker in structurally normal hearts
- Appearance of ECG marker after administration of sodium channel blockers

Minor criteria
- Family history of sudden cardiac death
- Syncope of unknown origin
- Documented ventricular tachycardia/fibrillation
- Genetic mutation of ion channels
- Positive programmed electrocardiostimulation test on VT / VF

MANAGEMENT

Implantable cardioverter-defibrillator implantation is the mainstay of treatment. Expert consensus recommendations have recently been published by Priori SG et al[4].

Table 1: Expert consensus recommendations on Brugada Syndrome therapeutic interventions

Class I	ICD is recommended in patients with a diagnosis of BrS who: a) are survivors of a cardiac arrest, and/or b) have documented spontaneous sustained VT with or without syncope
Class IIa	ICD can be useful in patients with a spontaneous diagnostic Type I ECG who have a history of syncope judged to be likely caused by ventricular arrhythmias
Class IIb	ICD may be considered in patients with a diagnosis of BrS who develop VF during programmed electrical stimulation (inducible patients)
Class III	ICDs are not indicated in asymptomatic BrS patients with a drug-induced type 1 ECG and on the basis of a family history of sudden cardiac death alone

SUDDEN CARDIAC DEATH

With an annual incidence of 0.1-0.2% , sudden cardiac death claims seven million lives per year worldwide. Males are affected three times as much, with a peak incidence between 45 and 75 years. The commonest cause is coronary artery disease, followed by cardiomyopathies and channelopathies. The most common cardiomyopathies are dilated, hypertrophic, arrythmogenic right ventricular, restrictive and left ventricular non-compaction. Channelopathies include Brugada syndrome, long and short QT syndromes, idiopathic VF and short-coupled variant of Torsades de Pointes[6].

Figure 2: Chain of Survival[7]

CONCLUSION

The educated eye should look out for the Brugada sign in every electrocardiogram, in order to diagnose and appropriately manage these patients. In addition, the chain of survival following cardiac arrest should be well known to all.

ABBREVIATIONS
BrS - Brugada Syndrome
ECG - Electrocardiogram
ICD - Implantable cardioverter-defibrillator
RBBB - Right bundle branch block
SCD - Sudden cardiac death
VT - Ventricular tachycardia
VF – Ventricular fibrillation

REFERENCES CAN BE ACCESSED ON THESYNAPSE.NET