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Case Report

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Unexplained Syncope in a 32-Year Old Joiner: Brugada Syndrome

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1. Summary

A 32-year old Caucasian male presented to the Emergency Department with a new two-day history of syncope. On first presentation he felt thirsty and hot and lost consciousness after having a drink and fell down the stairs. Initial investigations including blood tests, chest x-ray and ECG were reported as normal. He was discharged as having experienced a vagal episode worsened by dehydration. He presented again two days later having experienced another syncopal event while working at height on a scaffold. No prodromal symptoms or palpitations were described. There was no relevant family pedigree on initial questioning. He was admitted for observation and referred to cardiology. Cardiac monitoring indicated self-terminating ventricular tachycardia. A full range of blood tests were normal, as was echocardiography. A possible Type 2 Brugada pattern on ECG changes in V1, V2 prompted a normal cardiac MRI scan to rule out arrhythmogenic right ventricular cardiomyopathy (ARVC). A Flecainide provocation study unmasked Type 1 Brugada Syndrome (BrS).

2. Background

Syncope is a common cause for patients to present to the Emergency Department (ED). Brugada syndrome is uncommon (≤0.25% of European population) **[1]**

but well described. Emergency medical staff should be aware of the clinical signs of Brugada syndrome as a missed diagnosis may prove fatal.

3. Case Presentation

A 32-year Caucasian old male presented to the Emergency Department (ED) after waking with worsening of longstanding chest pain and feeling thirsty. The chest pain had no typical cardiac features and had recently been investigated with OGD that demonstrated a previous Mallory-Weiss tear. On taking a long drink, he suddenly felt hot and lost consciousness resulting in a fall down the stairs without sustaining injury. There was no, tongue biting, loss of bladder control, or palpitations and recovery was instantaneous with no neurological deficit.

The patient was normally fit and well with his only pre-existing medical history of gastro-oesophageal

reflux disease (GORD) treated with omeprazole. There was no history of syncope, epilepsy or unexplained familial sudden death. The patient occasionally experienced self-terminating palpitations lasting for "a few minutes only" with no associated pre-syncope or syncope. 12-lead ECG showed a shortened PR interval (99ms), left ventricular hypertrophy by voltage criteria with a non-specific intraventricular conduction delay with an early repolarisation pattern in V2. QTc (B) was within acceptable parameters at 444ms. The ECG had been reported as normal by the ED team. No abnormalities were identified on routine bloods for urea and electrolytes, liver function, CRP or full blood count. Troponin T was also normal. He was afebrile and chest x-ray was normal. He was discharged from the ED after treatment for presumed dehydration (even though urea and electrolytes did not confirm dehydration) with vagal syncope and arrangements for a 24-hour outpatient ambulatory ECG. He was advised to return if the symptoms recurred.

Two days later he presented again to the ED with a history of five syncopal episodes. These were preceded by palpitations on all occasions. The first episode occurred whilst working at height on scaffolding resulting in a fall. Again, no serious traumatic injury was sustained. He was found to be mildly hypoglycaemic (3.7mmol/L) and givenoral glucose replacement but other than this all his blood results, including Troponin T, where normal. He was normotensive at 121/76 mmHg. He was afebrile. 12-lead ECG demonstrated an incomplete right bundle branch block (RBBB), a new feature of saddleback ST elevation in V1 and V2 with >1mm in V2 at the J point with positive T waves. Advice was sought from the Cardiology Advanced Clinical Practitioner (ACP), who noticed this feature was new to the ECG compared to two days previously, and believed the ECG could be consistent with a Type 2 Brugada pattern. The ED team had planned to admit for a period of observation, but had not considered Brugada. Initially, the patient reported there was no family pedigree of sudden death and there were no known heart rhythm problems in family members. However, on probing, his father had died 20 years earlier from an out of hospital cardiac arrest that has been recorded as myocardial infarction on the death certificate (this is likely to have been Brugada that was largely unrecognised in a Caucasian population at this time). The patient did not associate his presentation with his father on first questioning as his father had died of a "Heart Attack".

4. Investigations

Inpatient ambulatory ECG monitoring showed three symptomatic episodes of self-terminating ventricular tachycardia (VT).Echocardiography was undertaken due to the left ventricular hypertrophy (LVH) by voltage on the 12-lead ECG. This heart was structurally normal. LVH by voltage is commonly described in young fit adults with low body fat **[2]**. Alternative differential to Brugada were ischaemia and arrhythmogenic right ventricular cardiomyopathy (ARVC) which cannot always be seen on an echocardiogram. Hence, a stress cardiac MRI (cMRI) scan was undertaken. The cMRI indicated a structurally normal heart with no fibrosis, infarction or ischemia. A flecainide provocation study was undertaken. Concurrent standard and superior (2^{nd} intercostal space) ECG lead placement in V1 and V2 was used (superior ECG position is reported to increase the sensitivity of testing in BrS). See Figure 2.A Type 1 Brugada pattern emerged firstly in the superior leads, and then in the standard leads. This confirmed a diagnosis of Brugada.

5. Treatment

Current European Society of Cardiology (ESC) guidelines **[3]** in Brugada stress risk stratification as imperative in determining treatment. A confirmation of Brugada does not equate to identifying a patient at high risk of sudden cardiac death (SCD). Evidence for interventions is Level C (expert consensus) with accordant recommendations. The conclusion was that this patient had a class I indication for implantable cardiac defibrillator (ICD) owing to induced Type 1 Brugada pattern with symptoms of arrhythmia induced syncope. An ICD was implanted as an in-patient. Advice was given in regards to medications that may increase the risk of ventricular arrhythmias in BrS **[9]** and on the management of pyrexia and infection. Following discussion, he was referred for genetic testing as the patient had a child.

6. Discussion

Brugada Syndrome was first identified in 1992 by the Brugada brothers **[4]** as a new disease entity with characteristic ECG changes of right bundle branch block and persistent ST-segment elevation and sudden cardiac death. There were originally x3

identified Brugada type patterns on ECG. Latterly Type 2 and 3 have been amalgamated **[5]**. Only Type 1 is diagnostic of BrS. Type 1 ECG shows J point elevation >2mm in right precordial leads V (1 and/or V2) with coved downward ST segment followed by a negative T wave. Type 2 pattern has an 'RSR' pattern in V1 and V2. The 'R' is at least 2mV amplitude. There is right precordial ST elevation with a saddled ST segment ≥0.5mm followed by positive T wave in V2. T wave morphology in V1 can be variable. The duration of the QRS is greater in V1 than in V6 in the Type 2 pattern **(Figure 1)**.

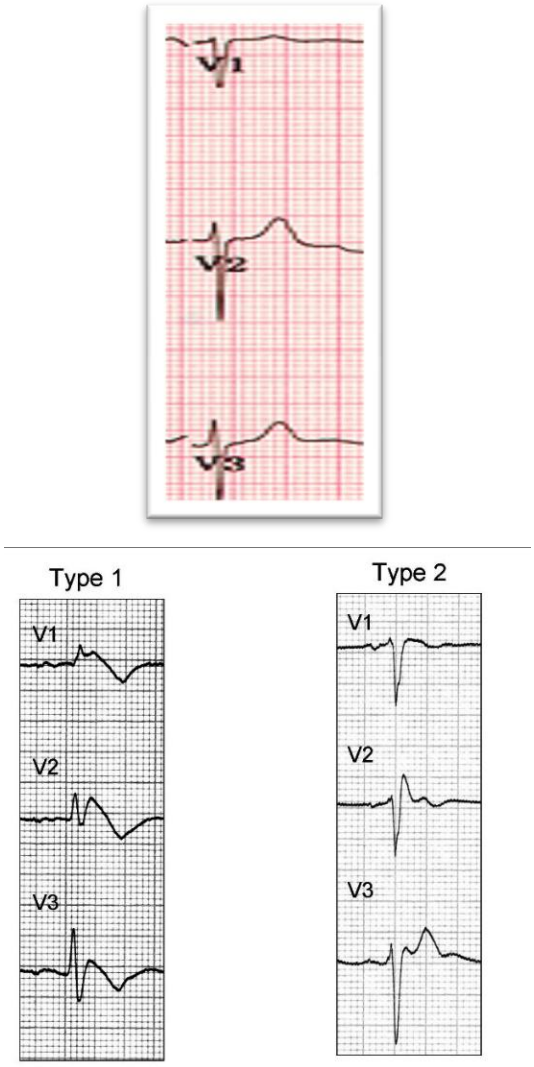


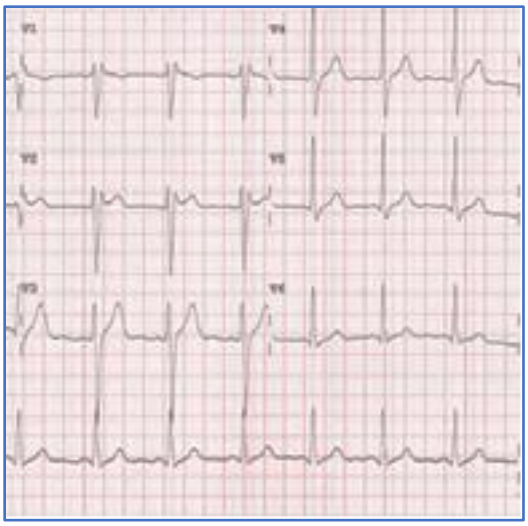
Figure 1: ECG Characteristics of Type 1 and Type 2 Brugada. The first image represents a normal pattern. Type 1 presents as ST-segment elevation followed by a symmetric negative T wave in the right precordial leads. Type 2 is characterized in V1 and V2 with the presence of terminal positive wave called *r'*, although in fact, it is a mixture of final QRS and beginning of repolarization. This r' presents a high take-off of at least 0.2 mV of amplitude, followed by elevated ST segment with saddle-back pattern, and by a T wave that is positive in V2 .

Only Type 1 pattern is diagnostic of Brugada Syndrome. Type 1 can be unmasked by pyrexia, some anaesthetic drugs or class 1 antiarrhythmics. The recognised test for Brugada in type 2 pattern is testing with a class 1a (e.g. ajmaline) or class 1c (e.g. flecainide) antiarrhythmic to promote the sodium channel pathway. Superior precordial chest lead positioning (2^{nd} or 3^{rd} intercostal space) may increase ECG sensitivity. Once diagnosis is established patients are assessed for risk of Sudden Cardiac Death (SCD) according to current guidelines **[3]**. The only definitive treatment for prevention of SCD is ICD. ICD is recommended in patients with aborted SCD or spontaneous ventricular arrhythmias, and "can be useful" for syncope judged likely to be ventricular arrhythmias.

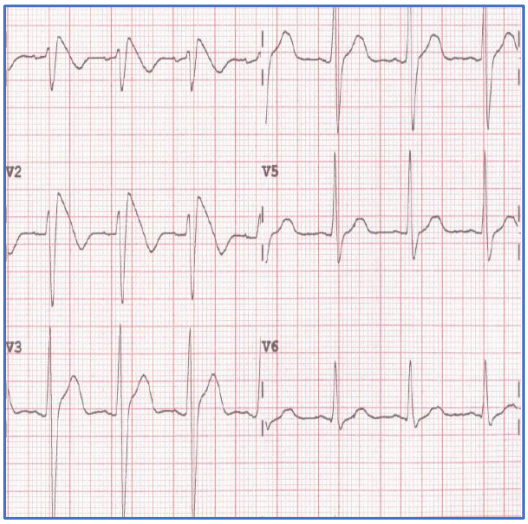
First manifestations of Brugada syndrome are usually in adulthood with a mean age of sudden death of 41+/- 15years **[6]**. Clinical manifestations are eight times more prevalent in men **[6]**. There are a number of identified genetic mutations associated with Brugada Syndrome **[7,8]**. Prevalence in a European population is ≤0.25% rising to up to 0.36% in Asian populations **[1]**. Clinical symptoms include ventricular fibrillation and aborted SCD. Palpitations, dizziness, recurrent syncope and nocturnal agonal respirations are listed as common symptoms. These symptoms are more commonly associated with rest and sleep (periods of increased vagal tone) or with pyrexia **[8]**.

The right ventricular outflow tract (RVOT) is cited as the source of suggested depolarisation disturbance **[8]**. One hypothesis is an imbalance in inward (Na+ and Ca+) and the outward potassium depolarisation currents during early repolarisation. This is thought to create a transmural gradient on the action potential in this area and sustained ST segment elevation. Another hypothesis suggests conduction slowing in the RVOT **[8]**. Diagnosis requires either spontaneous or induced Type 1 ECG changes in only one right precordial lead **[5]**. Once Brugada syndrome is confirmed ICD is recommended only with higher risk features of VT or aborted SCD (Class I recommendation), or syncope (IIa) **[3]**. The initial syncope in this patient was attributed to poor dietary

and fluid intake that day. There was not an awareness of palpitations on first presentation. In retrospect it is reasonable to suspect this was also a Brugada-related incident, but there were fewer clues in the history and ECG. It seemed reasonable to discharge the patient **(Figure 2)**.



(A)



(B)

Figure 2: (A**)** Chest Leads prior to Flecanide Challenge and (B) 15 minutes into Flecainide provocation study. With V1 and V2 in superior position.

The second presentation to the ED with palpitations, recurrent syncope and pseudo Type 2 Brugada pattern made for easier decision-making process. Whilst Brugada was established as a differential, other causes of syncope still required consideration. The European Society of Cardiology (ESC) guidelines on Syncope **[9]** identify the causes for consideration: reflex syncope (vasovagal, situational, carotid sinus syndrome): syncope due to orthostatic hypotension (drug-induced, volume depletion, neurogenic); and cardiac. The history of the situation, posture and prodrome are helpful in suggesting the likelihood of these causes. In this case there was much less evidence to suggest non-cardiac causes, and more to suggest arrhythmia due to rapid palpitations preceding the syncope, and documented symptomatic VT once cardiac monitoring was initiated. Although the diagnosis was far from secure, the symptoms represented a high risk should there be a BrS diagnosis. Once BrS was confirmed the risk stratification was a Class I recommendation for ICD due to documented VT. Syncope alone would have been class IIa recommendation for ICD. Current recommendations **[3]** also focus on reducing conditions that may induce ST elevation or ventricular arrhythmias. Therefore patients must avoid the drugs listed with potential to increase or induce ST elevation in right precordial leads **[10]**. They should also avoid excessive alcohol intake and treat fever promptly with antipyretic medication. Family history of sudden cardiac death is not an indication for ICD in asymptomatic BrS **[3]**. Genetic testing is not recommended for risk stratification, but as a diagnostic tool **[7,8]**.

7. Learning Points

- Type 1 Brugada syndrome with syncope is associated with adult sudden death.
- Brugada should be considered in unexplained syncope. Where there are ECG features suggestive of Brugada expert opinion should be sought
- Emergency medical staff should be aware of the clinical signs of Brugada syndrome as a missed diagnosis may prove fatal.

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