Is this a case of Brugada syndrome?

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Articles in this section are inspired by, but not based on, real cases to illustrate the importance of knowledge about ECGs in relation to clinical situations in general practice. Management is not discussed in detail.

Your first patient on a Monday morning is booked in for a health screen. He is a seemingly well 33-year-old Japanese man who has recently been sent to Australia by his company for two years. As part of his initial work arrangement he needs a health screen before starting his new job, hence his presence today at your practice.

You start your review of this patient. He speaks English quite well and there is no problem with communication. He is living alone in Australia. He is a nonsmoker, social drinker and has never used any recreational drugs. He is physically active and does 20 to 30 minutes daily of moderate intensity jogging and weight lifting at the gym. He is not taking any medication and does not have allergies to any medications. He does not complain of any symptoms. He sleeps well and is not under much stress at work.

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On examination, the patient looks well, his height is 1.70 m and his weight is 65 kg. You perform a thorough physical examination. His blood pressure is 110/65 mmHg and pulse rate is 60 beats per minute (bpm). There are no positive findings. As part of your health screen you perform a full blood count, measurement of urea, electrolyte and creatinine levels, as well as blood urea concentrations, a liver function test, lipid profile and an ECG (see Figure 1).

How do you describe this ECG?

The ECG shows a regular sinus rhythm with a rate of 60 bpm. There is a P wave prior to each QRS complex and the P wave is positive in leads I and II and negative in aVR. Axis is normal. A quick and easy way to determine the axis is:

- if lead I is positive and leads II and III negative, then there is left axis deviation
- If lead I is negative and leads II and III positive, then there is right axis deviation.

Waves

The P and Q waves appear normal. There is an R wave in leads V1 and V2, and widening and poor progression in the precordial leads. The T wave is inverted in leads V2.

Intervals

The PR is normal (<200 msec) and the QRS is prolonged at 128 msec (normal, <120 msec). QT, machine calculated and corrected for the rate is not prolonged (if >500 msec this is concerning and will increase the risk of torsade de points). As a rough estimation of QT on the ECG, QT should be less than half of RR interval, between rates of 60 and 90 bpm. There is ST segment elevation in leads V1, V2 and V3.

What is your interpretation of the ECG?

The ECG is in regular sinus rhythm and the axis is normal. There is a right bundle branch block (RBBB) pattern in leads V1 and V2, no right axis deviation, and ST segment elevation in leads V1 to V3. This particular pattern in leads V1 and V2 (and sometimes lead V3) is suggestive of Brugada syndrome.

What specific questions do you now ask the patient?

You ask the following specific questions.

- Is there any history of palpitations?
- Is there any history of syncope or episodes of presyncope?
- Do you have any previous ECGs for comparison?
- Is there any family history of cardiac

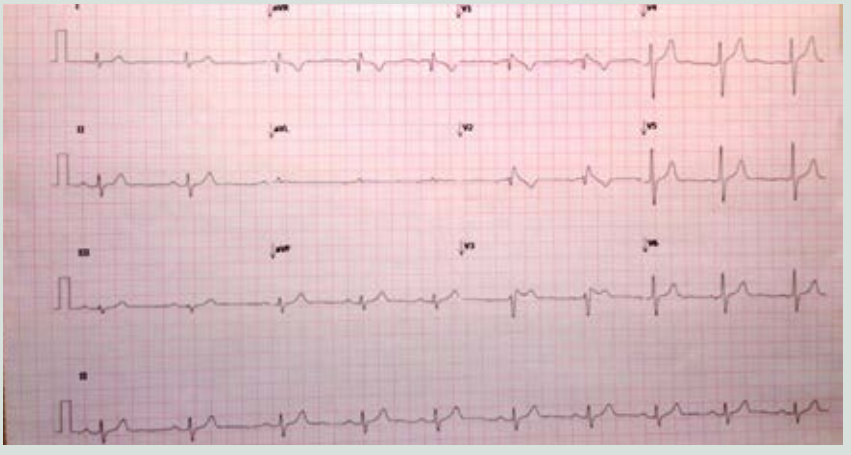

Figure 1. An ECG showing right bundle branch block pattern in leads V1 and V2, no right axis deviation and ST segment elevation in leads V1 and V2. This particular pattern is suggestive of Brugada syndrome.

disease, sudden death or sudden infant death syndrome?
- Has any of your siblings been told of any heart abnormality?

What is your next step?

Patients with Brugada syndrome are at risk of sudden cardiac death due to ventricular tachycardia, ventricular fibrillation and cardiac arrest. You contact your usual cardiologist for his opinion and send him a picture of the ECG. The cardiologist confirms the Brugada pattern on the ECG and organises to see the patient as a priority.

What is Brugada syndrome?

The first patient with Brugada syndrome was identified in 1986, with the first paper on the topic being published in 1992. Brugada syndrome accounts for approximately 4% of all sudden deaths and 20% of sudden deaths in people with structurally normal hearts. Brugada syndrome is one of the leading causes of natural death in men younger than 50 years in southeast Asia.

Brugada syndrome is an autosomal dominant genetic disorder that predisposes the person to ventricular tachycardia, ventricular fibrillation and sudden cardiac arrest. It is more common in men, and is usually diagnosed at about 40 years of age. It is more common in people with schizophrenia and is not due to use of antipsychotic medications; the cause is unclear.

The two types of Brugada are type 1 in which there is only the pattern of the Brugada on the ECG and no symptoms, and type 2 in which there is the ECG abnormality and associated symptoms.

Brugada syndrome is caused by defective myocardial sodium channels, which reduces sodium inflow currents, thereby reducing the duration of normal action potentials. It is not usually associated with structural heart disease.

What are the clinical features?

Most clinical manifestations of Brugada syndrome are related to life-threatening ventricular arrhythmias. Sudden cardiac arrest may be the initial presentation in as many as one-third of patients with the condition and it happens more often during the night. Patients may also present with an episode of syncope.

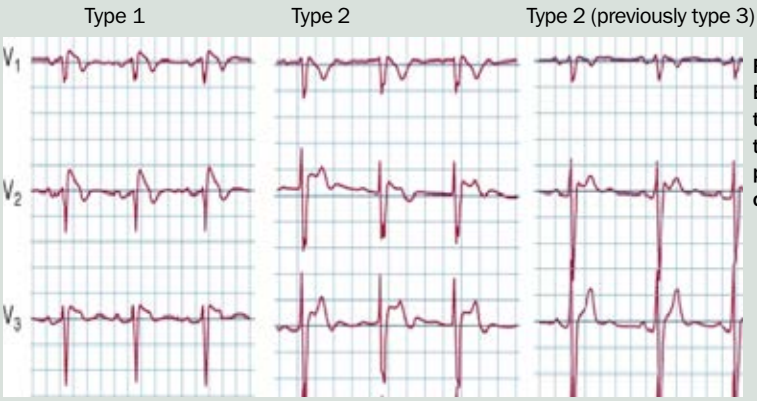

Figure 2. Brugada type 1 and type 2 pattern ECG changes.

The initial presentation may also be palpitations related to atrial fibrillation, which is associated with Brugada syndrome. Patients with Brugada syndrome are at increased risk of atrial arrhythmias, most notably atrial fibrillation. Palpitations related to ventricular tachyarrhythmia are not common in patients with Brugada syndrome.

Nocturnal agonal respiration with gasping breaths during sleep has been reported and may represent aborted cardiac arrhythmias. The risk of cardiac arrest is much lower in asymptomatic patients.

What are the ECG changes of a Brugada pattern?

These are pseudo-RBBB (i.e. the presence of ECG changes suggestive of RBBB but no axis deviation) and persistent ST segment elevation in leads V1 to V2 and sometimes V3.

In the classic Brugada type 1, the elevated ST segment (≥2 mm) descends with an upward convexity to an inverted T wave on the ECG. This is referred to as the 'coved type' Brugada pattern.

In the type 2 pattern (combined from the original designation of types 2 and 3 patterns), the ST segment is 2 mm or more elevated and has a 'saddle back' ST-T wave configuration, in which the elevated ST segment descends toward the baseline but remains at least 0.5 mm above the isoelectric baseline and then rises again to an upright or biphasic T wave (see Figure 2).

Moving the right precordial chest leads superiorly to the second or third intercostal space or using bipolar chest leads may increase the sensitivity of detecting these abnormalities and should be performed if there is doubt about the diagnosis.

The widened S wave in left lateral leads that is characteristic of RBBB (waveform 2) is absent in most patients with Brugada patterns on ECG.

What are the diagnostic criteria?

Brugada syndrome type 1 is diagnosed in patients with ST segment elevation of more than 2 mm in more than one lead among the right precordial leads V1 to V2 positioned in the second, third or fourth intercostal space occurring either spontaneously or after provocative drug test with intravenous administration of class I antiarrhythmic drugs.

Brugada syndrome type 2 is diagnosed in patients with ST segment elevation in more than one lead among the right precordial leads V1 to V2 positioned in the second, third or fourth intercostal space when a provocative drug test with intravenous administration of class I antiarrhythmic drugs induces a type 1 ECG morphology.

What are the provoking factors for Brugada pattern?

Characteristic ECG abnormalities may be exposed by a sodium channel blocker, thereby identifying patients at risk. Pacing, vagal manoeuvres and increased alpha-adrenergic tone may also provoke the typical ECG changes of Brugada syndrome.

Other factors that can unmask or modulate the Brugada ECG pattern are use of beta blockers, tricyclic or tetracyclic antidepressants, lithium and local anaesthetics, fever, hypokalaemia, hyperkalaemia, hypercalcaemia, alcohol and cocaine toxicity.

What are the diagnostic tests?

Holter monitoring

The ECG pattern of Brugada syndrome can change during the day. It is recommended to obtain a 24-hour holter monitor reading in patients who are at low risk but have ECG changes of type 2 Brugada syndrome.

Drug challenge

Once the diagnosis of Brugada syndrome is suspected based on the clinical presentation and ECG findings, additional testing may be considered to further confirm the diagnosis and to provide an estimate of the risk of ventricular arrhythmias and sudden cardiac death in the individual patient.

In general, the first test is drug challenge testing for patients whose resting ECG shows the type 2 Brugada pattern and who have a family history of sudden cardiac death at under 45 years of age and/or a family history of type 1 Brugada pattern ECG changes. The drugs that are usually used are sodium channel blockers such as flecainide, ajmaline or procainamide (only flecainide is available in Australia).

The patient should be monitored during the administration of the drug and for the duration of its action (e.g. flecainide infusion occurs over 20 to 30 minutes and monitoring is required, especially as changes may become evident early). These tests are preferably carried out as an inpatient with all the appropriate safe guards.

Some cardiologists also proceed with electrophysiological studies to determine whether an implantable cardiac defibrillator (ICD) should be considered. Drug challenge is not recommended for asymptomatic patients with type 2 Brugada pattern without a family history of sudden cardiac death.

Genetic testing

Brugada syndrome is caused by an autosomal dominant inherited gene mutation. Genetic testing for Brugada syndrome is commercially available and can be useful in confirming the presence of a mutation in a patient with a suspected diagnosis of Brugada syndrome. The decision for genetic testing should be made in conjunction with the treating cardiologist, as well as involving genetic counselling before and after the test.

What are the mimics of the Brugada pattern on ECG?

- Atypical RBBB
- Arrhythmogenic right ventricular cardiomyopathy
- Early repolarisation
- Acute pericarditis
- Acute myocarditis
- Acute myocardial ischaemia or infarction
- Hypothermia
- Conditions that impinge on the right ventricle (tumours, pericardial effusion).

What are the prognostic factors?

The most important prognostic risk factor for patients with the Brugada ECG pattern or Brugada syndrome appears to be a history of ventricular tachyarrhythmias leading to sudden cardiac arrest or syncope. Other less powerful predictors of future events may include atrial fibrillation, male gender and a family history of sudden cardiac arrest.

What are the precipitating causes of sudden death in this syndrome?

There is a long list of medications that can increase the risk of ventricular tachycardia, ventricular fibrillation and sudden cardiac death. (A complete list can be found at www.brugadadrugs.org.)

Fever is a precipitant of cardiac arrest and during a febrile illness it is important to remind the patient to control his temperature with antipyretic medications. Sudden cardiac arrest in patients with Brugada syndrome is usually not related to exercise.

What are the treatment options?

Pharmacological therapy for arrhythmia prevention has been tried in patients with the Brugada syndrome with relatively little success. Treatment for patients diagnosed with Brugada syndrome is primarily focused around termination of any ventricular arrhythmias with an ICD.

In patients who refuse ICD implantation or are not considered suitable candidates due to reduced life expectancy or significant comorbidities, initial therapy with either amiodarone or quinidine (not TGA approved for use in Australia) is recommended.

Patients with only the Brugada ECG pattern do not require any specific therapy. However, there are many drugs (including antiarrhythmic, psychotropic and anaesthetic drugs) that need to be avoided by these asymptomatic patients.

What are the implications of a diagnosis of Brugada syndrome for relatives?

As Brugada syndrome follows an autosomal dominant genetic pattern with variable penetrance, all first-degree relatives of patients with confirmed Brugada syndrome should undergo screening with a clinical history and 12-lead ECG.

A high suspicion for the Brugada syndrome should continue in first-degree relatives with a concerning history of syncope but a normal appearing ECG and an indeterminate screening result. Such patients should have ongoing screening with serial ECGs performed over three to four visits over the course of one to two years. First-degree relatives with indeterminate screening should also be considered for provocative testing with a pharmacological challenge.

As the diagnostic ECG changes of Brugada syndrome can appear later in life in the fourth and fifth decades, symptomatic younger patients with a first-degree relative with Brugada syndrome should continue to receive annual ECGs. First-degree relatives with no history of syncope and a normal ECG are considered to have a negative screening result and do not require ongoing surveillance.

Outcome

The patient was reviewed by the cardiologist and his ECG showed type 1 Brugada syndrome. He does not have any concerning family history or any symptoms in his history. It was decided that at this stage he can be monitored with yearly ECG screening and that he should seek medical attention if he develops any symptoms. He was advised to monitor his temperature, to treat pyrexia early and to remember to inform any treating doctor of his syndrome before taking any medication. **CT**

Further reading

A list of further reading is included in the website version (www.medicinetoday.com.au) of this article.

COMPETING INTERESTS: None.

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Further reading

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