Aborted sudden death in a young male

Q1: What is the ECG (fig 1; p 660) diagnosis? Why is it important to recognise this condition?

The ECG done on his arrival at the emergency room (see questions) shows (i) sinus tachycardia, (ii) a QRS complex that ends with a positive deflection (or prominent J wave) that is, a rsR' pattern in V1 and V2, and (iii) an elevated downsloping ST segment ending in a small negative T-wave deflection. This ECG pattern in someone with a history of syncopy and documented ventricular fibrillation/aborted sudden death, is most consistent with the eponymous Brugada syndrome. Described first in 1992 by Brugada and Brugada, Brugada syndrome is an inherited arrhythmogenic disease, which may presage ventricular fibrillation and sudden cardiac death.1,2

The Gussak diagnostic criteria3 for Brugada syndrome are shown in box 1. One must be aware that ST elevation in the right precordial ECG leads occurs in a variety of clinical conditions, as shown in box 2, and hence clinical correlation with diligent characterisation of the ECG is mandatory before a diagnosis of Brugada syndrome is made. 2,4

Brugada syndrome is a recognised cause of sudden cardiac death, and hence the need for prompt recognition and treatment. Every year, in the United States alone, there are about 300 000 new cases of sudden death due to cardiac arrest. Altogether 3%–9% out-of-hospital cases of ventricular fibrillation, unrelated to myocardial infarction, occur in those with minimal or no structural heart disease.5 Such cases may include those with Brugada syndrome, congenital and acquired long QT syndromes, pre-excitation states such as Wolff-Parkinson-White syndrome, and cases where no ready cause is apparent (so called “idiopathic” ventricular fibrillation). Though seen worldwide, Brugada syndrome is endemic in Southeast Asia and Japan, where it is known as sudden unexplained nocturnal death syndrome and sudden unexplained nocturnal death syndrome, and the incidence has been estimated to range between five and 66 events per 100 000 people.1 In some countries, the prevalence of Brugada-type ECG changes among those who were diagnosed with “idiopathic ventricular fibrillation”, has been estimated to be as high as 40%–60%.6 Studies quote an incidence of sudden cardiac death varying between 44%–62% in those with Brugada-type ECG and history of aborted sudden death/syncopy.7 Considerable variation exists in the clinical presentation, and several “forms” of Brugada syndrome have been described: manifest, concealed, asymptomatic, suspected, and simulated.8 Brugada syndrome affects males preferentially, and the mean age of those affected tends to be in the mid to late thirties. Clinical manifestation of Brugada syndrome are attributed exclusively to the malignant ventricular arrhythmias that occur in this condition. Tragically, sudden death may be the first and only clinical event. These arrhythmias often occur at rest, and in some at night-time. High sympathetic tone, anxiety, and alcohol consumption have all been proposed as possible provocative factors.7

Q2: What is the pathophysiological basis of this condition? What further diagnostic tests would you consider doing in this patient?

Genetic studies have shown that Brugada syndrome and chromosome 1-linked long QT syndrome (LQTS) are allelic disorders of the cardiac channel gene (SCN5A, 3p21). The inheritance is autosomal dominant with variable penetrance. The SCN5A gene codes for the alpha subunit of the sodium channel. Mutations of this gene results in abnormalities of the sodium channel, with abnormal ion conductance patterns and can be demonstrated in up to 25% Brugada syndrome cases.4,5 Brugada-type downsloping ST segment is a normal feature of the ECG in some rodents, whereas in higher mammals, the ST segment is usually isoelectric in the normal state. Figure 1 (below) describes the various phases of the cardiac ventricular action potential. Failure of the plateau phase or “dome” to develop occurs when the transient outward currents, termed I_{Na} (phases 1 and 3; fig 1) overwhelms the inward current, mainly the calcium current termed I_{Ca} (phase 2; fig 1). This results in a 40%–70% abbreviation of the action potential in some, but not all epicardial sites (schematically represented by the dotted line in fig 1), resulting in a marked dispersion of repolarisation within the ventricular muscle. This is manifest on the ECG as marked QT-dispersion. Propagation of the dome from sites where it is maintained to sites where it is abolished (termed phase 2 re-entry) can result in local re-excitation, producing closely coupled extrasystoles, which in turn may initiate fibrillation or re-entry.9 In those cases where the typical ECG changes are evanescent, programmed electrical stimulation (PES) with or without chemical challenge with certain drugs may unmask the ST segment elevation in V1–V3 and right bundle branch block-like pattern in many patients.1 Sodium channel blockers

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**Box 1: Gussak’s criteria**

- **Major criteria**:  
  1. Presence of the ECG marker of Brugada syndrome in patients with structurally normal heart.  
  2. Appearance of the ECG marker of Brugada syndrome after administration of sodium channel blocker.

- **Minor criteria**:  
  1. Family history of sudden cardiac death.  
  2. Syncopy of unknown origin.  
  3. Documented episodes of ventricular tachycardia/ventricular fibrillation.  
  4. Positive programmed electrocardiogram stimulation test on ventricular tachycardia/ventricular fibrillation.  
  5. Genetic mutations of ion channels (yet to be fully defined).

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**Box 2: Causes of ST segment elevation in right precordial ECG leads**

- Anterior myocardial infarction.  
- Right or left bundle branch block.  
- Right ventricular infarction.  
- Left ventricular aneurysm.  
- Exercise stress induced.  
- Acute myocarditis.  
- Dissecting aortic aneurysm.  
- Acute pulmonary thromboembolism.  
- Right ventricular outflow tract obstruction (tumour, etc).  
- Various central and autonomic nervous system disorders.  
- Duchenne’s muscular dystrophy.  
- Friedreich’s ataxia.  
- Hypercalcaemia and hyperkalaemia.  
- Heterocyclic antidepressant overdose.  
- Cocaine intoxication.  
- Thiamine deficiency (beriberi).

Adapted from Gussak et al.2
SCB) such as procainamide, ajmaline and flecainide, \( \beta \)-blockers such as propranolol, \( \alpha \)-adrenergic and muscarinic stimulation— all may bring out the typical ECG features, and indeed induce ventricular tachyarrhythmia and/or ventricular fibrillation in those with Brugada syndrome. While PES and SCB challenge may be useful in risk stratifying patients with Brugada syndrome, their ability to identify the symptomatic (cardiac arrest, syncope) cases is at best modest for (PES, positive and negative predictive values and overall accuracy 50%, 46% and 49% respectively, for SCB challenge, positive predictive value 35%). A complete workup of a symptomatic patient with Brugada syndrome may also include echo-cardiography, coronary angiography, stress testing, magnetic resonance imaging, and rarely, myocardial biopsy.4 This patient underwent PES with procainamide challenge, which resulted in inducing the ventricular tachyarrhythmia. He underwent cardiac catheterisation, which revealed normal coronary artery anatomy and left ventricular function.

**Q3: How is this condition treated? What is the prognosis?**

For the symptomatic Brugada patients (syncope or sudden death) the treatment of choice is placement of an implantable cardioverter-debrillator (ICD) device. The incidence of arrhythmic events is similar in patients receiving either an ICD device, \( \beta \)-blocker or amiodarone, but only the ICD device protects patients with Brugada syndrome from sudden death. To this date, there is no pharmacological agent that has been shown to confer a survival benefit to patients with Brugada syndrome.

In some countries such as Japan, the incidence of asymptomatic Brugada syndrome cases is very high and far exceeds those with symptoms. In as much as the ICD device prevents death in symptomatic cases, many lives could be potentially saved if we could successfully identify the high risk, asymptomatic patients as well.5 There is some evidence that asymptomatic patients with Brugada syndrome who have a positive provocative test may benefit by placement of an ICD device. When followed up for over 33 months, 17% of inducible Brugada syndrome patients had an arrhythmia compared with only 3.5% among those who were not inducible.6 As to what constitutes optimal therapy for non-inducible cases of Brugada syndrome, it is still unclear and more studies are required to address this question.7

Regardless of the presence or absence of symptoms, the prognosis of Brugada syndrome is poor, with a 10% per year mortality.8 While no correlation between right bundle branch block and SCD has yet been established in a population other than those with Brugada syndrome, the magnitude of ST segment elevation has been linked to the incidence of life threatening arrhythmias, especially in Brugada syndrome.9 Careful attention to the ECG is mandated in every case of aborted sudden cardiac death in order to recognise and treat the patient with the Brugada syndrome.

**Final diagnosis**

Brugada syndrome.

**Acknowledgements**

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**References**


An unusual cause of abdominal pain

**Q1: What is the diagnosis and what are the clinical features of this condition?**

The underlying diagnosis is tuberous sclerosis. Tuberous sclerosis complex (TSC), described by Bourneville in 1880, is one of the neurocutaneous syndromes. Inheritance is autosomal dominant with spontaneous mutation in 60%. Two loci on chromosomes 9 and 16 produce the phenotype, both encoding proteins with tumour suppressor function.1 Incidence is estimated as one per 6000 live births and a prevalence of one in 10 000.2 Diagnostic criteria were reviewed in 1998.3 Clinical features result from hamartomas affecting various organ systems. Cerebral manifestations occur in up to 95% of patients, which include cortical tubers, subependymal nodules, giant cell astrocytomas, epilepsy (60%), learning difficulties (40%), and autism (40%–45%). Skin involvement (90%–95%) includes facial angiofibroma, hypomelanotic macules, forehead fibrous plaques, Shagreen’s patches, ash leaf spots, and perungual fibromas (fig 1; p 661). Renal involvement involves cysts and angiomylipomatosis (45%–66%), composed of blood vessels, smooth muscle, adipose and connective tissue. Type I lesions are benign and may be asymptomatic, though may differentiate to renal cell carcinoma in well under 5% and may occur bilaterally. Renal disease is a leading cause of death in patients with TSC.7 Pulmonary lymphangiomyomatosis and lymphangioleiomyomatosis occur exclusively in women.8 Retinal phakomas, dental pitting, cardiac rhabdomyomas, gingival fibromas, and rectal polyps are recognised features.9

**Q2: What does the computed tomogram of the abdomen (fig 2; p 661) show?**

The non-contrast computed tomogram shows grossly abnormal kidneys with enlarged focal areas of fatty change surrounded by streaky material largely replacing the renal tissue. A large uniform soft tissue mass is seen to arise from the anteromedial aspect of the right kidney.

**Q3: What do the renal ultrasound scans (figs 3, 4, 5; p 661) show and what is the likely diagnosis?**

The initial ultrasound (fig 3; p 661) shows a homogenous 10 cm mass in the mid-lower abdomen. Subsequent scans (fig 4 and 5; p 661) over a six week period show the mass to be reduced in size, with a more loculated irregular echo pattern consistent with resolving haematoma within a large section of angiomylipoma. The diagnosis is spontaneous haemorrhage into a renal angiomylipoma in a patient with tuberous sclerosis. Intrarenal, perirenal, retroperitoneal, and intraperitoneal haemorrhage are well recognised complications of angiomylipoma.10 Bleeding risk increases when they exceed 4 cm in size, and if asymptomatic may require intervention with embolisation or nephrectomy surgery.11

**Q4: What is the cause of the clotting abnormality?**

A normal prothrombin time and prolonged activated partial thromboplastin time which is not reversed when the patients plasma is diluted 1:1 with normal platelet free plasma suggests lupus anticoagulant activity. Anticardiolipin antibodies were subsequently negative in this case, and clotting studies require follow up.

**Final diagnosis**

Spontaneous haemorrhage into a renal angiomylipoma in a patient with tuberous sclerosis.

**References**


A case of severe, unexplained breathlessness

**Q1: What is the mechanism of this patient’s breathlessness and how would you confirm this?**

This man is breathless due to bilateral diaphragmatic paralyisis, which causes profound orthopnoea and paradoxical abdominal motion, unlike other common causes of breathlessness. The clinical picture differs from orthopnoea of cardiorespiratory origin in its strikingly rapid onset on lying flat, with rapid and complete recovery on sitting up. Paradoxical abdominal motion (that is, movement of the abdominal contents inward during inspiration) is an important physical sign of diaphragmatic weakness. The diagnosis is suggested in the absence of other signs indicating a respiratory or cardiovascular cause for the
orthopnoea, a careful search for paradoxical abdominal movement is important. Fluoroscopic screening of the diaphragms can be set to confirm bilateral paresis and paradoxical movement.

Q2: What is the likely clinical diagnosis. How would you try to establish this?

Bilateral diaphragmatic weakness is most often observed in the context of generalised neurological illnesses affecting muscle (for example, polymyositis or muscular dystrophies), neuromuscular transmission (for example, myasthenia gravis), inflammatory polyneuropathies (for example, Guillain-Barré syndrome), or anterior horn cell disease. However, involvement of the diaphragm in association with the rapid onset of diaphragmatic weakness and weak, and variable sensory loss around the shoulder girdle. Typically, sudden deep pain around the shoulder girdle—described as sharp, aching, boring, or throbbing—is associated with muscle weakness either simultaneously or after a variable period of several days to weeks. Commonly affected muscles include the deltoid, triceps, serratus anterior, spinati, biceps, triceps, and wrist and finger extensors; sensory deficit is usually less conspicuous. The annual incidence is approximately 1.64 per 100,000.1 Men are more commonly affected, with the highest prevalence in the 20–50 year age group.2 Unilateral or bilateral diaphragmatic weakness is found in about 7% of patients, and may dominate the clinical presentation.3 The precise location of the lesion, and its progression remain puzzling; viral and autoimmune processes have been suggested but not confirmed.

Nerve conduction studies (NCS) and electromyography (EMG) are the most helpful diagnostic tests. Extensive needle electrode examination may be required. In this patient NCS/EMG revealed normal sensory and motor conduction velocities, but no evidence of a neuromuscular junction transmission disorder. There was complete denervation of the right deltoid muscle, and milder neurogenic changes in the right supraspinatus, biceps, and brachioradialis. The EMG findings of active, patchy denervation strongly favoured the diagnosis of brachial neuritis, and helped to exclude peripheral nerve or root involvement.

Routine laboratory studies on blood, and examination of the cerebrospinal fluid are unremarkable in brachial neuritis. Magnetic resonance imaging may be helpful in excluding local neoplastic, infiltrative, traumatic, and musculoskeletal conditions.

Q3: What is the treatment and prognosis for this patient?

Accurate and prompt diagnosis of brachial neuritis can help to avoid potentially hazardous investigations and treatment. Treatment is mainly supportive, including analgesics, physiotherapy, and reassurance. Corticosteroids (for example, prednisolone, 60 mg daily tapering over two weeks) may be given to accelerate recovery and reduce pain, but they have not been shown to clearly influence the course of the illness. The clinical outcome with diaphragm involvement is variable. Some degree of recovery is usual but may be slow or incomplete.7 The patient described was treated conservatively with analgesics and physical therapy, and advised regarding sleeping posture. Three months after discharge, he remained well with only mild orthopnoea.

Final diagnosis

Brachial neuritis (neuralgic amyotrophy).

References


An unusual case of relapsing Graves’ disease

Q1: What is the diagnosis and how frequently is this condition encountered?

The patient had developed thyroid storm secondary to radioiodine therapy. Thyroid storm is a rare, life threatening complication of hyperthyroidism with an incidence of 1%–2% in hospitalised patients with hyperthyroidism, although it has a high mortality of around 15%. The incidence of the thyroid storm after RAI is variable because of variations in the regimens of RAI, in patient selection, and in the use of thyrrostatic medications before and after RAI. The overall incidence is low and in one series only one patient out of 525 patients treated with 550 MBq RAI developed thyroid storm.8 The risk of thyroid storm after RAI treatment is difficult to predict in an individual patient but appears to be higher in patients with severe hyperthyroidism, in older patients, and in the presence of cardiovascular and cerebrovascular disease.9

Q2: What is the mechanism and what are the criteria for diagnosis of this condition?

The mechanism of thyroid storm is either a reduction in levels of binding proteins or the release of preformed thyroid hormones. Examples of the former include postoperative state or a major systemic illness; the latter is encountered as a result of injury to the follicular cells after RAI treatment or even after vigorous manipulation of the thyroid gland. Other precipitating factors include radiation, diabetic ketoacidosis, toxaemia of pregnancy, and parturition. Diagnosis is entirely based on typical clinical features in an appropriate setting. Suspicious thy-roid stimulating hormone and raised thyroid hormone levels support the diagnosis but the degree of elevation of the latter is not always exceptional.

Q3: How is this condition managed and how can one prevent it?

Management of thyroid storm precipitated by RAI therapy is along similar lines as that of thyroid storm caused by any other precipitant. Thyroid storm should preferably be managed in conjunction with an endocrinologist and management includes the administration of Lugol’s iodine, high dose propylthiouracil, corticosteroids, and supportive measures. There are no specific recommendations for prevention of thyroid storm after RAI, although, in high risk patients, prior hospitalisation,5 rendering patients euthyroid,2 and use of antithyroid drugs after RAI therapy have been recommended.10 Our patient developed thyroid storm even though she had been rendered euthyroid before RAI therapy and did not have any associated comorbidity. After recovery from thyroid storm, carbimazole was continued till May 1984 for persistent hyperthyroidism when RAI was readministered at a very high dose of 1110 MBq in view of an isotope uptake study showing an extremely high radioiodine turnover. On this occasion she was hospitalised before the administration of RAI therapy and carbimazole was recommenced five days after RAI. There was no recurrence of thyroid storm and three months later the patient became hypothyroid, requiring thyroxine replacement. It is likely that thyroid storm was successfully prevented by early reintroduction of carbimazole after the RAI treatment.

Final diagnosis

Thyroid storm secondary to radioiodine therapy.

References

An unusual case of relapsing Graves' disease

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