We describe the successful administration of a combined general and epidural anaesthetic for laparotomy in a patient with Brugada syndrome.1

Case report
A 52-yr-old man presented with acute small bowel obstruction for a laparotomy. Eighteen months before admission, the patient had suffered an unheralded episode of a pulseless cardiac arrhythmia (recognized by a relative trained in basic life support) at home. Recovery occurred after basic cardiopulmonary resuscitation, before the arrival of the paramedic ambulance crew. A further episode of monitored ventricular fibrillation (VF) in the ambulance required a single 200 J cardioversion. He had no history of angina or previous syncope and there was no family history of sudden death. His father had suffered a myocardial infarction at the age of 50 and died. The patient had been a smoker until 3 months before admission and had a history of peptic ulcer that had been treated with ranitidine.

On investigation, the patient had a 12-lead ECG showing a partial right bundle branch block with a ‘coved’ pattern of ST elevation in leads V1 to V3 (Fig. 1). Cardiac enzymes were not elevated. Subsequent cardiac catheterization showed normal left ventricular function and coronary arteries. The patient underwent a flecainide challenge with an i.v. bolus of 150 mg. This produced accentuation of the ST elevation, consistent with Brugada syndrome. In view of the documented VF arrest, characteristic ECG features, and the absence of underlying structural heart disease, a diagnosis of Brugada syndrome was made. A single-chamber implantable cardioverter–defibrillator (ICD) was inserted under local anaesthesia and sedation. The patient was discharged home on aspirin, ranitidine, nadolol (subsequently changed to bisoprolol) and amiloride.

Before arrival in the anaesthetic room during this admission, the question of postoperative analgesia was discussed with the patient. Having been informed of the various options and their associated risks, the patient consented to the placement of a thoracic epidural catheter after induction of general anaesthesia. After the patient had arrived in the anaesthetic room, and with the patient fully monitored, the ICD was externally disabled. A right radial arterial cannula and a right internal jugular triple-lumen cannula were inserted under local anaesthetic. The patient underwent rapid sequence induction with thiopental 5 mg kg⁻¹ and succinylcholine 100 mg. After intubation of the trachea, the patient was given fentanyl 100 μg and a thoracic epidural catheter was inserted aseptically at the T8/9 space with the patient in the left lateral position. Cefuroxime 1.5 g, metronidazole 500 mg and gentamicin 320 mg were then administered. Anaesthesia was maintained using an oxygen–nitrous oxide–isoflurane mixture with increments of vecuronium 2 mg for neuromuscular block. Epidural analgesia was provided with 0.25% bupivacaine 10 ml and fentanyl 20 μg. An external defibrillator, connected to defibrillation pads placed on the patient, was present in theatre during the laparotomy. At operation, some minor small bowel adhesions were divided. No other abnormality was found. Neostigmine 2.5 mg–glycopyrrolate 0.5 mg solution was used at the end of the procedure to antagonize the neuromuscular block. Continuous monitoring of the ECG showed no abnormalities as a result of the anaesthetic or the operation. The internal defibrillator was re-enabled in the recovery room, and the patient went on to recover successfully from the operation.

Discussion
Brugada syndrome is characterized by an ECG pattern of right bundle branch block and ST segment elevation in the
right precordial leads (V₁ to V₃), without evidence of underlying structural heart disease. It is associated with a significant risk of ventricular tachyarrhythmias and sudden death. It was first recognized as a distinct clinical entity in 1992. The syndrome is familial (although this was not observed in our patient), with an autosomal dominant mode of transmission and incomplete penetrance. Arrhythmic events are observed at an average age of approximately 40 yr, but have been reported over a wide range of ages from 2 to 77 yr.

Establishing the diagnosis of Brugada syndrome can be difficult. The electrocardiographic signature is concealed in up to 30% of affected individuals and can only be seen after administration of potent sodium channel blockers, such as flecainide, propafenone and procainamide. However, recent follow-up data indicate that the risk of ventricular tachyarrhythmias is low in the absence of a resting ECG abnormality. In patients with an abnormal resting ECG, electrophysiological study incorporating programmed electrical stimulation is recommended to further define the risk of malignant tachyarrhythmia. In the presence of inducible VT/VF, the risk of sudden death is 5–10% per year and ICD implantation is recommended, as it is in any Brugada patient with a history of documented VT/VF or resuscitated cardiac arrest.

The molecular basis for the ventricular arrhythmias remains uncertain. Mutations have been identified in patients with Brugada syndrome in the SCN5A gene, which codes for the tetrodotoxin-‘insensitive’ human cardiac sodium channel (hH1). The functional abnormalities of the expressed mutant channels are opposite to those found in sodium channel mutants associated with long-QT syndrome. In Brugada syndrome, as in some of the other idiopathic ventricular fibrillation syndromes, the sodium channels show loss-of-function features, such as enhanced inactivation. However, it is difficult to see how these features give rise to ventricular arrhythmias. A clue may come from the finding that calmodulin, a ubiquitous calcium-sensing protein, binds to the carboxy-terminal IQ domain of the hH1 channel in a calcium-dependent manner. A naturally occurring mutation (A1924T) in the IQ domain alters hH1 function in a manner characteristic of...
the Brugada syndrome, but at the same time inhibits slow inactivation induced by calcium–calmodulin, yielding a clinically benign (arrhythmia-free) phenotype. Further studies will be required to elucidate the precise mechanism(s) by which the other mutations in hH1 give rise to Brugada syndrome.

So far as we can ascertain, this is only the third report of a general anaesthetic having been administered to a patient with Brugada syndrome. The first case report describes a 47-yr-old Japanese male undergoing hemilaminectomy. Anaesthesia was induced with fentanyl 50 μg, droperidol 2.5 mg and propofol 120 mg, and the neuromuscular blocking drug used was vecuronium 8 mg. Maintenance of anaesthesia continued with the use of sevoflurane and further fentanyl 150 μg. Antagonism of the neuromuscular block was accomplished using neostigmine 2.5 mg and atropine 1.0 mg; during antagonism the authors noted an elevation of the ST segments on the ECG.

A second case report describes a 49-yr-old man with Brugada syndrome who had surgery for a polyp on the vocal cords. Despite episodes of vertigo and an ECG showing a right bundle branch block with elevation of the ST segments in leads V1 and V2, the cardiologist did not consider that there was an indication for an ICD. The patient was given diazepam 10 mg orally as a premedication and monitored using ECG, a non-invasive blood pressure cuff, pulse oximetry and capnography. Induction of anaesthesia was carried out using fentanyl 0.2 mg, propofol 200 mg, mivacurium 18 mg and glycopyrrolate 0.3 mg. A portable defibrillator was placed in theatre in case ventricular dysrhythmias developed. Anaesthesia was maintained using 1% isoflurane with a nitrous oxide–oxygen gas mixture. After surgery, the patient was transferred to the recovery room and monitored for 2 h. No problems were reported with this anaesthetic.

Both sets of authors in these case reports note that the administration of drugs that block sodium channels, such as procainamide and flecainide, are contraindicated in patients with Brugada syndrome.

Miyazaki and colleagues describe four patients who underwent investigation for Brugada syndrome. They noted that selective α-adrenoceptor stimulation by i.v. norepinephrine in the presence of propranolol or by i.v. methoxamine consistently augmented ST segment elevation whereas α-adrenoceptor block reduced it in three of the patients. Additionally, i.v. neostigmine and class IA antiarrhythmic drugs augmented ST elevation without inducing coronary spasm, but class IB antiarrhythmic drugs had no effect on ST elevation. However, the number of patients was very small and it is difficult to draw firm conclusions from this study, especially in the light of the heterogeneous nature of the mutations leading to Brugada syndrome.

In the case described by Lafuente Martin and colleagues and in our case, isoflurane was administered as an anaesthetic agent. It is perhaps surprising (and illustrates the lack of detailed understanding of the physiology and pharmacology behind Brugada syndrome) that no cardiac arrhythmias were detected during anaesthesia in these cases, in the light of recent evidence suggesting that isoflurane should be avoided in patients with prolonged QTc syndrome.

Administration of i.v. neostigmine with glycopyrrolate in our patient did not give rise to any detectable cardiac arrhythmia. Likewise, bupivacaine given via the epidural route did not cause problems. However, in view of the fact that drugs that block the sodium channels may cause problems in patients with Brugada syndrome, it may be wise in future to avoid systemic administration of local anaesthetics by routes that cause a rapid increase in serum concentrations of local anaesthetic.

Reported experience of general anaesthesia in Brugada syndrome is limited at present. However, it is an increasingly recognized disorder, and one which many anaesthetists are likely to encounter in their clinical practice in the future. Caution should be exercised when using α-agonists or neostigmine, while class I antiarrhythmic drugs must be avoided. In any patient with an ICD, the device must be disabled immediately before surgery. Close cooperation of the anaesthetist with a cardiologist is essential both before and after surgery. In patients with Brugada syndrome in whom no ICD has been fitted, recovery should take place in either a coronary care unit or a high-dependency unit. This will permit detection and treatment of cardiac arrhythmias, which are most likely to occur in the postoperative period, in a timely manner.

References

Balser JR. Sodium ‘channelopathies’ and sudden death: must you be so sensitive? Circ Res 1999; 85: 872–4


