Cardiothoracic Anesthesia, Respiration and Airway

General anesthesia for patients with Brugada syndrome. A report of six cases

[L'anesthésie générale chez des patients atteints du syndrome de Brugada.

Présentation de six cas]

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Purpose: To review six cases of Brugada syndrome presenting for insertion of a cardioverter-defibrillator under general anesthesia.

Clinical features: All patients had a history of syncope, ST segment elevation in the right precordial lead of the electrocardiogram (ECG) which became prominent after a pilsicainide challenge test. Routine monitors, right precordial lead of the ECG and an external defibrillator were installed prior to anesthesia. We administered propofol/midazolam for induction, and propofol/sevoflurane combined with fentanyl for maintenance of anesthesia. Atropine and ephedrine were administered to decrease vagal tone. No ECG change or arrhythmia was observed perioperatively. After the successful implantation of the defibrillator, all patients were discharged without any adverse event.

Conclusion: By avoiding agents or conditions that may exacerbate Brugada syndrome during anesthesia, we were able to manage the patients uneventfully for implantation of a cardioverter-defibrillator.

Objectif : Passer en revue six cas de syndrome de Brugada admis pour l'insertion d'un défibrillateur à synchronisation automatique sous anesthésie générale.

Éléments cliniques : Les patients avaient des antécédents de syncope, d'élévation du segment ST dans la dérivation précordiale droite de l'électrocardiogramme (ECG) qui est devenu proéminent après le test de provocation à la pilsicainide. Les moniteurs réguliers, la dérivation précordiale droite de l'ECG et un défibrillateur externe ont été installés avant l'anesthésie. Un mélange de propofol/midazolam a été administré pour l'induction de l'anesthésie et de propofol/sévoflurane combiné à du fentanyl pour son maintien. De l'atropine et de l'éphédrine ont permis de diminuer le tonus vagal. Aucune modification de l'ECG, ni arythmie périopératoires n'ont été observées. Après l'implan-

tation réussie du défibrillateur, tous les patients ont pu quitter l'hôpital sans complication.

Conclusion : En évitant les médicaments ou les conditions qui pourraient exacerber le syndrome de Brugada pendant l'anesthésie, nous avons pu procéder sans incident à l'implantation d'un défibrillateur à synchronisation automatique.

BRUGADA syndrome is a distinct form of an arrhythmic disease characterized by right bundle branch block and ST segment elevation in the right precordial leads (V1–V3) of the electrocardiogram (ECG).¹ This syndrome is clinically important because of the high incidence of sudden death by ventricular fibrillation (VF) without any structural heart disease, and is seen especially in the Asian populations including Japanese people.² Recently, it has been demonstrated that Brugada syndrome is genetically linked to the mutation of the alpha subunit of the sodium channel gene, SCN5A,³ and the use of certain anti-arrhythmic sodium channel blockers (class IA and IC) accentuates the ECG manifestations.⁴ To date, an implantable cardioverter-defibrillator (ICD) is the sole medical intervention which effectively protects patients with Brugada syndrome from sudden cardiac death.⁵ Although a few single case reports of general anesthesia have been published,^{6–8} there is no report of general anesthesia in a series of patients with Brugada syndrome. We herein report six patients with Brugada syndrome who underwent implantation of an ICD under general anesthesia.

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TABLE I Preoperative clinical characteristics of six patients with Brugada syndrome

No.	Age, sex (yr)	Cardiac history (medication)	Electrophysiology				Echocardiography	Cardiac catheterization
			RBBB	ST segment elevation	EPS	Pilsicainide (Ic) challenge test		
1	60, M	Documented VF Post CPR	IRBBB	V1 coved V2 saddleback	VF -	positive	normal	normal
2	51, M	Syncope	IRBBB	V2-3 saddleback	VF +	positive	normal	normal
3	56, M	Convulsion hypertension	CRBBB	V1-2 coved V3 saddleback	VF +	positive	IVS thickening	normal
4	59, M	Syncope hypertension	IRBBB	V1 coved V2-3 saddleback	VF +	positive	Small AR	normal
5	63, M	Syncope	IRBBB	V2-3 saddleback	VF +	negative	normal	normal
6	63, M	Syncope (Diltiazem)	IRBBB	V1-2 saddleback	VF +	positive	Small AR, MR	Normal spasm +

RBBB = right bundle branch block; CRBBB = complete RBBB; IRBBB = incomplete RBBB; EPS = electrophysiological study; VF = ventricular fibrillation; CPR = cardiopulmonary resuscitation; IVS = interventricular septum; AR = aortic regurgitation; MR = mitral regurgitation.

TABLE II Anesthesia technique, perioperative use of drugs, and perioperative complications in six patients with Brugada syndrome

	Anesthesia				Anti-arrhythmic drug	Vasoactive drugs	Complications	
	Premedication	Induction	Muscle relaxant	Maintenance			ECG change	Others
1	Diazepam	Propofol	Vecuronium	Propofol fentanyl		Atropine ephedrine	-	Bradycardia hypotension
2	Diazepam	Propofol	Vecuronium	Sevoflurane N ₂ O fentanyl			-	-
3	Diazepam	Midazolam	Vecuronium	Sevoflurane N ₂ O fentanyl	Lidocaine	Ephedrine	-	Hypotension
4	Diazepam	Propofol	Vecuronium	Propofol fentanyl		Atropine	-	Bradycardia
5	Diazepam	Propofol	Vecuronium	Sevoflurane N ₂ O fentanyl			-	-
6	Diazepam	Propofol	Vecuronium	Sevoflurane N ₂ O fentanyl	Lidocaine	Diltiazem	-	-

ECG = electrocardiogram

Clinical features

The following criteria were used to diagnose Brugada syndrome:⁹ 1) history of cardiac arrest or aborted sudden death or syncope of unknown origin with or without documentation of VF; 2) ST segment elevation (coved or saddleback type) in V1–V3 with or without a certain degree of right bundle branch block (RBBB); 3) no prolongation of the QT interval (QTc < 440 msec); 4) no structural and ischemic heart disease demonstrated by echocardiography and cardiac catheterization. An electrophysiological study (EPS) was conducted in which the VF inducing and class IC drug, pilsicainide was administered for a challenge test.¹⁰ Thereafter, informed consent for ICD implantation was obtained. As shown in Table I, all patients were males, and their age ranged from 51 to 63 yr. One patient (patient 1) had a history of documented

VF and cardiopulmonary resuscitation. Two patients had untreated hypertension. Regarding ECG findings, all patients had RBBB, either complete or incomplete. Coved type ST segment elevation was seen in three patients and saddleback type elevation was seen in the other three patients. VF was induced in five patients in EPS and five patients developed ST segment elevation after the administration of pilsicainide, a sodium channel blocker (Figure). Echocardiography revealed a slight thickening of the interventricular septum in one patient and minimal mitral or aortic regurgitation in two patients but, otherwise, were normal. No patient had coronary disease but patient 6 had coronary spasm induced by mechanical stimulation during cardiac catheterization (diltiazem was prescribed for this patient). Perioperative data for the six patients are shown in Table II. We monitored direct arterial blood

TABLE III Acceptable and contraindicated drugs for Brugada syndrome

	Drugs	Acceptable	Contraindicated
<i>Anti-arrhythmic drugs</i>	procainamide		+ 4, 9
	ajimarine		+ 4, 9
	quinidine	+ 11	
	disopyramide	+ 11	+ 14
	lidocaine	+ * 12	
	mexiletine	+ 12, 14	
	flecainide		+ 4, 9, 11, 14
	pilsicainide		+ * 10
	amiodarone	+ 1, 5	
	noradrenaline		+ 12
<i>Autonomic nervous system-related drugs</i>	isoproterenol	+ * 12	
	ephedrine	+	
	propranolol	+ 5	+ 2, 12
	atropine	+ * 6	
	acetylcholine		+ 11, 12
	neostigmine	+ 8	+ 12
<i>General anesthetics</i>	fentanyl	+ * 6, 7, 8, 13	
	propofol	+ * 6, 7, 13	
	thiopental	+ 8	
	midazolam	+ * 13	
	isoflurane	+ 7, 8	
	sevoflurane	+ * 6, 13	
	N ₂ O	+ * 7, 8	
<i>Muscle relaxants</i>	vecuronium	+ * 6, 8	
	mivacurium	+ 7	
	rocuronium	+ 13	
	bupivacaine (epidural)	+ 8	+ 13

Acceptable = alleviates ST segment elevation or has no significant effect. Contraindicated = induces ventricular fibrillation or ST segment elevation. *Described in the present report, number = reference number.

pressure, right precordial lead V1 or V2, bispectral index (BIS), and near infrared oximetry to measure regional cerebral oxygen saturation, in addition to routine monitoring. An external defibrillator connected to defibrillation pads was installed. Following oral diazepam (5 ~ 10 mg) for premedication, propofol (five patients) or midazolam (one patient) was used for induction of anesthesia. Neuromuscular blockade was provided by *iv* vecuronium and tracheal intubation was performed in every patient. Anesthesia was maintained with propofol and fentanyl (total *iv* anesthesia) in two patients, or with sevoflurane and N₂O with fentanyl in the other four. Lidocaine was administered in two patients in order to alleviate hemodynamic changes during intubation. Atropine was used in two patients because of bradycardia (< 45 beats·min⁻¹) during tracheal intubation, and ephedrine was used in two patients to reverse hypotension (systolic pressure < 80 mmHg) during

FIGURE Typical recording of precordial electrocardiogram (V1-V6) during class IC drug challenge test. At control, coved type ST-segment elevation is seen in leads V1 and V2. Following the administration of flecainide, further elevation of the ST-segment is observed. The ST-segment elevation returned to control level after the administration of isoproterenol.

the procedure. No patient developed VF unrelated to electrophysiological stimulation. No ST segment change was detected in any patient throughout the anesthetic. The ICD was implanted successfully in all patients who were discharged from the hospital without any adverse event.

Discussion

The anesthetic considerations for general anesthesia in patients with Brugada syndrome have not yet been fully established because of the restricted number of reports on this condition.⁶⁻⁸ To our knowledge, we are the first to report on more than a single patient with Brugada syndrome undergoing general anesthesia. Based on our experience and other reports, sevoflurane [five patients (pts)], N₂O (6 pts), fentanyl (9 pts), propofol (8 pts) and vecuronium (7 pts) have been administered uneventfully; no patient developed VF or further ST segment elevation that lead to VF.⁶⁻⁸ According to Antzelevich's theory, intrinsic heterogeneity produces the transmural dispersion of repolarization between the epicardium and endocardium, which may lead to local pre-excitation termed phase 2 reentry, triggering VF.¹¹ Ionic mechanisms such as decrease of sodium current or calcium current, an increase in transient outward current or adenosine triphosphate-sensitive potassium (K-ATP) current or calcium-activated chloride current have been shown to be capable of developing phase 2 reentry,

which underlies VF. Several drugs such as class IC or IA anti-arrhythmic drugs (flecainide, pilsicainide, ajmaline, and procainamide), acetylcholine, beta-adrenergic antagonists (propranolol; not arrhythmogenic per se), K-ATP opener (pinacidil, nicorandil) may interfere with the ionic conditions mentioned above and may exacerbate Brugada syndrome. Therefore, these drugs should be avoided during anesthesia. For this reason, we did not use neostigmine to reverse the effect of vecuronium, and we used a vagolytic agent, atropine, to antagonize bradycardia. Although we could not use mivacurium because it was unavailable, its short duration of action secondary to its spontaneous degradation would make it the neuromuscular blocker of choice. Beta-adrenergic stimulation (e.g., isoproterenol) has been reported to ameliorate the ECG manifestations of Brugada syndrome.¹² Consistent with previous reports, isoproterenol successfully restored the elevated ST segment to the pretreatment level in all patients following the pilsicainide challenge test (Figure). In two patients, ephedrine was administered to treat hypotension because of its beta-adrenergic effect. Lidocaine, a class IB anti-arrhythmic agent and also a local anesthetic, had no effect on the ECG, as shown previously.¹² However, it is noteworthy that another local anesthetic, bupivacaine has recently been reported to unmask Brugada-like ECG patterns when administered epidurally.¹³ Therefore, profound sympathetic blockade with thoracic epidural anesthesia especially with bupivacaine should be avoided. In Table III, acceptable and contraindicated drugs^{1,2,4-14} are listed for the reader's sake. During the ICD implantation, we feel that BIS monitoring was useful to avoid deep anesthesia that may increase vagal tone by suppressing sympathetic nervous system outflow. In our point of view, light general anesthesia or local anesthesia with sedation may be preferable. Also, right precordial ECG leads and an external defibrillator are highly recommended during the procedure unless they interfere with the surgical field.

In summary, we report our experience in six patients with Brugada syndrome who underwent ICD implantation under general anesthesia. Although it is too early to draw a conclusion on the safety of this technique because of the limited number of patients and anesthetics employed in the present report, we were able to administer general anesthesia uneventfully in these patients by avoiding agents or conditions that may exacerbate the syndrome.

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