Ventricular tachycardia during general anesthesia in a patient with congenital long QT syndrome

[La tachycardie ventriculaire pendant l'anesthésie générale chez une patiente atteinte du syndrome congénital du QT long]

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Purpose: Congenital long QT syndrome is characterized by a corrected QT interval of at least 440 msec on the electrocardiogram and has been associated with recurrent syncope, documented ventricular arrhythmia and sudden death. There have been numerous articles over the past 20 years describing isolated instances of surgical and anesthesia related complications but the general anesthetic management of the condition remains unclear.

Clinical features: An 11-yr-old female with documented long QT syndrome, with two episodes of syncope in the past, was admitted for emergency drainage of left periorbital cellulitis. Anesthesia was induced with propofol, fentanyl and rocuronium, and initially maintained with nitrous oxide and halothane. After 20 min, the patient developed ventricular tachycardia (torsade de pointes). Lidocaine 1 mg·kg⁻¹ iv was given and the rhythm reverted to normal sinus. Halothane was discontinued and the surgery proceeded without further incident.

Conclusions: Our review of the literature revealed that patients with long QT syndrome whose symptoms are well controlled prior to surgery tend to do well regardless of the anesthetic chosen. There are, however, theoretical reasons to avoid anesthetics which either sensitize the myocardium to catecholamines or which cause an increase in circulating levels of catecholamines.

Objectif : Le syndrome congénital du QT long est caractérisé par un intervalle QT corrigé d'au moins 440 msec à l'électrocardiogramme et est associé à des syncopes récurrentes, de l'arythmie ventriculaire reconnue et la mort subite. Au cours des 20 dernières années, de nombreux articles ont présenté des cas isolés de complications reliées à la chirurgie et à l'anesthésie, mais la prise en charge anesthésique est encore indéterminée dans ces conditions.

Éléments cliniques : Une fillette de 11 ans atteinte du syndrome du QT long, ayant subi deux épisodes de syncope dans le passé, a été admise pour un drainage de cellulite périorbitaire gauche en urgence. L'anesthésie a été induite avec du propofol, du fentanyl et du rocuronium

et maintenue d'abord avec du protoxyde d'azote et de l'halothane. Après 20 min, une tachycardie ventriculaire (torsade de pointes) s'est développée. Une dose iv de 1 mg·kg⁻¹ de lidocaïne a été administrée et le rythme est revenu à la normale. L'halothane a été stoppé et l'intervention chirurgicale s'est déroulée sans incident.

Conclusion : Notre examen des publications a révélé que les patients atteints du syndrome du QT long, dont les symptômes sont bien contrôlés avant une opération, réagissent bien, peu importe l'anesthésique choisi. Il y a, toutefois, des raisons théoriques d'éviter l'anesthésie qui sensibilise le myocarde ou cause une augmentation des niveaux de catécholamines sériques.

CONGENITAL long QT syndrome (LGTS) can be inherited either in association with congenital deafness (Jervell and Lange-Nielson syndrome),¹ or with no other associated physical anomalies (Romano-Ward syndrome).² During the past decade, at least six different genetic defects, all involving potassium or sodium transmission, have been discovered to lead to one form or another of LQTS.³ The most common, LQT 1, is a defect on chromosome 11, encoding for the potassium channel. The next most common, LQT 2, is a defect on chromosome 7, again encoding for the potassium channel. It is thought that LQT 1 and 2 together represent approximately 95% of all cases. LQT 3 (3–4% of cases) is a defect on chromosome 3, encoding for the sodium channel. LQT 4, 5 and 6 all involve defects in potassium transmission, are located on chromosomes 4, 21 and 21, respectively, and are quite rare. All the genetic subtypes are characterized by a corrected QT interval of at least 440 msec on the

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Accepted for publication July 10, 2002.

Revision accepted December 13, 2002.

electrocardiogram (ECG), and the condition has been associated with recurrent syncope, documented ventricular arrhythmia and sudden death.⁴

There have been numerous articles over the past 20 years describing isolated instances of surgical and anesthesia related complications but the general anesthetic management of the condition remains unclear. We present the case of an 11-yr-old child presenting for emergency surgery requiring general anesthesia, who suffered ventricular tachycardia during surgery. We also present a review of the literature and recommendations for dealing with such cases in the future.

Case report

An 11-yr-old female was admitted to the pediatric service with a four-day history of left eye swelling and pain, accompanied by fever. Her past medical history was significant for documented LQTS, with two episodes of syncope in the past. Her mother and two siblings had also been diagnosed with LQTS (Romano-Ward). The patient had begun taking atenolol approximately two years prior to the current admission. A few months after beginning therapy with atenolol, she suffered an episode of syncope, and the dose was then increased.

She was brought to the operating room for left ethmoidectomy and drainage of periorbital abscess. The patient's preoperative ECG (Figure 1) revealed prolonged QT interval with no arrhythmia.

The patient weighed 46 kg. She received midazolam 1 mg intravenously prior to anesthetic induction. She was given oxygen 100% by mask and anesthesia was induced with fentanyl 200 µg and propofol 80 mg, with rocuronium 20 mg for muscle relaxation. Tracheal intubation was easily accomplished and anesthesia initially maintained with nitrous oxide, fentanyl and oxygen. Vital signs remained stable, with heart rate (HR) at 82 beats·min⁻¹. She was given *iv* labetalol 5 mg and HR decreased to approximately 60 beats·min⁻¹. Prior to the start of surgery, halothane 0.8% was initiated. Vital signs remained stable until approximately 20 min into the case, when the patient developed, first bigeminy, then ventricular tachycardia (torsade de pointes) at a rate of 130 beats·min⁻¹. Blood pressure decreased to a mean of 45 mmHg. Lidocaine 40 mg was given intravenously on the advice of cardiology. Halothane and nitrous oxide were discontinued and isoflurane 1% substituted. Cardiac rhythm returned to normal sinus and there were no further arrhythmias throughout the case. Muscle relaxation was reversed with neostigmine 2.0 mg and glycopyrrolate 0.4 mg and the trachea extubated. ETCO₂ remained between 32 and 34 mmHg and oxygen sat-

FIGURE 1 Leads II and AVF of the patient's preoperative electrocardiogram, clearly showing both QT prolongation and bifid T-waves characteristic of long QT 2.

uration was 99–100% for the entire case. No further adverse events occurred. End-tidal halothane concentration was measured but not recorded, and until discontinued, was thought to be appropriate to the vaporizer settings. The patient was transferred to the pediatric intensive care unit in stable condition.

A few months after discharge, the patient's younger brother suddenly died, presumably secondary to an episode of ventricular tachycardia. Her older brother then had an automatic implantable cardioverter defibrillator (AICD) placed but the patient was at that time unwilling to accept such a procedure for herself. Her dosage of atenolol was again increased but the patient suffered an episode of syncope approximately one year after the drainage of her periorbital abscess. She was admitted to a neighbouring hospital where an esmolol infusion was started. While in the hospital, she suffered an episode of ventricular tachycardia and was transferred to our institution. The esmolol was continued, the atenolol dosage again increased and a lidocaine

FIGURE 2 Electrocardiogram strip (lead II) from the pediatric intensive care unit, obtained prior to AICD placement, showing the patient's typical arrhythmia.

infusion started. The patient again suffered an episode of ventricular tachycardia (Figure 2) and the decision was made to place an AICD. For this procedure, she received midazolam 2 mg, diphenhydramine 25 mg, fentanyl 100 µg, and propofol by infusion. She suffered no untoward incident during the procedure. Subsequent to these events, genetic testing revealed a defect on chromosome 7, leading to a diagnosis of LQTS type 2 (LQT 2).

Discussion

Idiopathic LQTS is characterized by episodes of syncope, more commonly in females, and has been associated with sudden death, particularly in the pediatric population.⁴ Increased levels of catecholamines have been associated with arrhythmias, and LQTS is thought to be one of many possible etiologies of sudden infant death syndrome.⁵

Once diagnosed, the standard treatment for LQT 1 and 2 is beta-adrenergic blockade, which has been shown to significantly reduce morbidity.⁶ Beta-blockade may, however, be contra-indicated in LQT 3, since bradycardia in these patients can further prolong the QT interval and lead to ventricular arrhythmias.⁷ In 1991, Moss *et al.*, showed that cardiac pacing at a rate sufficient to shorten the QT interval could prove useful.⁸ However, at the time this study was done, the various genetic sub-types of LQTS had not yet been identified, and recent data suggests that increasing the HR would probably be beneficial only in LQT 3.⁷

Refractory acute arrhythmic episodes in association with LQTS may be treated by resection of the left stellate ganglion.⁹ Intravenous magnesium has been used to break refractory arrhythmias¹⁰ and treatment with an AICD has recently become a viable therapeutic option.¹¹ Procainamide and lidocaine have been thought to be contraindicated, due to their propensity to prolong the QT interval.¹² Nevertheless, lidocaine has been reported to successfully treat ventricular arrhythmias in LQTS.¹³

The anesthetic management of these patients is controversial. The condition is rare, and there are no controlled clinical trials pointing to the advisability of one technique over another. Our patient arrived in the operating room at night and without prior warning. A MEDLINE search back to 1995 through the hospital Internet connection revealed no articles specifically dealing with the anesthetic management of her condition. However, we discovered an article by Michaloudis *et al.*, examining the effect of both isoflurane and halothane on the QT interval in normal, healthy patients, which concluded that halothane would most likely be superior for patients with prolonged QT syndrome, since halothane shortened the QT interval more than did isoflurane.¹⁴ A review of other sources available to us in the operating room revealed contradictory recommendations. Reich, Brooks and Kaplan recommend the use of high dose narcotics without nitrous oxide.¹⁵ Stoelting, Dierdorf and McCammon give the opinion that nitrous oxide plus isoflurane or enflurane are acceptable, but state that "halothane is a less attractive alternative," due to the tendency of halothane to predispose to arrhythmias in the presence of catecholamines.¹⁶

A postoperative search of the literature going back to 1977 revealed a number of reports that perhaps shed light on the question (Table). Including our own, ten cases have been reported of patients receiving halothane.^{17–23} Of these, four underwent surgery without incident,^{17,18} all four were taking medication and asymptomatic prior to surgery. In six cases,^{19–23} patients who were either not under treatment or whose symptoms were not well controlled by treatment, suffered arrhythmias during surgery.

Eight patients received isoflurane,^{21,24–27} six of whom suffered no untoward incident. Five of these six had been considered asymptomatic on medication.

Two patients received enflurane. One, whose symptoms were well controlled prior to surgery, suffered no untoward incident during two anesthetics.²⁸ One patient was symptomatic prior to surgery and had ventricular tachycardia during surgery.²⁹

Two patients received sevoflurane. Both were symptomatic prior to surgery. One had premature ventricular contractions (PVCs)³⁰ and the other suffered ventricular fibrillation during surgery.³¹

Four patients had a nitrous oxide/narcotic anesthetic. All four were taking medication and asymptomatic prior to surgery.^{18,32} Three suffered no untoward incident. One had PVCs.³²

Three patients suffered arrhythmias during anesthetic induction.^{33–35} All were symptomatic prior to surgery, though one had reportedly³⁴ undergone two

TABLE Number of reported episodes of arrhythmias in LQTS patients during anesthesia, by anesthetic agent and according to preoperative control of symptoms

	Symptoms controlled		Symptoms poorly controlled	
	Arrhythmias	No arrhythmias	Arrhythmias	No arrhythmias
Halothane ¹⁷⁻²³		4	6	
Isoflurane ^{21,24-27}	Arrhythmias	No arrhythmias	Arrhythmias	No arrhythmias
		5	2	1
Sevoflurane ^{30,31}	Arrhythmias	No arrhythmias	Arrhythmias	No arrhythmias
			2	
Enflurane ^{28,29}	Arrhythmias	No arrhythmias	Arrhythmias	No arrhythmias
		1	1	
N ₂ O/narcotic ^{18,32}	Arrhythmias	No arrhythmias	Arrhythmias	No arrhythmias
	1	3		
On induction ³³⁻³⁵	Arrhythmias	No arrhythmias	Arrhythmias	No arrhythmias
		1	3	2
Ketamine ¹⁹	Arrhythmias	No arrhythmias	Arrhythmias	No arrhythmias
	1		1	

earlier successful surgeries, and again had surgery after treatment, without untoward incident. In none of these three anesthetics was the specific anesthetic technique described.

One patient received ketamine twice,¹⁹ on both occasions suffering significant arrhythmias. She was diagnosed with LQTS after the first incident and propranolol was begun. Nevertheless, she again suffered a life-threatening arrhythmia during surgery, after having received 10 mg·kg⁻¹ oral ketamine.

An article by Galloway and Glass, published in 1985, gives the opinion that isoflurane is most likely a safer anesthetic than halothane.³⁶ Though this opinion may be true, a review of the literature does not necessarily support such a conclusion. On the other hand, our review of the literature suggests that patients whose symptoms are not well controlled prior to surgery are likely to suffer arrhythmias during surgery, regardless of the anesthetic technique chosen.

Unfortunately, genetic testing is still not readily available, and it may not be possible to determine with certainty a particular patient's genotype. However, at least one recent article claims that LQT 1, 2, and 3 can frequently be identified by the ECG pattern.³⁷ LQT 1 has a prolonged QT interval with a normal to high T wave amplitude, a broad based T wave, and an indistinct T wave onset. LQT 2 is characterized by a prolonged QT interval, low amplitude T waves, and bifid T waves in over 60% of cases. LQT 3 shows a prolonged QT interval with late onset, peaked T waves and a long, isoelectric ST segment. Of note, our patient does have the bifid T wave pattern supposedly characteristic of LQT 2 (Figure 1).

Since LQT 1 and 2 are the most common forms, preoperative beta-adrenergic blockade would certain-

ly seem advisable if a diagnosis of LQTS has been confirmed but the specific genetic abnormality has not yet been identified. If known to be LQT 3, however, beta-blockade should probably be avoided, and during surgery, rapid cardiac pacing should be available in the operating room. It would perhaps be prudent to avoid both halothane and ketamine, and also, as far as possible, situations involving stress and subsequent catecholamine release. If a patient's symptoms can be controlled prior to surgery - by whatever means - it would seem advisable to do so. Numerous drugs prolong the QT interval, and should be avoided. An excellent listing of such drugs is contained on the website <http://www.torsades.org/druglist.cfm>, but among those most likely to be encountered in the operating room are amiodarone (Cordarone®), bepredil (Vascor®), cisapride (Propulsid®), chlorpromazine (Thorazine®), disopyramide (Norpace®), dolasetron (Anzemet®), droperidol (Inapsine®), erythromycin, flecainide (Tambocor®), fluoxetine (Prozac®), fosphenytoin (Cerebryx®), gatifloxacin (Tequin®), haloperidol (Haldol®), levofloxacin (Lecaquin®), nicardipine (Cardene®), paroxetine (Paxil®), procainamide (Pronestyl®, Procan®), risperidone (Risperdal®), salmeterol (Serevent®), sertraline (Zoloft®), sotalol (Betapace®), sumatriptan (Imitrex®), tamoxifen (Novadex®) and thioridazine (Mellaril®). QT interval should be monitored during surgery and the patient's cardiac rhythm should be monitored for a prolonged period after surgery. If arrhythmias occur - most typically torsade de pointes - *iv* lidocaine or *iv* magnesium may prove effective, as may rapid cardiac pacing in LQT 3. If these fail, electrical defibrillation may be necessary.

References

- 1 Gordon N. The long Q-T syndromes. *Brain Dev* 1994; 16: 153–5.
- 2 Eggeling T, Hoher M, Osterbues HH, Kochs M, Weismuller P, Hombach V. The arrhythmogenic substrate of the long QT syndrome: genetic basis, pathology, and pathophysiologic mechanisms. *Eur Heart J* 1993; 14(Suppl E): 73–9.
- 3 Vincent GM, Timothy K, Zhang L. Congenital long QT syndrome. *Card Electrophysiol Rev* 2002; 6: 57–60.
- 4 Garson A Jr, Dick M II, Fournier A, et al. The long QT syndrome in children. An international study of 287 patients. *Circulation* 1993; 87: 1866–72.
- 5 Berger S, Dhala A, Friedberg DZ. Sudden cardiac death in infants, children, and adolescents. *Pediatr Clin North Am* 1999; 46: 221–34.
- 6 Moss AJ, Zareba W, Hall WJ, et al. Effectiveness and limitations of β -blocker therapy in congenital long-QT syndrome. *Circulation* 2000; 101: 616–23.
- 7 Schwartz PJ, Priori SG, Locati EH, et al. Long QT syndrome patients with mutations of the SCN5A and HERG genes have differential responses to Na⁺ channel blockade and to increases in heart rate. Implications for gene-specific therapy. *Circulation* 1995; 92: 3381–6.
- 8 Moss AJ, Lin JE, Gottlieb S, Locati EH, Schwartz PJ, Robinson JL. Efficacy of permanent pacing in the management of high-risk patients with long QT syndrome. *Circulation* 1991; 84: 1524–9.
- 9 Moss AJ, Robinson J. Clinical features of the idiopathic long QT syndrome. *Circulation* 1992; 85(Suppl I): II40–4.
- 10 Hasegawa J, Takami T, Kaneda T, et al. Treatment of torsade de pointes with intravenous magnesium in idiopathic long QT syndrome. *Jpn Circ J* 1991; 55: 1057–60.
- 11 Brugada P, Brugada R, Brugada J, Geelan P. Use of the prophylactic implantable cardioverter defibrillator for patients with normal hearts. *Am J Cardiol* 1999; 83: 98D–100D.
- 12 Otteni JC, Pottecher T, Bronner G, Flesch H, Diebold JR. Prolongation of the Q-T interval and sudden cardiac arrest following right radical neck dissection. *Anesthesiology* 1983; 59: 358–61.
- 13 Sakurada H, Tejima T, Hiyoshi Y, Motomiya T, Hiraoka M. Association of humps on monophasic action potentials and ST-T alternans in a patient with Romano-Ward syndrome. *Pacing Clin Electrophysiol* 1991; 14: 1485–91.
- 14 Michaloudis D, Fraidakis O, Lefaki T, Kanadonakis F, Askitopoulou H. Anaesthesia and the QT interval in humans: effects of halothane and isoflurane in premedicated children. *Eur J Anaesthesiol* 1998; 15: 623–8.
- 15 Reich DL, Brooks JL III, Kaplan JA. Uncommon cardiac diseases. In: Katz J, Benumof JL, Kadis LB (Eds.). *Anesthesia and Uncommon Diseases*, 3rd ed. Philadelphia: W.B. Saunders Company; 1990: 373–4.
- 16 Stoelting RK, Dierdorf SF, McCammon RL. *Anesthesia and Co-Existing Disease*, 2nd ed. New York: Churchill Livingstone; 1988.
- 17 Freshwater JV. Anaesthesia for caesarian section and the Jervell, Lange-Nielson syndrome (prolonged Q-T interval syndrome). *Br J Anaesth* 1984; 56: 655–7.
- 18 O'Callaghan AC, Normandale JP, Morgan M. The prolonged Q-T syndrome. A Review with anaesthetic implications and a report of two cases. *Anaesth Intensive Care* 1982; 10: 50–5.
- 19 Joseph-Reynolds AM, Auden SM, Sobczyk WL. Perioperative considerations in a newly described subtype of congenital long QT syndrome. *Paediatr Anaesth* 1997; 7: 237–41.
- 20 Adu-Gyamfi Y, Said A, Chowdhary UM, Abomelha A, Sanyal SK. Anaesthetic-induced ventricular tachyarrhythmia in Jervell and Lange-Nielsen syndrome. *Can J Anaesth* 1991; 38: 345–6.
- 21 Medak R, Benumof JL. Perioperative management of the prolonged Q-T interval syndrome. *Br J Anaesth* 1983; 55: 361–4.
- 22 Holland JJ. Cardiac arrest under anaesthesia in a child with previously undiagnosed Jervell and Lange-Nielsen syndrome. *Anaesthesia* 1993; 48: 149–51.
- 23 Wig J, Bali IM, Singh RG, Kataria RN, Khattri HN. Prolonged Q-T interval syndrome. Sudden cardiac arrest during anaesthesia. *Anaesthesia* 1979; 34: 37–40.
- 24 Nair L, Tseng PS, Manninen PH, Teo WS. Anaesthetic management of idiopathic long QT syndrome—a case report. *Ann Acad Med Singapore* 1994; 23: 582–5.
- 25 Peral A, Martinez MV, Garcia del Valle S, Carrera A. Two cases of anesthesia in long-QT syndrome (Letter; Spanish). *Rev Esp Anesthesiol Reanim* 2000; 42: 193–5.
- 26 Wilton NCT, Hantler CB. Congenital long QT syndrome: changes in QT interval during anesthesia with thiopental, vecuronium, fentanyl, and isoflurane. *Anesth Analg* 1987; 66: 357–60.
- 27 Carlock FJ, Brown M, Brown EM. Isoflurane anaesthesia for a patient with long Q-T syndrome. *Can Anaesth Soc J* 1984; 31: 83–5.
- 28 Owitz S, Pratilas V, Pratila MG, Dimich I. Anaesthetic considerations in the prolonged Q-T interval (LQTS): a case report. *Can Anaesth Soc J* 1979; 26: 50–4.
- 29 Brown M, Liberthson RR, Ali HH, Lowenstein E. Perioperative anesthetic management of a patient with long Q-T syndrome (LQTS). *Anesthesiology* 1981; 55: 586–9.
- 30 Gallagher JD, Weindling SN, Anderson G, Fillinger MP. Effects of sevoflurane on QT interval in a patient

- with congenital long QT syndrome. *Anesthesiology* 1998; 89: 1569–72.
- 31 *Pleym H, Bathen J, Spigset O, Gisvold SE.* Ventricular fibrillation related to reversal of the neuromuscular blockade in a patient with long QT syndrome. *Acta Anaesthesiol Scand* 1999; 43: 352–5.
- 32 *Lloyd Jones S, Mason RA.* Laser surgery in a patient with Romano-Ward (long QT) syndrome and an automatic implantable cardioverter defibrillator. *Anaesthesia* 2000; 55: 362–6.
- 33 *Forbes RB, Morton GH.* Ventricular fibrillation in a patient with unsuspected mitral valve prolapse and a prolonged Q-T interval. *Can Anaesth Soc J* 1979; 26: 424–7.
- 34 *Callaghan ML, Nichols AB, Sweet RB.* Anesthetic management of prolonged Q-T interval syndrome. *Anesthesiology* 1977; 47: 67–9.
- 35 *Ponte J, Lund J.* Prolongation of the Q-T interval (Romano-Ward syndrome): anaesthetic management. *Br J Anaesth* 1981; 53: 1347–9.
- 36 *Galloway PA, Glass PSA.* Anesthetic implications of prolonged QT interval syndromes. *Anesth Analg* 1985; 64: 612–20.
- 37 *Moss AJ.* T-wave patterns associated with the hereditary long QT syndrome. *Card Electrophysiol Rev* 2002; 6: 311–5.

Resisting the winter season