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Torsades de pointes during laparoscopic adrenalectomy of a pheochromocytoma: a case report

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Abstract
We describe the case of a 42-year old Caucasian female who developed recurrent
torsades de pointes during laparoscopic removal of a pheochromocytoma. The
literature available on torsades de pointes occurring in patients with
pheochromocytoma is limited and as far as we are aware there are no reports
describing this dysrhythmia in a pheochromocytoma patient under anaesthesia.
Torsades de pointes mainly occurs in the setting of a prolonged QT interval. This
patient neither had a prolonged QT preoperatively, nor was her family history
suspect for a congenital long QT syndrome. We show that, in the case of a surgical
pheochromocytoma removal, perioperative conditions can elicit an acquired or
previously unknown congenital long QT syndrome. Preoperative α- and β-blockade is
advised and QT-prolonging drugs should be avoided.
Introduction

Pheochromocytomas are catecholamine-producing neuroendocrine tumours, arising from the chromaffin cells of the adrenal medulla or extra-adrenal paraganglia. A pheochromocytoma is a potential life-threatening disease with a high risk of cardiovascular complications such as myocardial infarction, arrhythmias, catecholamine-induced cardiomyopathy, stroke and pulmonary oedema. It is a rare neoplasm, occurring 1-2 per 1000 patients suffering from hypertension. The relatively high prevalence of pheochromocytoma in autopsy studies (about 0.05%) indicates that the diagnosis is often missed\(^1\); overall incidence is estimated on 1.6 - 8 cases per million people per year\(^1\).

Traditionally, adrenalectomy for pheochromocytoma has been performed by open lateral retroperitoneal surgery\(^2\). Nowadays, laparoscopic removal of intra-adrenal and extra-adrenal pheochromocytomas is the preferred surgical treatment, since it reduces postoperative morbidity, hospital stay and costs compared with conventional laparotomy\(^1\). Induction of general anaesthesia and surgical tumour manipulation are the most well-known stimuli to evoke an acute catecholaminergic crisis. Twenty-five to fifty percent of hospital deaths of patients with pheochromocytoma occur during surgery\(^3\). This report describes torsades de pointes (TdP) in a patient during laparoscopic removal of a pheochromocytoma, as a rare perioperative complication.
Case presentation
A 42-year old woman was referred to our university hospital because of a pheochromocytoma of the left adrenal gland. For a year she had suffered from episodic headaches, palpitations, sweating, chest discomfort, orthostatic hypotension and fatigue. CT-scan showed a large adrenal mass, and urine and blood tests confirmed the diagnosis of a catecholamine producing mass (mainly epinephrine, in a lesser degree norepinephrine). For symptomatic treatment, combined α- and β-blockade was started with Doxazosin (8 mg 1dd per os (p.o.)) and Propranolol (20 mg 3dd p.o.). Since electrocardiography showed atrial fibrillation, she was also treated with Flecainide (100 mg 1dd p.o.) and Acenocoumarol (p.o., INR-conducted: 2.5 – 3.5).

Preoperative exam revealed a blood pressure of 130/75 mmHg in supine position (120/85 mmHg standing upright), under combined α- and β-blockade. At admission, she had a sinus bradycardia of 58 beats/min, with a normal QRS-width (110 ms) without prolonged corrected QT interval (QTc 435 ms) (figure 1a).

[figure 1]

Blood count and serum electrolytes were all within normal ranges; however serum magnesium level was not determined.

Anaesthesia was performed with Propofol (2.5 mg/kg intravenously (iv)), Sufentanil (0.4 µg/kg iv) and Rocuronium (0.6 mg/kg iv). Isoflurane (1.1-1.3%) was used for maintenance, along with increments of Sufentanil and Rocuronium when appropriate. A central venous line (16 fr, double-lumen, right internal jugular vein), an arterial line (20 G, left radial artery) and two peripheral IV’s (14 G/20 G) were inserted. To perform a left laparoscopic adrenalectomy she was placed in right
lateral position. Blood pressure and heart rate remained stable during induction and positioning.

Immediately after surgical manipulation of the tumour the blood pressure increased from 155/95 to 200/105 mmHg. To control hypertension, Nitroprusside (25 µg/kg/hr iv) was started and an extra Propofol bolus (100 mg iv) was administered. Despite these measures, the second surgical manipulation of the tumour resulted in a blood pressure of 245/110 mmHg, immediately followed by a TdP (figure 1b). On request of the anaesthetist the surgeons stopped manipulating the tumour, resulting in a spontaneous return to sinus rhythm within a few seconds and a gradual normalization of the blood pressure. However, each time the surgeons tried to ligate the tumour's venous return, blood pressure rose. Nitroprusside infusion rate was increased up to 130 µg/kg/hr and 2 Esmolol boluses of 20 mg each were administered. Also, anaesthesia was deepened with Propofol (100 mg, thrice) and 2 sufentanil boluses of 20 µg and 10 µg. Despite these interventions, blood pressure did not drop below a diastolic 105 mmHg. On each blood pressure peak (max 254/112) the patient showed a TdP. In total she suffered 4 times from this arrhythmia, all returning to sinus rhythm.

The total period of arrhythmias lasted 15 minutes and ended abruptly when the venous return of the tumour was ligated. Subsequently, the tumour was successfully removed. Serum electrolytes were tested directly after removal of the tumour and revealed a slight hypomagnesaemia (0.54 mmol/L), a normokalaemia and normal sodium. Pupillary reflexes were found normal during the whole procedure. To prevent hypotension after tumour ligation, the patient was administered intravenous Norepinephrine (10 mg/50 ml), which was stopped at the end of the
operation. The postoperative ECG showed sinus rhythm with 77 beats/min, but in contrast to the preoperative ECG, now with prolonged QT interval (QTc 505 ms) and U-waves (figure 1c). Her postoperative stay was uneventful. Pathological examination confirmed the diagnosis of a pheochromocytoma.
Discussion

We describe a patient without QT prolongation preoperatively, with recurrent TdP during laparoscopic removal of a pheochromocytoma. TdP is a form of polymorphic ventricular tachycardia, predominantly occurring in the setting of a prolonged QT interval, T wave abnormality and/or increased U wave amplitude.\(^8\) It occurs frequently in the presence of (severe) bradycardia and often precedes ventricular fibrillation. Electrocardiographically, TdP is a pattern of continuously changing morphology of the QRS complexes twisting around an imaginary baseline. In most cases, including our patient, TdP is preceded by a characteristic sequence of a long RR interval, followed by a short extrasystolic interval with premature depolarization interrupting the preceding repolarization, called the short-long-short phenomenon (figure 1b).

The QT interval represents the depolarization and repolarization of the ventricles.\(^9-12\) Prolongation of the QT interval is caused by an increase in action potential duration of ventricular myocytes\(^10-12\). The ventricular myocardium is predominantly composed of three cell types which are histologically alike, yet vary electrophysiologically and pharmacologically. These three cell types may respond differently to drug or disease-mediated action potential prolongation and hence differences in repolarization (‘inhomogeneous prolongation of repolarization’). Transmural dispersion of repolarization may occur\(^11\), which may be considered as the electrophysiological cause of TdP. Transmural dispersion of repolarization may be increased by an adrenergic agent like Isoproterenol\(^10-12\).
In contrast to the patient’s normal preoperative QT interval, the postoperative QT interval was prolonged. A QT interval can be prolonged congenitally or acquired. The congenital long QT syndrome (LQTS) is subdivided into 10 genotypes. With the LQT1 and LQT2 genotypes cardiac events may be precipitated by physical or emotional stress. These patients are treated with anti-adrenergic therapy, like β-blockers. Identification of the congenital long QT syndrome genes uncovered groups of patients with a normal resting ECG. It is thought that these patients have an incomplete penetrance, that they are mutation carriers or are carrying polymorphic congenital long QT syndrome disease genes. They are at risk of developing TdP when exposed to certain drugs.[9] Nothing, however, is known about adrenergic stimulation in this group of patients. An ‘epinephrine stress test’ is sometimes performed to unmask this group of patients with a supposed congenital long QT syndrome and normal QT interval. In this provocative test epinephrine is administered intravenously, whether by bolus infusion (Shimizu protocol) or by incremental escalating infusion (Mayo protocol), while ECG changes are measured. A paradoxical response characterized by QT lengthening (rather than expected shortening) is seen more frequent in patients with LQT1.[13].

Our patient neither had a prolonged QT preoperatively, nor was her family history suggestive of a congenital LQTS. Moreover, in a follow-up study, exercise test and echocardiography were also normal and a 24-hours ambulatory monitoring only showed a short episode of a spontaneous supraventricular tachycardia, probably originated by atrial tachycardia. Possibly, she had a LQTS1 during surgery originated by excessive adrenergic stimulation. We did not perform genetic testing afterwards to confirm this because non-invasive cardiac evaluation was normal and her family
history was negative. Most likely, our patient suffered from an acquired LQTS. An acquired LQTS is predominantly elicited by drugs that prolong the ventricular action potential and/or by an electrolyte imbalance (www.torsades.org\textsuperscript{14}). In the present case, the combination of flecainide\textsuperscript{14}, hypomagnesaemia and adrenergic stimulation may have elicited increased transmural dispersion of repolarization resulting in TdP \textsuperscript{10-12}. The increased adrenergic stimulation during manipulation of the tumour then likely resulted in premature ventricular beats either by abnormal automaticity or by early after depolarizations inducing a pause (long RR interval) and increased transmural dispersion of depolarization resulting in TdP.

Anaesthetic guidelines on managing patients with pheochromocytoma stress the importance of preoperative treatment with α-blocking and, if necessary, with β-blocking agents. Often Phenoxybenzamine or Doxazosin is advised \textsuperscript{2;3;15}. Peroperative haemodynamic changes are preferably controlled with Phentolamine, Nitroprusside and short-acting β-blockers like Esmolol \textsuperscript{2;3;15}. Since no prospective, controlled, randomized trials have been performed on almost any aspect of the diagnosis or treatment of pheochromocytoma, guidelines are based on expert opinions and case reports. TdP occurring in patients with pheochromocytoma is not expected and specific combinations of drugs to minimize the risk of TdP are unknown. We suggest that QT-prolonging drugs should be avoided (www.torsades.org). Moreover, potassium - and magnesium plasma levels should be kept on a normal to high level.
Conclusion

A laparoscopic adrenalectomy of a pheochromocytoma in a patient without pre-operative QT interval prolongation may result in TdP, most likely elicited by excess of adrenergic stimulation. Thorough preoperative α- and β-blockade is advised and QT-prolonging drugs should be avoided.
Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The author(s) declare that they have no competing interests

Authors’ contributions

KvdH, AdH and HGDH were present during the event described in this case report. KvdH and AdH collected the literature and the patient data, KvdH was the major contributor in writing the manuscript. Reviewing the manuscript was mostly done by KvdH, JKGW and HGDH. ACPW was asked for her expertise on torsades de pointes and, by this, also contributed to reviewing the manuscript. All authors read and approved the final manuscript.

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References


[14]. QT drug list by risk group. 15-2-2008. Ref Type: Internet Communication

Figure legends

Figure 1: perioperative electrocardiographic recordings

Figure 1a: Preoperative ECG.

Sinus rhythm, 58 bpm. Without QT-prolongation (QTc 440 ms)

Figure 1 b: Two recordings of torsades de pointes episodes.

Note the short-long-short phenomenon preceding the arrhythmia in the upper recording.

Figure 1 c: Postoperative ECG.

Sinus rhythm, 77 bpm. With prolonged QT interval (QTc 505 ms), best seen in aVF. In leads V1-4 there are possible U-waves, merging into the P wave.