CASE REPORT

Perioperative management of a large, late presenting phaeochromocytoma

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SUMMARY

A 77-year-old man presenting to the emergency department with an acute coronary syndrome was later found to have a phaeochromocytoma. The lateness of this presentation was likely due to the protective α blocking effects of long-term terazosin therapy for his prostatism. α blockers such as terazosin are a well-recognised medical therapy in the perioperative optimisation of phaeochromocytoma because they treat the adrenergic effects of catecholamine release from the tumour such as hypertension. This patient was diagnosed with an ST elevation myocardial infarction (STEMI). A cardiac angiogram showed no evidence of vessel occlusion. A right adrenal mass of 9×8×9 cm was incidentally found and confirmed as a phaeochromocytoma with raised plasma metanephrines and normetanephrines. Following preoperative optimisation and multidisciplinary team involvement, an open right adrenalectomy was performed successfully some months later.

BACKGROUND

Phaeochromocytoma is a rare catecholamine secreting neuroendocrine tumour.¹ It usually presents with recurrent symptoms such as headaches, sweating and signs such as hypertension.² This particular case presented as a STEMI. It is wise to keep an open mind for differential diagnoses and other underlying causes, especially prior to final confirmatory tests (a coronary angiogram in this case). It is also important to recognise that signs or symptoms of a disease may be masked by treatments for other diseases. In this case, the clinical features of phaeochromocytoma were blinded by long-term terazosin therapy.

CASE PRESENTATION

This 77-year-old man presented to the emergency department with squeezing central chest pain, nausea and diaphoresis. Having stood up from a chair at home he had then collapsed and become unresponsive for 10 s, he then proceeded to walk to the hospital in which time his chest pain had developed. He denied any previous chest pains or cardiac history. He frequently worked in the garden and went swimming up to 2 km four times a week. He was an ex-smoker having stopped 35 years ago. His medical history comprised benign prostatic hypertrophy for which he had been on a 2 mg daily dose of terazosin for many years, and hyperlipidaemia for which he took 20 mg of simvastatin daily. He also took alendronate every 2 weeks and monthly cholecalciferol for osteoporosis. He had

an allergy to aspirin, which involved his tongue swelling. On examination, he had on-going severe central chest pain, a blood pressure of 180/80 mm Hg, a heart rate of 70 bpm, oxygen saturations of 100% in room air, a respiratory rate of 20 breaths per minute and a GCS of 15/15. Focusing on the cardiovascular system, his heart sounds were dual with no peripheral oedema or raised jugular venous pressure. His peripheries were warm, and his heart rate was regular. Respiratory and gastrointestinal examinations were unremarkable. Regarding investigations, his ECG showed a 3 mm ST elevation in the aVL lead and a 2 mm ST depression in leads II, III, aVF and leads V4–V6 (figure 1). His portable chest X-ray displayed clear lung fields with a normal mediastinum. Full blood count, urea and electrolytes, and coagulation screen were largely normal. Creatine kinase was raised at 339, and troponin I was slightly raised at 50 (normal <40) on presentation. The diagnosis in the emergency department was an inferolateral STEMI. The patient was treated with 180 mg of ticagrelor and 5000 IU of intravenous heparin. Furthermore, 1–2 mg boluses of intravenous morphine were administered until the chest pain resolved 3 hours after its onset, with a total of 5 mg of morphine having been administered. Then, 8 mg of ondansetron was administered for nausea, which resolved after a similar amount of time. He was then transferred to a tertiary centre for consideration of primary percutaneous coronary intervention.

INVESTIGATIONS

At the tertiary centre, the patient underwent a coronary angiogram which showed mild diffuse coronary artery disease and no evidence of vessel occlusion. High-sensitive cardiac troponin T was 919 (normal <15) 8 hours after presentation, and troponin I was 3990 (normal <40) 36 hours after presentation. A private cardiac MRI showed no evidence of ischaemic scars, making a plaque rupture unlikely. It also showed left ventricular mid wall hypokinesis but well preserved left ventricular function. During the MRI, a right-sided adrenal mass was found incidentally. Plasma levels of metanephrines were >50 000 (normal <500) and normetanephrines 38 000 (normal <900), pathognomonic of a phaeochromocytoma. The mass was quantified with a CT scan and measured 9×8×9 cm (figure 2). The left kidney and adrenal gland were normal. Another MRI scan then confirmed that the mass was separate to the inferior cava and liver prior to surgery.

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Figure 1 ECG showing ST elevation in lead aVL.

Figure 2 CT axial showing large right adrenal mass.

DIFFERENTIAL DIAGNOSIS

Other causes of myocardial ischaemia associated with coronary vasospasm include:

- ▶ Stimulants such as cocaine³ and cannabis.^{4 5}
- ▶ Acute myocarditis.⁶
- ▶ Drugs such as methylphenidate,^{7 8} capecitabine⁹ and 5-fluorouracil.¹⁰⁻¹²
- ▶ Carcinoid tumour.^{13 14}
- ▶ A complication of coronary angiography.¹⁵

TREATMENT

Phenoxybenzamine 10 mg daily was started 2 months prior to surgery by the endocrinology team, replacing his terazosin.

Unfortunately, there was a delay in surgery due to unavailability of essential staff. The cardiologists decided that dual antiplatelet therapy was not required as his chest pain and raised troponin levels were likely to have been due to high catecholamines from the pheochromocytoma causing myocardial ischaemia via vasoconstriction. His cardiac MRI and coronary angiogram showed mild coronary artery disease only. Thus, the ticagrelor was discontinued a week prior to surgery with no bridging therapy required. At his anaesthetic clinic appointment 1 month prior to surgery, the patient fulfilled Roizen criteria for perioperative optimisation after phenoxybenzamine treatment and this was adhered to until surgery.¹ He was normotensive with a blood pressure of 110/62 dropping to 104/65 on standing. His heart rate was 55 bpm, thus he did not require any β blocker treatment. His ECG showed normal sinus rhythm with no ST changes and no premature ventricular contractions. He denied any history of symptoms of adrenergic activity other than his presentation to the emergency department. His haemoglobin had remained stable at 141 g/L throughout his phenoxybenzamine treatment. He confirmed there was no known family history of pheochromocytoma. There was nothing to suggest a multiple endocrine neoplasia syndrome in his history, and he had never had significant hypertension.

He was admitted 1 day prior to his operation for further surgical and anaesthetic review and preparation. On the day of surgery, phenoxybenzamine treatment was ceased and multiple intravenous access lines were inserted, including a central line for vasoactive medication administration and central venous pressure monitoring. The intensive care unit were contacted to confirm bed availability and regularly communicated with throughout the operation with updates on the patient's status. An arterial line was inserted for continuous blood pressure

monitoring and blood gas sampling. A thoracic epidural was sited at level T6–7 for postoperative pain control. Before induction for general anaesthesia, a remifentanyl (a rapid onset opioid) infusion was started, which allowed a judicious amount of propofol to be administered in slow boluses of 50 and 30 mg for cardiovascular stability (figure 3). A sodium nitroprusside infusion was used due to its immediate vasodilatory effects and short duration of action. A magnesium sulphate loading dose and infusion was used for further vasodilatation and as an anti-arrhythmic. An esmolol infusion was chosen as the β blocker of choice due to its rapid onset and offset and lack of α effects. There was a noradrenaline infusion on standby in case of any episodes of hypotension. This was in anticipation of refractory hypotension which can commonly occur during venous ligation of the tumour: this instantaneous blockage of venous drainage of the tumour results in a large drop in catecholamine release into the systemic circulation, and thus a large drop in blood pressure.² Vecuronium was our muscle relaxant of choice as it is one of the most cardiostable agents and can be rapidly reversed with sugammadex. This reversal is useful as large doses of magnesium sulphate administration prolong the action of most neuromuscular blocking drugs. Desflurane was used as the volatile anaesthetic agent due to its low blood gas partition coefficient, enabling a quicker emergence from anaesthesia. The tachycardia associated with desflurane at steady state does not occur until a MAC of 1.5 or above, thus it was deemed acceptable to use desflurane throughout the operation at low inspired concentrations of about 4 kPa (<1 MAC).¹⁶ The patient was catheterised for monitoring of urine output, and warming was achieved with an intravenous fluid warmer and a forced air warming blanket. Intraoperative monitoring included: neuromuscular transmission

monitoring, a nasal temperature probe, oxygen saturations, inspired and expired gases, bispectral index (depth of anaesthesia), invasive blood pressure, ECG and heart rate monitoring. Pulse pressure variation was monitored from the arterial line, and any more invasive forms of cardiac output monitoring were not deemed appropriate as the patient had a normal heart and a good exercise tolerance. Intubation and induction of general anaesthesia were uneventful. Throughout the operation, the patient was most haemodynamically unstable during periods of tumour manipulation. Maximum and minimum blood pressures were 210/105 and 50/30, and maximum and minimum heart rates were 110 and 46, respectively (figure 4). The tumour was adhered to the liver superiorly but with no invasion. It was extremely well vascularised and, although abutting the right hepatic vein, was not invading any major vascular structures. The tumour was removed successfully, with preservation of the right renal artery and vein. Extubation in theatre was uneventful.

OUTCOME AND FOLLOW-UP

In the immediate postoperative period, the patient was kept on a 5% dextrose infusion in the high dependency unit. Other than one low blood glucose measurement of 3 mmol/L taken 2 hours after the end of surgery, glucose levels were tightly controlled between 5 and 6 mmol/L for the next 24 hours. The patient was drowsy and not fully awake until 4 hours postoperatively. He was eating and drinking the following day. Vasopressor support was required for 24 hours postoperatively. The patient was then discharged to the surgical ward where he spent a further 5 days before returning home. Two weeks after discharge from hospital, the patient made a good recovery and was going for walks

Date: 18/08/2016			Page: 2			Anaesthetic Staff:				
NHI:			Signed.....			Anaesthetist				
Patient Name:										
DOB:			Age: 77			Sex: M				
Time	08:30	09:00	09:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00
										Total/Unit
0.125% Bupivacaine with 5 mcg/ml										
Fentanyl	10	10								20 ml
Cefuroxime		1.5								1.5 g
Droperidol								0.625		0.625 mg
Fentanyl	25									25 mcg
Magnesium Sulphate		1.44+1.44	1.44+1.44		1.44+1.44+1.44	1.44	1.44			12.96 g
Midazolam	2 1									3 mg
Ondansetron								4		4 mg
Paracetamol								1		1 g
Propofol		50 30								80 mg
Sugammadex										200 200 400 mg
Vecuronium		10			4					14 mg
0.125% Bupivacaine with 5 mcg/ml										
Fentanyl			5							ml
Esmolol					100+200+100+200+0+200	200				mcg/kg/min
Magnesium Sulphate		2					0			g/h
Noradrenaline			0.2+0.3+0.1+0+0.1	0.3	0	0.1+0.2+0+0.150.5+0.2	0.6+0.4+0.1+0+0.1+0.3+0.1+0+0.2+0.3+0.2+0+0.4+0.5+0.3+0.5+0+0.2+0.3+0.4+0.2+0.3+0.2+0+0.3+0.2+0			mcg/kg/min
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ANAESTHETIC RECORD

Figure 3 Anaesthetic drug chart.

ANAESTHETIC RECORD

Figure 4 Anaesthetic monitoring chart. Blood pressure (red lines) and heart rate (green dots).

outside of his house. His pain was manageable with just paracetamol. His wound was healing well with no signs of infection, and his full blood count and urea and electrolytes were grossly normal. Histology had showed a T2 N0 M0 phaeochromocytoma of low-grade malignancy. He is planned for a 1-year repeat CT scan as there was some capsular invasion of the tumour. At the time of writing, the patient has not had a repeat cardiac MRI or echocardiogram as functionally he has been very well. Levels of serum cortisol, plasma metanephrines and normetanephrines all were within normal limits 3 months postoperatively.

DISCUSSION

Phaeochromocytomas are catecholamine-secreting neuroendocrine tumours of the chromaffin cells, usually found in the adrenal medulla. They are responsible for about 0.2% of cases of hypertension.¹⁷ The preoperative optimisation of these patients cannot be understated: the mortality rate for phaeochromocytomas in elective surgery is <2%, rising to 50% in unoptimised emergency cases.² One of the main optimisation targets is treating hypertension to normalise the blood pressure, commonly performed with an α blocker such as phenoxybenzamine, started a month to 14 days before surgery. The mortality rate of surgery for phaeochromocytomas decreased from 13% to 45% before α blockade was introduced, to 0–3% after α blockade was introduced in the 1980s.¹ Although phenoxybenzamine is the most commonly used α blocker, other short-acting α blockers have been used such as doxazosin, prazosin and terazosin. The dose of terazosin given to these patients is 2–5 mg per day.¹⁸ Our patient took 2 mg per day for over 15 years for

his prostatism, so it is highly likely that this gave him a degree of protection from the adrenergic effects of excessive catecholamine release from his phaeochromocytoma. It would also make sense that in his history of presenting complaint he experienced syncope after getting up quickly from his chair, a symptom of orthostatic hypotension cause by α blockade. There are currently no reports of phaeochromocytoma blinded by prostatism treatment in the literature.

With regard to his presentation and diagnosis of a STEMI, there have been several reports in the literature about this. Five case reports over the last 4 years with phaeochromocytomas presenting as STEMIs all had chest pain with an acute rise in cardiac biomarkers. Similar to our patient, none had any evidence of coronary artery occlusion on angiogram.^{19–23} This is in keeping with the current theory of intense coronary vasospasm caused by direct toxic effects of catecholamines.²⁴ This would have resolved by the time the patient underwent an angiogram and would explain the negative findings on angiogram with these cases. Findings on echocardiography were more mixed. Like our patient who had left ventricular mid wall hypokinesis, three cases had mild-to-moderate wall motion abnormalities.^{20–21–23} One had ballooning of the cardiac walls sufficient for a diagnosis of takotsubo cardiomyopathy.²² Another had severe impairment of the left ventricle with a left ventricular ejection fraction of 25%, remaining at 25% after a year. Although that patient had presented multiple times with acute coronary syndromes as her diagnosis had been clouded by hyperthyroidism.¹⁹ Dilated cardiomyopathy and systolic dysfunction caused by excessive catecholamines damaging to cardiac myocytes is a known pathology, especially in cases of

phaeochromocytoma,²⁵ although this is usually reversible and only present in about 10% of phaeochromocytoma cases.²⁶

With regard to the surgical approach used, the size of the mass and its proximity to vasculature were the factors in deciding on open surgery in this patient. In general however, most centres prefer a laparoscopic approach due to evidence supporting earlier postoperative mobilisation, less postoperative pain, lower incidence of venous thromboembolism and overall shorter hospital stay.¹ Disadvantages of the laparoscopic approach include the higher level of technical skill required and a large catecholamine release from insufflation of gas.² Open procedures are usually reserved for large masses or extra-adrenal masses with limited access. Adrenal sparing surgery is also possible, particularly in cases with bilateral or familial phaeochromocytoma.¹⁸

This case highlights the importance of keeping other underlying causes in mind for commonly presenting diseases, especially when a presentation is atypical and before final confirmatory tests are performed. It also displays that other comorbidities and treatments can interfere with the clinical presentation and confuse the diagnostic process.

Learning points

- ▶ Pheochromocytoma can present as an acute coronary syndrome, clinicians should take a thorough history and be aware the common clinical features of phaeochromocytoma.
- ▶ Signs and symptoms of phaeochromocytoma can be blinded by common medications such as α blockers.
- ▶ Preoperative optimisation of these patients is essential. The mortality rate for unoptimised emergency phaeochromocytoma patients remains very high.
- ▶ The management of these complex cases is best performed with a multidisciplinary team approach, including surgeons, anaesthetists, endocrinologists and intensive care teams.

Contributors DM was responsible for consent, writing of case report, discussion and literature review. AL reviewed the article as a whole.

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Patient consent Obtained.

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