CHAPTER 11

Hypertensive Crisis during Adrenalectomy in a Patient with Pheochromocytoma and a HOCM with SAM

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Abstract

We describe the perioperative management of a patient with a norepinephrine producing pheochromocytoma complicated by a hypertrophic obstructive cardiomyopathy (HOCM) with systolic anterior motion (SAM) of the anterior mitral leaflet. The perioperative pass through Scylla (blunting catecholamine effects to allow adrenalectomy, potentially inducing hypotension and relative hypovolemia) and Charybdis (preventing hypovolemia and hypotension and maintaining sufficient afterload to prevent aortic outflow obstruction) in this patient lead to a hypertensive crisis during adrenalectomy. We conclude that preoperative preparation of a patient with a pheochromocytoma with a HOCM and SAM should be performed under invasive monitoring conditions.

Introduction

Adrenalectomy for pheochromocytoma generally is performed after preparation with α- and β-sympathicolytic agents to blunt the effects of the elevated catecholamine output.[1] In patients also known with hypertrophic cardiomyopathy this preoperative workup needs more attention than in other patients with pheochromocytoma.

Case report

A 41-year old woman was presented to the Emergency Department with severe dyspnoea, palpitations, nausea and vomiting. She reported to suffer from periods of sweating, palpitations, dyspnoea, nausea and vomiting and chest pain for a longer period. Her medical history included hypertension, diabetes mellitus type 2 and a small myocardial infarction five years earlier without significant stenosis on coronary angiogram. A diagnosis of transient stress cardiomyopathy (also known as Tako-Tsubo, transient apical ballooning or broken heart syndrome) was postulated at that time.

At presentation, the patient's blood pressure was 225/140 mmHg, heart rate 134 beats per minute (bpm), and the electrocardiogram (ECG) revealed a sinus tachycardia without signs of ischemia. She was admitted to the intensive care unit (ICU), where she was treated with intravenous (IV) diuretics, ß-blockade and nitroglycerine.

Urinary excretion rates of catecholamines and their metabolites were elevated: norepinephrine concentration was 12.91 µmol/24 h (reference range 0.06-0.47 µmol/24 h), epinephrine 0.18 µmol/24 h (reference range 0.00-0.06 µmol/24 h), dopamine 3.38 µmol/24 h (reference range 0.46-3.40 µmol/24 h), normetanephrine 57.6 µmol/24 h (reference range 0.0-0.3 µmol/24 h), and metanephrine 0.9 µmol/24 h (reference range 0.0-1.8 µmol/24 h). In addition, abdominal computed tomography showed a mass of 6 by 7 cm in the left adrenal gland, suggesting the presence of a pheochromocytoma.

Doxazosin 4 mg per os (PO), an α- sympathicolytic agent, was started and two days after admission the patient was discharged, awaiting adrenalectomy. The day after the patient collapsed in her bathroom. At readmission a loud systolic murmur, grade 4/6, maximum point of loudness 2nd intercostal space on the left, was noticed. Echocardiography showed a severe concentric hypertrophic left ventricle with a systolic obstruction of the left ventricular outflow tract due to a systolic anterior motion (SAM) of the mitral valve with a maximal velocity over the outflow tract of 6 m/s (corresponding with a pressure gradient of 144 mmHg) and a mitral valve insufficiency grade 2-3. With fluid therapy and temporarily termination of doxazosin the patient recovered. Based on the size of the pheochromocytoma and clinical impact of hormonal excess she was scheduled for an open adrenalectomy.

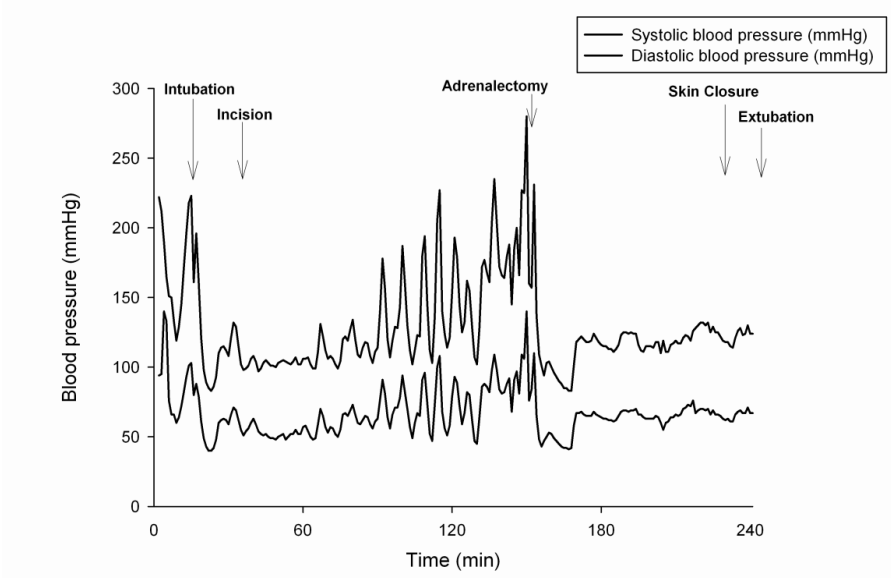
Preoperative preparation was started on the ward with doxasozin 4 mg PO 2 dd and, in view of the fact the patient had collapsed earlier while taking doxasozin, verapamil 120 mg PO. Metoprolol 50 mg PO 2 dd was added 2 days later because of a persisting heart rate > 100 bpm and the patient was intravenously hydrated. Blood pressure and heart rate reached near normal values but still periods of hypertension and tachycardia persisted. Because of the patients' history of hypertrophic obstructive cardiomyopathy (HOCM) with SAM resulting in cardiovascular collapse a further increase in the dosage of α- and β-sympathicolytic agents was determined undesirable and the intentional treatment goal; orthostatic hypotension, was not reached.

Preoperatively, an echocardiography under α- and β-sympathicolysis was repeated and now showed the gradient over the left ventricular out flow tract only 13 mmHg, and 34 mmHg after Valsalva in this catecholamine suppressed and unprovoked setting.

The day of surgery, 4 days after starting preoperative treatment and after administration of midazolam 7.5 mg PO, blood pressure was 125/73 mmHg and heart rate 73 bpm. An arterial line was placed. After infusion of 500 ml of colloids anesthesia was induced with IV etomidate 40 mg, 100 µg remifentanil and 70 mg rocuronium together with 50 mg esmolol. In spite of this high dose anaesthetic induction the intubation was accompanied with a period of hypertension reaching 230/110 mmHg with a heart rate of 110 bpm. Anesthesia was continued with propofol 10-12 mg/kg/h and remifentanil 0.3-0.5 µg/kg/min, in addition to sufentanil bolus doses of 10-25 µg. The bispectral index score (BIS) was kept below 50. A central venous line was placed and the central venous pressure was kept at 12-14 mmHg. Surgery passed uneventful until reaching the left adrenal gland when various periods of hyper-, normo- and hypotension followed (Figure 1).

Resection was hampered due to an overlying renal artery and vein that left no room for selective adrenal vein transsection, done routinely in pheochromocytoma surgery. Due to the varying intensity of surgical stimulation the blood pressure now varied between 230/120 mmHg and 70/40 mmHg, in the presence of esmolol 0-100 µg/kg/min and sodiumnitroprusside (SNP) 0-2.0 µg/kg/min in addition to extra bolus doses of esmolol (50-100 mg IV) and SNP (100 to 200 µg IV). Surgical pauses were needed to regain hemodynamic control but again were often complicated by hypotension requiring rapid reductions in the esmolol and SNP infusion. At the time the pheochromocytoma almost had been removed, the blood pressure reached 280/140 mmHg accompanied by a tachycardia of 140 bpm, refractory to medication. This ended when the remaining adrenal tumour was swiftly excised but, due to the need for speed of surgery, complicated by transsection of the left renal artery for which a primary repair was possible.

Figure 1: Intra-arterial systolic and diastolic blood pressure during adrenalectomy for pheochromocytoma. During the excision phase esmolol 0-100 µg/kg/min and sodiumnitroprusside (SNP) 0-2.0 µg/kg/min in addition to bolus doses of esmolol (50-100 mg intravenous (IV)) and SNP (100-200 µg IV) were infused to control hypertension. After adrenalectomy norepinephrine up to 0.6 µg/kg/min was infused to prevent hypotension.



After resection a period of hypotension followed that was treated with intravenous norepinephrine at 0.6 µg/kg/min. The adrenalectomy had taken 4 hours and 400 ml of blood loss. Postoperatively, the trachea was extubated and the patient transferred to the post anesthesia care unit (PACU). The postoperative ECG was conform preoperative. Norepinephrine infusion was terminated 12 hours postoperatively and the patient was discharged to the ward in a hemodynamically stable condition with diuresis exceeding 0.5 ml/kg/h and a plasma creatinin of 87 mmol/L. Eight days postoperatively the patient returned home in satisfactory condition. Pathological examination revealed a 6.5-5-6 cm pheochromocytoma that was fully extirpated. Postoperative 24 h urinary excretion of catecholamines and metanephrines were normal. Genetic testing for mutations causing inherited pheochromocytoma (succinate dehydrogenase, Von Hippel Lindau and Multiple Endocrine Neoplasia type 2a genes) was negative. Evaluation of the patient's cardiac function one month and one year after surgery repeatedly displayed a non-dilated, normal functioning left ventricle without significant hypertrophy.

Discussion

Pheochromocytomas are catecholamine-secreting tumours that originate from chromaffin tissue in the adrenal medulla. They may produce norepinephrine, epinephrine and/or dopamine, resulting in clinical findings as headache, palpitations, pallor and perspiration, accompanied by hypertension.[2]

Pheochromocytomas may be either inherited as autosomal dominant trait or found sporadically. Sporadic pheochromocytomas often generate more signs and symptoms, exhibit higher catecholamine excess and are larger tumours compared with pheochromocytomas detected by screening of patients with a hereditary predisposition.[3] In case a pheochromocytoma is detected, adrenalectomy is indicated after appropriate preoperative care.[1]

It is reported that cardiomyopathy, resulting from catecholamine-induced myofibrillar damage, occurs in 30% of patients with pheochromocytomas.[4;5] Sometimes dilated and hypertrophic variants of cardiomyopathy represent the only sign of the tumour.[2;6] Excess catecholamines contribute to myocardial hypertrophy not only indirectly via adrenergic receptor stimulation but also directly by stimulation of cardiac cell protein synthesis.[7] A complete cardiac evaluation is therefore recommended in the preoperative evaluation of a patient with pheochromocytoma.[8]

The main characteristic of HOCM is hypertrophy of the left ventricular chamber. Mitral regurgitation reflects the interference of the hypertrophied interventricular septum with the movement of the anterior leaflet of the mitral valve. Both septal hypertrophy and systolic anterior motion of the mitral valve may result in left ventricular outflow obstruction. Left ventricular outflow obstruction may vary rapidly with changing myocardial contractility, preload and afterload. In these patients drugs and interventions associated with enhanced myocardial contractility are therefore contraindicated, as they increase left ventricular outflow obstruction.[9] Perioperative anaesthetic management therefore aims to assure (supra)normal filling pressures, prevent tachycardia and maintain adequate afterload. Inotropic and vasodilatory forces should be guided and balanced continuously. Elevated catecholamine concentrations may be beneficial or detrimental depending on the balance between positive inotropy and peripheral vasoconstriction. α-Antagonists, of benefit in pheochromocytoma by blunting sympathetic tone, may in the presence of HOCM, through a decrease in pre- and afterload, increase outflow tract obstruction and thus decrease cardiac output.

No consensus exists regarding the precise timing or choice of agent for preoperative α- and β-sympathicolysis. In most medical centers sympathetic blockade starts 7-14 days preoperatively. Recommendations regarding treatment goals of blood pressure and heart rate control are supported by observational studies and personal experience rather than by data from prospective clinical studies.[1]

In this case the preoperative initiated level of α- and β-sympathicolysis proved insufficient intraoperatively. The preoperative α- and β-sympathicolytic dosage was kept low in fear of another cardiovascular collapse in this patient that was prepared on the ward. In retrospect, in this patient who collapsed preoperatively and was known with a HOCM and SAM and a transient Tako-Tsubo cardiomyopathy, it would have been better to preoperatively monitor and control blood pressure and fluid volume status invasively at an ICU or PACU and thus allow for a more sufficient α- and β-blockade preoperatively.

Interestingly, one month after surgery the left ventricle showed no signs of hypertrophy. This suggests that in our patient the left ventricular hypertrophy was a reversible condition, initiated by catecholamine excess and reversed after surgical removal of the pheochromocytoma. A few cases of reversible dilatation of hypertrophied left ventricle in pheochromocytoma have been reported before.[10;11]

In conclusion, this case stresses the importance of considering the presence of cardiomyopathy in any patient with pheochromocytoma. Preoperative preparation of a patient with a pheochromocytoma with this significant comorbidity (HOCM and SAM) should better be performed in an environment that allows invasive monitoring and control of blood pressure and fluid volume status.

Reference List

1. Pacak K., Eisenhofer G., Ahlman H. *et al*. (2007) Pheochromocytoma: recommendations for clinical practice from the First International Symposium. October 2005. *Nat Clin Pract Endocrinol Metab*, **3**, 92-102.
2. Di Palma G., Daniele G.P., Antonini-Canterin F., Piazza R., Nicolosi G.L. (2010) Cardiogenic shock with basal transient left ventricular ballooning (Takotsubo-like cardiomyopathy) as first presentation of pheochromocytoma. *J Cardiovasc Med (Hagerstown)*, **11**, 507-10.
3. van Duinen N., Steenvoorden D., Bonsing B.A. *et al*. (2010) Pheochromocytomas detected by biochemical screening in predisposed subjects are associated with lower prevalence of clinical and biochemical manifestations and smaller tumors than pheochromocytomas detected by signs and symptoms. *Eur J Endocrinol*, **163**, 121-7.
4. Gilsanz F.J., Luengo C., Conejero P., Peral P., Avello F. (1983) Cardiomyopathy and phaeochromocytoma. *Anaesthesia*, **38**, 888-91.
5. Park J.H., Kim K.S., Sul J.Y. *et al*. (2011) Prevalence and patterns of left ventricular dysfunction in patients with pheochromocytoma. *J Cardiovasc Ultrasound*, **19**, 76-82.
6. Von Bergen N.H., Lyon J.K., Edens R.E. (2009) Takotsubo-like cardiomyopathy in a 17-year-old male with a pheochromocytoma. *Pediatr Cardiol*, **30,** 184-7.
7. Hjalmarson A., Kallfelt B., Swedberg K., Waagstein F., Waldenstrom A. (1983) Possible adrenergic effects on heart protein metabolism. *Acta Med Scand Suppl*, **672**, 85-93.
8. Pacak K. (2007) Preoperative management of the pheochromocytoma patient. J Clin Endocrinol Metab, **92**, 4069-79.
9. Thompson R.C., Liberthson R.R., Lowenstein E. (1985) Perioperative anesthetic risk of noncardiac surgery in hypertrophic obstructive cardiomyopathy. *JAMA*, **254**, 2419-21.
10. Lam J.B., Shub C., Sheps S.G. (1985) Reversible dilatation of hypertrophied left ventricle in pheochromocytoma: serial two-dimensional echocardiographic observations. *Am Heart J*, **109**, 613-5.
11. Wiswell J.G., Crago R.M. (1969) Reversible cardiomyopathy with pheochromocytoma. *Trans Am Clin Climatol Assoc*, **80**, 185-95.