

Anaesthesia For Right Adrenalectomy In A Patient With Pheochromocytoma In A Resource-Challenged Facility- Case Report

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Abstract

We present a case of pheochromocytoma in a 22 year old female who had adrenalectomy done in our hospital as our first experience in 25 years.

The patient presented with 2 months history of low grade fever, excessive sweating and throbbing headache. Her blood pressure on presentation was 190/140 mm Hg. A diagnosis of pheochromocytoma was made from the history, clinical examination, ultrasound finding of a suprarenal mass and raised urine catecholamine levels.

Preoperatively, blood pressure was controlled with prazosin and propranolol. She had right adrenalectomy under general anaesthesia. Intraoperatively, blood pressure was controlled with infusion of hydralazine and intermittent bolus doses administered during surges in blood pressure. Adrenaline infusion and bolus doses were used to treat hypotension after excision of the tumour. The postoperative course was uneventful

Key words: Pheochromocytoma, anaesthetic management, resource-challenged facility

Introduction

Pheochromocytoma is a tumour arising from catecholamine-producing chromaffin cells in the adrenal medulla¹. Closely related tumours of extra-adrenal sympathetic and parasympathetic paraganglia are classified as extra-adrenal paragangliomas. They secrete epinephrine (adrenaline), norepinephrine (noradrenaline), and/or dopamine.

Patients with pheochromocytoma may develop complicated and potentially lethal cardiovascular and other complications, especially upon induction of anaesthesia or during surgery due to the potent effect of paroxysmal release of catecholamines. The released catecholamines cause severe hypertension, often refractory to conventional treatment^{2,3,4}.

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This makes anaesthetic management of these patients potentially hazardous. The first surgical excision of pheochromocytoma was reported in 1927 by Roux⁵ who described removal of a suprarenal tumor in a patient with a two-year history of episodic vertigo and nausea. Since then, successful surgical excision of the tumour has been achieved with careful perioperative use of rapidly acting cardiovascular drugs guided by invasive monitoring and other pertinent measures.

Pheochromocytoma is a rare catecholamine-secreting tumour arising from chromaffin tissue⁶. In Nigeria, its incidence is not known and only few cases have been reported in literature^{7,8,9,10}. The limited availability of invasive monitoring facilities and rapidly acting vasoactive drugs in most centers in addition to the rarity of the tumour have made management of this disease particularly challenging in our environment. A search through the literature and hospital records revealed that there had not been any surgical treatment of pheochromocytoma in the last quarter of a century in our centre. We describe a case of pheochromocytoma in which surgical excision of the tumour was successfully carried out in a Nigerian tertiary hospital despite challenges of drugs and facilities.

Case presentation

AG a 22year old female student was referred from a general hospital to our medical emergency on account of elevated blood pressure and ultrasonographic finding of a supra renal mass. She initially presented at the referral hospital with 2 months history of low grade fever, which was intermittent occurring more in the evenings. She had associated excessive sweating and throbbing headache.

Further history revealed that she had paroxysms of palpitations both at rest and on exertion but she did not have chest pain, orthopnoea or paroxysmal nocturnal dyspnoea. Her past medical history was not significant. Examination at presentation revealed a young woman who was conscious and alert. She was neither pale nor icteric but she was warm to touch with temperature of 37.4°C. Her weight was 47 kg and height 1.55 m. Examination of the cardiovascular system revealed that she was tachycardic with a pulse of 104/min which was regular. However the pulse showed occasional irregularities with rate as low as 60/min. Her blood

pressure was 190/140 mm Hg. There was praecordial hyperactivity and the apex beat was palpable at the 5th left intercostal space lateral to the mid clavicular line. She had fourth, first and second heart sounds with associated loud A₂ but there were no murmurs. The respiratory rate was 18 cycles per minute and the lung fields were clinically clear.

Examination of the abdomen revealed palpable right lumbar mass which was firm and tender. The patient was admitted and serum electrolytes and urea showed: Na⁺ 130 mmol/L, K⁺ 3.9 mmol/L, urea 2.5 mmol/L, creatinine 101 mmol/L, Ca²⁺ 2.24 mmol/L and phosphate 1.5 mmol/L. Complete blood count showed Hb 9.7 g/dL, packed cell volume 32%, white cell count of $6.5 \times 10^9/L$ (neutrophils 42%, lymphocytes 58%), platelet count of $276 \times 10^9/L$ and the ESR 60 mm/hr. Fasting blood sugar was 5.6 mmol/L and urinalysis was normal.

A repeat abdominal ultrasound scan done revealed a right supra renal mass, rounded, well circumscribed and separate from the kidney and the liver. It measured 77 x 64 x 66 mm in size with rich capsular vascularity but devoid of central vascularity. Computerised tomography scan showed a rounded thick walled mass measuring 5.1 x 4.9 cm arising from the right adrenal gland with hypodense central portion suggestive of necrosis. It also showed enhancement of its wall, normal liver, kidneys, spleen, pancreas and left adrenal gland. The mass was suspected to be an adrenal mass and based on persistent elevated blood pressure a presumptive diagnosis of pheochromocytoma was made. This was corroborated by the result of urinary catecholamine metabolites which were markedly increased (Table 1).

Within 7 days of admission, her blood pressure was controlled with oral prazosin 1 mg b.d. and propranolol 40 mg b.d. She was subsequently worked up for surgery.

Preanaesthetic review showed blood pressure of 120/90 mm Hg and the packed cell volume was 38% while the electrolytes and urea were within normal range. The patient was sedated with 10 mg oral

diazepam on the night before surgery. She had oral prazosin 1mg, propranolol 40mg and diazepam 10mg on the morning of surgery.

Intraoperative management

In the operating room, baseline vital signs using the DASH 4000 multiparameter patient monitor showed a non-invasive blood pressure of 130/90mmHg, pulse rate of 96 bpm and oxygen saturation of 98% on room air. Intravenous access was secured with an 18G cannula on the right forearm while an intra-arterial cannula was inserted into the right radial artery for invasive blood pressure monitoring. The patient was pre-oxygenated for three minutes with 100% oxygen, 2mg/kg of lidocaine was given to blunt the pressor response to laryngoscopy and intubation before anaesthesia was induced with i.v. propofol 2mg/kg and i.v. fentanyl 3 µg/kg. Vecuronium 0.15mg/kg was administered intravenously to facilitate endotracheal intubation. The patient was intubated with a size 7.5mm polyvinyl chloride endotracheal tube and mechanically ventilated with 50% oxygen in air supplemented with 1% isoflurane using a closed circuit breathing system. Muscle paralysis was maintained with supplemental doses of vecuronium as required while intra-operative analgesia was further ensured with titrated bolus doses of i.v. fentanyl. The patient had open adrenalectomy through an anterior approach. A vertical midline incision was used to gain access to the right adrenal mass which was excised and the wound closed in layers.

After the start of surgery, hydralazine infusion at 1.5µg/kg/min was given to maintain systolic blood pressure between 100 – 130 mmHg and diastolic pressures between 70 – 90 mmHg. Intraoperatively, blood pressure ranged between 34 mmHg and 220 mmHg systolic, and, between 20 mmHg and 140 mmHg diastolic. The pulse ranged between 90 and 110 bpm. There were surges in blood pressure (up to 220/140 mmHg) during manipulation of the tumour which were controlled with i.v. bolus doses of hydralazine in 5 mg aliquots. After tumour removal, there was a sharp reduction in blood pressure down to 34/20 mmHg which lasted up to 5 minutes. The hypotension was managed with rapid intravenous infusion of 0.9% saline, adrenaline infusion at 1

Table 1: showing 24 hr urine assay for creatinine and catecholamines

TEST	VALUE	REFERENCE RANGE
Volume (ml)	2660	600 – 2400
Creatinine (mmol/l)	8	9.0 – 17.7
Normetanephrine (nmol/l)	43,417	573 – 1932
Normetanephrine: Creatinine ratio	5441	26 – 200
Metanephrine (mmol/l)	1519	375 – 1506
Metanephrine: Creatinine ratio	190	5 – 90

$\mu\text{g/kg/min}$ and intermittent i.v. bolus adrenaline 0.1mg given at one minute interval until hypotension was corrected. Adrenaline infusion was subsequently continued at 0.2 $\mu\text{g/kg/min}$ to maintain blood pressure between 95 and 105 mmHg systolic and 55 and 70 mmHg diastolic. Estimated blood loss using the number of soaked swabs and amount in suction bottle was 1,300 ml and 2 units of whole blood were transfused intraoperatively.

At the end of the surgery muscle paralysis was reversed with 1.2mg of atropine and 2.5mg of neostigmine. The patient was extubated and transferred to the intensive care unit. Postoperatively, cardiovascular system monitoring was continued and adrenaline infusion was gradually tailed off over 18 hours. Postoperative course was uneventful. She was discharged to the ward from the intensive care unit after forty-eight hours. She had an uneventful postoperative course and was discharged home on the 17th post-operative day. She had been regular on prazosin 1mg daily with blood pressure range between 90 and 100 mmHg systolic and 60 to 75 mmHg diastolic

Discussion

Phaeochromocytomas are rare with a reported incidence of 0.13% in the general population⁶, but despite their rarity, they are an important secondary cause of hypertension¹¹. The rarity of these tumours means that most clinicians would be lacking in direct experience relevant to its management and many will have their knowledge and information of its clinical management indirectly based on literature such as this reported case.

Operative management of phaeochromocytoma presents difficulties, because of its accompanying complications and potential for emergent cardiovascular events which include hypertension, tachycardia and dysrhythmias, cardiac ischaemia or myocardial dysfunction, hyperglycaemia, contracted intravascular volume and lactic acidosis. In addition the emotional and physical stress of surgical intervention, intraoperative handling of the tumour and anaesthetic drugs and techniques may also precipitate adrenergic crisis in the perioperative period.

It has been reported that 25% to 50% of hospital deaths in patients with phaeochromocytoma occur during induction of anaesthesia^{12,13,14}, therefore the correct pharmacological management is of great importance. The result of urinary analysis for catecholamines in our patient suggested that the tumour was a predominantly norepinephrine secreting tumour and she presented with the typical features of excessive sweating, throbbing headache and hypertension. This implied that she was a patient at risk of cardiovascular or haemodynamic perturbations in the perioperative period.

The aims of preoperative preparation are to prevent an acute hypertensive crisis and to minimize catecholamine-induced haemodynamic changes during anaesthesia. Phenoxybenzamine has been widely used since the early 1950s¹⁵ as the mainstay of pre and perioperative control of blood pressure in patients with phaeochromocytoma. It has a long duration of action, which allows twice daily oral dosing. However, being a non-selective α adrenoceptor antagonist, it also blocks the α_2 adrenoceptors on the presynaptic membrane of adrenergic neurone terminals which are part of a negative feedback loop regulating release of norepinephrine. Consequently, the release of norepinephrine at cardiac sympathetic nerve endings is uninhibited, leading to an undesirable chronotropic and inotropic effects. Prazosin, a selective competitive α_1 adrenoceptor blocker was used in combination with propranolol for successful control of blood pressure in this patient preoperatively. Because of its high clearance (4–5 ml/min/kg) and its short elimination half life (2–3 h), the blood concentrations may decrease to ineffective levels at the time of surgery if the last dose was given on the previous night. The last dose was given to this patient on the morning of surgery. Cubeddu et al reported that combined use of prazosin and propranolol was effective in preoperative management of three patients with norepinephrine(NE)-secreting phaeochromocytoma¹⁶.

The adrenal gland can be removed through an open surgical technique or laparoscopic technique. The patient presented had an open surgery. For open surgery, the anterior, posterior or thoraco-abdominal approach can be used. The choice of approach depends on size, location, possibility of malignancy and surgeon's experience with the different techniques. The anterior approach is ideal for large tumours like in the patient presented and also if malignancy is suspected. Anaesthetic techniques that have been used for excision of phaeochromocytoma in our environment include general anaesthesia¹⁷, regional anaesthesia¹⁸ or combined general and epidural anaesthesia⁸.

The fundamental principle in anaesthetic management is the provision of a standard stable general anaesthetic and the prevention and treatment of catecholamine surges due to anaesthetic drugs or manoeuvres, surgical stimulation, tumour handling and clamping with ligation of venous drainage of tumour.

Anaesthesia induction and tracheal intubation must be smooth to avoid hypertension and tachycardia. Propofol used for induction of anaesthesia in this patient is one of several drugs used to blunt this sympathetic response¹⁹. Suxamethonium was not used for tracheal intubation because of its undesirable sympathetic stimulation and associated muscular

fasciculation, which may mechanically squeeze the tumour. Vecuronium used to facilitate endotracheal intubation and maintain neuromuscular blockade was suitable in this patient as a cardiostable neuromuscular blocking agent. Isoflurane was used for maintenance of anaesthesia because it does not sensitize the myocardium to circulating blood catecholamines.

The ideal agent for the treatment of hypertensive emergencies should be rapid acting, predictable and easily titrated, safe, inexpensive and convenient for use. Hydralazine infusion and bolus doses were used successfully to manage intraoperative hypertensive episodes as it was the only readily available agent at the time of the surgery. Hydralazine is a direct-acting arteriolar vasodilator with onset of action of 5 to 15 minutes. Tietjen et al²⁰ reported that 2-3 mg boluses of hydralazine could allow for a more controlled reduction in blood pressure in the perioperative setting. In pheochromocytoma surgery, hypertension control is often attained by nitroprusside, nicardipine, nitroglycerine, and/or deepening anaesthesia²¹. Adrenaline was infused to manage hypotension. After the adrenal gland has been removed, hypotension may be severe as was seen in this report with BP as low as 34/20 mmHg. This hypotension can be controlled by adrenaline, noradrenaline, ephedrine, dopamine and vasopressin²¹.

The successful management of this patient despite the rarity of the pathology and the lack of desirable agents like nitroprusside, nitroglycerine and nicardipine has shown that adequate preoperative preparation, use of intraoperative invasive monitoring and aggressive management of blood pressure fluctuations is critical to outcome in anaesthetizing a patient with pheochromocytoma in a resource-challenged facility.

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