A case study: Anesthesia for pheochromocytoma

A case study is presented of a 34-year-old female who was diagnosed with a markedly hydronephrotic right kidney. The patient underwent a cystoscopy and a right nephrectomy during which a pheochromocytoma was suspected and subsequently confirmed by postoperative histologic examination. No laboratory analysis for urinary metanephrines or vanillylmandelic acid was carried out.

Major problems associated with anesthesia during the perioperative period included uncontrolled hypertension, acute hypotension after ligation of venous return from the tumor and acute dysrhythmias. Since the pheochromocytoma was unsuspected preoperatively, the patient had no adrenergic blockade with concomitant volume loading. Consequently, she experienced wide fluctuations in blood pressure, heart rate and ventricular arrhythmias. Following venous ligation of the tumor, the patient experienced marked hypotension that readily responded to vasopressors and bolus IV fluid therapy. The patient experienced no medical problems postoperatively, even though she did require intravenous fluid volume with colloid and packed cells.

Pheochromocytoma is a chromaffin tissue catecholamine-producing tumor. Although usually found in the adrenal medulla it may arise anywhere along the sympathetic ganglia. The clinical features and the surgical and anesthetic management have been well described since Dr. Charles Mayo performed the first resection of such a tumor in 1926. The author will present a case of a previously undiagnosed pheochromocytoma found in a patient undergoing surgery for a hydronephrotic kidney.

Case report

A 34-year-old 78 kg obese female patient presented with a 3 day history of severe right flank and right upper quadrant pain with associated symptoms of nausea and vomiting. A similar episode had occurred approximately five months prior to the current admission; however, the etiology was undetermined. A series of gall bladder studies were performed, but no pathology was revealed. An intravenous pyelogram and tomograms were done, showing a markedly hydronephrotic right kidney with a very small rim of functioning tissue around the hydronephrotic mass. The presentation of the kidney was thought to be consistent with long-standing uretero-pelvic dysfunction. The left kidney was unremarkable. The patient was admitted for necessary surgery to include cystoscopy and right nephrectomy.

An anesthesia consultation was obtained. Pertinent findings included hemoglobin 13.1, hemato-
crit 38.1, white blood cell count 9.4, and normal chest x-ray and ECG. The patient was allergic to codeine. At the time of admission she was taking atenolol 50 mg by mouth daily. Past medical history included hypertension for the previous eight months, hiatal hernia (symptomatic) and hydrocephalus for which a shunt had been inserted four years ago. Past anesthetic history was unremarkable.

**Preoperative medication**

Medication included atenolol 50 mg by mouth, and intramuscular injection of meperidine 75 mg, promethazine 25 mg and glycopyrrolate 0.2 mg the morning of surgery.

The patient presented to the operating suite in an awake and alert state, but with some preoperative anxiety. Preinduction signs were as follows: blood pressure 140/80, heart rate 72, respirations 20/minute. ECG leads and an automatic blood pressure cuff were applied. A 16-gauge venous catheter with D5W and subsequently lactated Ringer’s solution was started.

A rapid sequence induction was carried out due to the presence of a symptomatic hiatal hernia. The patient was pretreated with d-Tubocurarine 3 mg IV and preoxygenated with 100% oxygen by mask. Induction was completed with sodium thiopental 450 mg and succinylcholine 100 mg. Cricoid pressure was applied and a 7.5 mm cuffed endotracheal tube was inserted. Blood pressure following induction and laryngoscopy was 110-140/76-80 and heart rate was 78-80, with normal sinus rhythm. Anesthesia was maintained with isoflurane and nitrous oxide. The patient was placed in the lithotomy position and a urethral cystoscopy was performed. An indwelling urethral catheter was inserted.

Following this procedure the patient was transferred from the cystoscopy room to the operating room for the surgical removal of the right kidney. The patient was placed in the left lateral position and supported by the kidney rest. Anesthesia was maintained with isoflurane 1-1.5%, 60% nitrous oxide and pancuronium 4 mg. A primary incision was made in the right flank over the twelfth rib. The patient remained normotensive initially. However, after 10-15 minutes, there was a steady rise in the systolic and diastolic blood pressure with a concomitant increase in heart rate. The blood pressure increased to 180/120-140 and a sinus tachycardia developed, with the rate ranging between 120 and 130. Occasional premature ventricular contractions were detected on the ECG.

Isoflurane was discontinued due to its inability to satisfactorily control the hypertension and sinus tachycardia, and enflurane 2-3% was administered. When this proved to be unsuccessful, propranolol 1 mg IV was administered in divided doses of 0.5 mg. The result was a slight reduction in heart rate with little or no effect on blood pressure. As these events were occurring the kidney was visualized. Because of the appearance of the kidney and the instability of the blood pressure and heart rate following surgical manipulation, a pheochromocytoma was suspected. A 20 gauge arterial line was then inserted in order to more closely monitor the blood pressure.

Following ligation of the venous drainage, resection of the kidney and removal of the tumor were accomplished. Immediately afterwards there was a precipitous fall in the blood pressure to 40 systolic. All anesthetics were discontinued and 100% oxygen was administered. At this time direct aortic compression was applied by the surgeon. Ephedrine sulfate was administered in 10 mg and 25 mg increments IV. Arterial blood gases were found to be normal; pH 7.40, PCO₂ 34, PO₂ 412, HCO₃ 24, base excess 0, SAT 99%. Blood pressure was restored to 130-140/80-100. Once hemodynamic stability was restored, anesthesia was maintained with enflurane and nitrous oxide.

The remainder of the case was unremarkable. The patient was given atropine sulfate 0.6 mg and edrophonium 35 mg IV as a reversal for the residual pancuronium. Upon her reaction to stimuli she was extubated and taken to the postoperative recovery unit. During the immediate postoperative period blood pressure remained in the low 90s systolic, for which hetastarch Hespan® and bolus IV fluids were administered. The patient was discharged to the surgical intensive care unit where she remained for two days. Subsequently her recovery was uneventful and she was discharged on the tenth postoperative day. Oncological follow-up was continued and a review by the institution’s tumor review board was carried out.

**Pathophysiology**

Although usually found in the adrenal medulla, pheochromocytoma may also be found along the cells of the extra-adrenal paraganglion system which are disseminated along the paravertebral axis from the pelvis to the base of the skull. Another extra-adrenal site is the organ of Zuckerkandl, a complex of para-aortic and paraganglion cells extending from the origin of the inferior mesenteric artery to the bifurcation of the abdominal aorta. Pheochromocytoma may also be found at the
bifurcation of the carotid artery. Ninety percent of pheochromocytomas are located within the adrenal glands with the right adrenal gland being more commonly affected.\(^2\) Familial pheochromocytoma may be associated with multiple endocrine neoplasms (MEN, type IIa, IIb).\(^4\) Familial pheochromocytoma also has an association with the neuroectodermal dysplasias which include Von Hippel-Lindau's disease, tuberous sclerosis, Sturge-Weber syndrome and Lindau-von Hippel disease.\(^1\)

Pheochromocytomas are characterized by a number of symptoms, the most important of which is hypertension. The hypertension is characterized by a great variability and associated paroxysms that occur unpredictably. Paroxysms may be precipitated by such things as emotion, exercise, drugs, changes in posture and abdominal palpation. Among the features most commonly recognized by patients are palpitations, headaches, sweating and pallor that develop suddenly.\(^2\)

Clinical features of pheochromocytoma are related to the production and release of excessive catecholamines; epinephrine and norepinephrine are usually both present in an adrenal medullary tumor, but norepinephrine is predominant. Occasionally each may be secreted exclusively.\(^2\) The epinephrine and norepinephrine are metabolized by monamine oxidase and catechol-O-methyl transferase to vanillylmandelic acid and metanephrines. These inactive metabolites along with a small portion of unaltered catecholamines are excreted by the kidney.\(^2\)

**Diagnosis**

The main biochemical diagnostic tool during the past decade has been the determination of urinary metanephrines and vanillylmandelic acid. Measurements of urinary catecholamines and their metabolites will establish the correct diagnosis in 95% of patients with pheochromocytoma.\(^4\)

Radiographic studies may be conducted for diagnosis and localization of pheochromocytoma. Selective arteriography, venography and nephrotomography are useful diagnostic tools. Other radiologic tests include roentgenograms of the chest and abdomen and intravenous pyelography. Although frequently used, intravenous pyelography has a low yield for tumor localization.\(^5\)

**Treatment**

Surgical removal remains the obvious treatment of choice for pheochromocytoma. The flank approach appears to offer certain advantages: risk of injury to the spleen is greatly reduced by elimination of unnecessary contralateral exploration and easier mobilization of the adrenal gland. The postoperative convalescence may be shortened due to greater comfort in respiration. Flank incisions correspond to a lower incidence of postoperative ileus.\(^8\)

**Anesthetic consideration**

Anesthetic management of the patient with pheochromocytoma is directed towards the control of the cardiovascular system. Vigilant electrocardiographic monitoring with direct arterial and pulmonary pressure measurements is strongly recommended.\(^2\) General anesthesia is the usual technique chosen. Virtually all anesthetic agents have been used at some time with success,\(^2,5,10\) although enflurane currently appears to be the safest anesthetic agent.\(^9\) Halothane sensitizes the myocardium to the effects of catecholamines by decreasing the dyssrhythmic threshold, and is therefore not recommended.\(^2\)

Prompt management of cardiovascular disturbances during surgery is critical. Pharmacologic agents such as phenolamine, nitroprusside, propranolol, lidocaine and blood volume expanders should be readily available. Increase in arterial pressures may occur during endotracheal intubation, skin incision, abdominal exploration and surgical manipulation of the pheochromocytoma. Presumably, cardiovascular changes result from release of catecholamines from the excessive stores in adrenergic nerve endings and may be blocked in some cases by deepening the level of anesthesia. Therefore the depth of anesthesia as opposed to the specific anesthesia agent may be of greatest importance.\(^2,5,8\)

Immediately following excision of the tumor or ligation of the venous drainage of the tumor, hypotension may result. Rapid infusion of colloid products (blood, albumin, plasma) and saline is recommended for reversal of the hypotension.\(^9\)

Hypertension may persist or recur during the postoperative period. Causative factors include excessive treatment with volume expanders, return of autonomic influences creating a hypovolemic state, residual pheochromocytoma tissue and renal/arterial/vascular hypertension. As many as 25% of patients remain hypertensive postoperatively without residual tumor. Treatment with the usual antihypertensive agents may be indicated. The possibility of myocardial infarction, cardiac failure, sepsis and retroperitoneal bleeding must also be considered if hypotension and tachycardia occur postoperatively and are unresponsive to therapy. Hypoglycemia may result due to sudden decreases in catechola-
mine levels and enhanced insulin secretion following tumor removal.2

Discussion
The incidence of pheochromocytoma among hypertensive patients ranges from 0.2% to 0.7%. Pheochromocytoma is a most hazardous and dramatic cause of hypertension. It may occur at any age but occurs more frequently between the third and fifth decades. Approximately 800 new cases are diagnosed each year. The five-year survival rate of patients with benign tumors is 96% and for those with malignant tumors it is 44%.3

Interest in the many problems involved in anesthesia for the surgical removal of pheochromocytoma has continued since the first such operation was performed by Mayo in 1926.7

Alpha receptor blockade has improved the preoperative and perioperative management of these patients. Phenoxybenzamine is a potent alpha-blocking agent that may be given orally or intravenously. Phentolamine may also be used, but it is shorter acting. Opponents of complete alpha blockade are concerned that changes in blood pressure and pulse during the operation will be masked and tumor localization may be difficult. Propranolol, a non-selective beta blocker, is indicated for persistent tachycardia, arrhythmias or angina. It should never be used without prior alpha blockade. With unopposed beta blockade, alpha effects predominate, resulting in intensification of vasoconstriction and hypertension.7,9

However, controversy remains regarding the role of preoperative adrenergic blockade, the significance of hypovolemia, the relative merits of arteriography, the use of postoperative vasopressors and the operative technique.8 Harrison et al. recommend the use of phenoxybenzamine if the blood pressure is uncontrolled and greater than 200/130 mmHg, if frequent severe uncontrolled hypertensive crises occur, or when the hematocrit is greater than 50%. Perry and Gould report that preoperative oral administration of phenoxybenzamine results in decreased incidence of tachycardia with no significant change in the incidence of intraoperative hypertensive episodes.7 Deoreo et al. do not advocate the routine use of phenoxybenzamine and report excellent survival rates with no deaths in 46 patients.8

Preoperative preparation with alpha and beta adrenergic blockade is recommended by most authors. However, controversy remains regarding their efficacy in the prevention of intraoperative cardiovascular disturbances. According to a 1984 study by Desmonte and Marty, operative mortality does not appear to have been influenced by the use of preoperative alpha and beta adrenergic blockade. However, preoperative therapy is mandatory in patients with sustained or paroxysmal hypertension.10

Conclusion
Pheochromocytoma may stimulate any hypertensive syndrome. Although it is an uncommon cause of high arterial pressure, its recognition is important because of possible serious anesthetic problems if its diagnosis is missed before any surgical procedure.10

Effective preoperative correction of hypovolemia, electrolyte disturbances and a blockade regimen has decreased the surgical mortality once experienced with pheochromocytoma. Once diagnosed, pheochromocytoma requires immediate treatment and life-time follow-up.

REFERENCES

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