The anaesthetic management of a patient with a phaeochromocytoma and acute stroke

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A case is reported of a young woman in whom the diagnosis of a phaeochromocytoma was made after a major stroke. Preoperative preparation included the introduction of phenoxybenzamine, 10 mg · day⁻¹, and propranolol, 80 mg · day⁻¹, over a two-week period. The presence of cerebrovascular disease and the marked orthostatic changes in blood pressure and heart rate to low-dose phenoxybenzamine prevented the establishment of full alpha blockade. Incomplete alpha blockade probably contributed to the hypertensive response to manipulation of the tumour (220/150 mmHg) and hypotension occurred after removal of the tumour (80/45 mmHg). An anaesthetic technique was chosen to provide haemodynamic stability as well as protection against cerebral ischaemia. Invasive haemodynamic monitoring, a four-channel processed electroencephalograph and somatosensory evoked potentials were used to accomplish these goals.

On rapporte le cas d'une jeune femme chez qui le diagnostic de phéochromocytome fut fait après une crise majeure d'apoplexie. La préparation préopératoire incluait l'introduction de phénoxybenzamine 10 mg · jour⁻¹ et propranolol 80 mg · jour⁻¹ pour une période de deux semaines. La présence de maladie cérébrovasculaire et les changements orthostatiques importants dans la pression artérielle et la fréquence cardiaque avec des doses faibles de phénoxybenzamine ont empêché l'installation d'un blocage alpha complet. Un blocage alpha incomplet a probablement contribué à la réponse hypertensive lors de la manipulation de la tumeur (220/150 mmHg) et l'hypotension survenant après l'exérèse de cette tumeur (80/45 mmHg). Une technique anesthésique fut choisie afin d'établir la stabilité

hémodynamique et une protection cérébrale contre l'ischémie. La surveillance hémodynamique invasive et l'électro-encéphalogramme à quatre canaux et des potentiels somatosensoriels évoqués furent employés afin d'atteindre ces buts.

Phaeochromocytoma is a rare tumour with an incidence of approximately 0.13% in the general population.¹ Neurological events can complicate the diagnosis and treatment of these patients.²⁻⁵ Although the anaesthetic management of a patient with a phaeochromocytoma has been well described previously,⁶⁻⁹ the management of a patient with a phaeochromocytoma and a recent cerebral infarction has not.

Case report

A 26-yr-old, 55 kg female nurse with a ten-day history of recurrent headaches was transferred from a local hospital for investigation. The headaches were increasing in frequency and unresponsive to medical therapy. Before transfer her vital signs had been normal except for one recorded systolic blood pressure of 200 mmHg.

Her past medical history included occasional palpitations which were not associated with syncope. She had received L-thyroxin for treatment of hypothyroidism for the previous year. This medication was stopped prior to her transfer in an attempt to eliminate it as a contributing factor to her headaches. On admission, she demonstrated marked orthostatic changes in blood pressure and heart rate; supine blood pressure was 110/60 mmHg and heart rate 85 beats per minute (bpm); sitting blood pressure 80/50 mmHg; and heart rate was 150 bpm. The remainder of her physical examination, including an extensive neurological assessment, was unremarkable. Routine laboratory investigations including complete blood count, electrolytes, serum glucose, blood urea nitrogen, and creatinine concentrations were normal. A 12-lead electrocardiogram (ECG) revealed diffuse nonspecific ST segment and T wave changes.

Shortly after admission to the neurological observation unit she had several episodes of transient neurological dysfunction ranging from blurred vision to motor and

Key words

BRAIN: infarction;

SURGERY: phaeochromocytoma.

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sensory abnormalities involving all four limbs. An initial computed tomographic scan (CT) of her head was normal and an electroencephalogram (EEG) was suggestive of a severe migraine attack. Holter monitoring of her heart recorded multiple episodes of supraventricular tachycardia. Frequent 12-lead ECG demonstrated fluctuating ST segment and T wave abnormalities. A two-dimensional echocardiogram was normal.

On her seventh day in hospital she developed profound right hemiparesis and global aphasia compatible with a left hemispheric stroke. At the time of her stroke her blood pressure was 110/60 mmHg and heart rate was 84 bpm. Magnetic resonance imaging (MRI) confirmed the presence of a stroke involving the globus pallidus and adjacent subcortical white matter. Subsequent cerebral angiography demonstrated numerous areas of segmental stenosis involving the vessels of both cerebral hemispheres as well as numerous occlusions in distal branches of the middle cerebral artery. On the basis of her cerebral angiogram a presumptive diagnosis of cerebral vasculitis was made and she was treated with methylprednisolone 500 mg · day⁻¹ *iv* for five days.

On the day she experienced her stroke, the results of her urinary catecholamine assays returned. The metanephrine concentration was 66.2 µmol · L⁻¹ (normal 0–4.95) and the vanillylmandelic acid concentration was 42.4 µmol · L⁻¹ (normal 0–40.4). A CT scan of her abdomen showed a single left adrenal mass and an ¹³¹I-metaiodobenzylguanidine (MIBG) scan subsequently demonstrated the presence of a single focus of uptake near the left adrenal. The diagnosis of pheochromocytoma was made and she was booked for surgery.

In preparation for surgery, alpha blockade in the form of phenoxybenzamine was started at 10 mg · day⁻¹. In spite of *iv* fluid replacement, she continued to have considerable orthostatic hypotension (systolic pressure <70 mmHg) and thus the dosage of phenoxybenzamine could not be increased. Propranolol was gradually introduced and successfully controlled her tachyarrhythmias. After two weeks of treatment, additional manipulations of her therapy were not attempted due to the risk of further cerebral compromise. It was decided to proceed to surgery 20 days after her stroke recognizing that her adrenergic blockade was not complete. Before surgery she was receiving propranolol 80 mg · day⁻¹ and phenoxybenzamine 10 mg · day⁻¹.

The evening before surgery she was admitted to the intensive care unit for insertion of an intraarterial line and pulmonary artery catheter for assessment of her haemodynamic variables (Table). She received her last dose of phenoxybenzamine and propranolol at 2200 hr on the night before surgery. Attempts at fluid loading with crystalloid produced an equivalent volume diuresis and no

TABLE Haemodynamic variables

	A	B	C	D
Heart rate (bpm)	68	80	92	101
Blood pressure (mmHg)	109/68	130/68	95/56	99/42
Central venous pressure (mmHg)	13	19	6	5
Pulmonary artery pressure (mmHg)	47/17	31/17	30/12	23/8
Pulmonary capillary wedge pressure (mmHg)	15	18	16	11
Cardiac index (L · min ⁻¹ · m ²)	3.3	3.0	5.4	6.4
Systemic vascular resistance index (dynes · sec · cm ⁻⁵)	1590	1901	965	671
Pulmonary vascular resistance index (dynes · sec · cm ⁻⁵)	122	132	74	62

Times of measurement: A = preoperative, B = after induction, C = immediately after tumour removal, D = end of procedure.

change in pulmonary capillary wedge pressure or central venous pressure. She was premedicated with diazepam 10 mg *po* and methylprednisolone 100 mg *iv* two hours before surgery.

On arrival in the operating room her blood pressure was 160/70 mmHg and heart rate was 90 bpm (Figure). Additional monitors included a lead II ECG, pulse oximeter, end tidal capnograph, urinary catheter, and oesophageal temperature probe. Induction of anaesthesia consisted of midazolam 3 mg, fentanyl 1.25 mg, vecuronium 8 mg and xylocaine 100 mg *iv*. Her trachea was intubated without changes in her blood pressure or heart rate. Anaesthesia was maintained with nitrous oxide 50%, oxygen 50%, fentanyl (total dose 2 mg), vecuronium, and isoflurane (0.6–1.0 vol%). Intermittent positive pressure ventilation was used to obtain a PETCO₂ of 40 mmHg. Arterial blood for gas analysis was drawn to ensure adequate oxygenation and to correlate arterial and PETCO₂ levels. Blood sugar concentrations were monitored. To maintain normal central venous and pulmonary capillary wedge pressures, she was given seven litres of crystalloid (two litres normal saline, and five litres Ringer's lactate). Intraoperative fluid loss consisted of two litres of urine and an estimated blood loss of 350 ml.

Monitoring of cerebral function was performed with an automated EEG and somatosensory evoked potentials (SSEP) using the Nicolet Pathfinder I. Four channel compressed spectral array analysis of EEG was performed continuously with the montage of F3-C3, C3-P3, F4-C4, C4-P4. Except for bilateral symmetrical changes in the spectral edge frequency corresponding to changes in the level of anaesthesia, there were no focal signs of

FIGURE Intraoperative blood pressure recordings from time of arrival in the operating room. Event 1 = manipulation of the tumour. Event 2 = removal of the tumour. SNP = sodium nitroprusside. B, C, and D refer to haemodynamic measurements in Table.

ischaemia. The SSEP were obtained by the stimulation of the median nerve at the wrist with needle electrodes and were recorded from scalp disc electrodes at C3' and C4' in reference to the forehead and from the cervical spine (C7). There were no changes in the SSEP throughout the procedure.

The patient was haemodynamically stable until the surgeon manipulated the tumour. This produced a sudden increase in blood pressure to 220/150 mmHg. Concurrently, there was a modest rise in heart rate from 70 to 90 bpm. Sodium nitroprusside and isoflurane were used intermittently over the next 30 min to control haemodynamic responses to tumour manipulation (Figure). There was no dramatic change in heart rate during this interval. Upon removal of the tumour the blood pressure decreased suddenly to 80/45 mmHg and heart rate gradually increased to 100 bpm in spite of adequate fluid loading and cessation of vasodilators. This responded rapidly to levophed. She then continued to require levophed 2–4 $\mu\text{g} \cdot \text{min}^{-1}$ to maintain blood pressure for the remainder of her surgery.

Following completion of surgery the patient was returned to the intensive care unit. She gradually awoke from the anaesthetic and the trachea was extubated five hours after surgery. Levophed was gradually withdrawn over the next four hours. Followup neurological examinations revealed no new abnormalities; however, she did demonstrate continued improvement in her previous deficits. Her postoperative course was uneventful and she was discharged home after six days.

Discussion

Improvements in the diagnostic abilities and pharmacological management have reduced the morbidity and

mortality associated with a pheochromocytoma and its surgical removal.⁹ The occurrence of neurological symptoms, including a preoperative stroke in this patient, increased her perioperative risk and complicated her anaesthetic management.

The clinical manifestations of a pheochromocytoma are often mistaken for other neurological, cardiovascular or psychiatric disorders. It is only with a high degree of suspicion that the diagnosis of this rare tumour is entertained and subsequently investigated. Furthermore, the morbidity and mortality of patients coming to surgery with an undiagnosed pheochromocytoma is increased. A recent review of patients with an unsuspected pheochromocytoma coming to the operating room stated that 27% of them died from hypertensive or hypotensive crisis occurring during a minor operation.¹ In contrast, the operative mortality of patients with known disease and preoperative preparation has recently been reported as 1.3%.⁹

Neurological symptoms, though less common, have been reported. Thomas *et al.* in a series of 100 patients described 11 patients with transient visual abnormalities ranging from snowy vision to almost complete visual loss.² Eleven patients also experienced numbness and paraesthesia in the hands and face. The author suggested that these symptoms could have been due to hyperventilation. Three patients had cerebral infarctions and two had an intracerebral bleed. No comment was made concerning the aetiology of these intracranial events. A case report in 1958 demonstrated angiographic cerebral vasospasm in a patient with pheochromocytoma and a three-week history of headaches.¹⁰ Other case reports have also linked cerebrovascular events to the presence of a pheochromocytoma.^{3–5} In one case, a stroke was thought to be the result of an embolic event. However, angiograms were not done and other vascular causes of stroke could not entirely be eliminated.⁴ Another patient had an acute stroke while concomitantly showing signs of peripheral vasoconstriction and acute ischaemic changes on her ECG suggesting an element of widespread vasospasm.³

Our patient suffered several transient neurological events before developing global aphasia and right hemiplegia. The cause of her stroke was uncertain. An embolus from her heart was unlikely as she did not have a cardiomyopathy or atrial fibrillation. The cerebral angiograms did not reveal proximal carotid artery disease that could have been a source of embolic material. The angiograms did show numerous areas of segmental stenosis suggesting a form of vasculitis. Speculating that the high catecholamine concentrations were inducing a form of cerebral vasculitis, rather than simple vasospasm, a course of steroids was given to our patient empirically.

The introduction of preoperative adrenergic blockade

has been a contributing factor to the reduction of perioperative morbidity and mortality.⁶ Arguments have been made both for partial and full alpha blockade prior to the removal of the tumour.⁷ Complete alpha blockade may mask the presence of a second tumour but incomplete blockade may not prevent hypertensive crises during induction of anaesthesia or during the manipulation of the tumour. In an effort to avoid episodes of worsening orthostatic hypotension and compromise of her cerebral perfusion, complete alpha blockade was not established. Full beta blockade in the presence of an incomplete alpha blockade raises the risk of unopposed alpha mediated vasoconstriction and severe hypertension.⁸ As a result, beta blockade was advanced cautiously to control her tachyarrhythmias but was withheld the morning of her surgery to complement the incomplete alpha blockade.

Preoperative institution of invasive haemodynamic monitoring in the intensive care unit provided baseline values as well as an opportunity to adjust her volume status. It has been proposed that the central venous pressure may not reflect left-sided filling pressures, even in apparently uncompromised patients with phaeochromocytoma and that pulmonary artery catheters should be inserted preoperatively.¹²

The induction of anaesthesia was smooth. However, manipulation of the tumour could not be accomplished without the use of vasodilating agents to control blood pressure. Sodium nitroprusside is most commonly used.¹¹ An increased concentration of isoflurane in combination with sodium nitroprusside was effective in controlling hypertension in our patient.

The presence of a preoperative stroke and stenotic lesions on the cerebral angiogram further complicated the intraoperative management of our patient. To protect against cerebral ischaemia, we attempted to maintain normal cerebral perfusion and monitored cerebral function. The patient's blood pressure was maintained as close to normal as possible with the use of vasoactive agents. Adequate oxygenation was monitored by the use of pulse oximetry and arterial blood gases. To protect against the adverse effects of hypocarbia and hypercarbia, PaCO₂ was maintained at normal values.^{13,14} A common method of detecting cerebral ischaemia in patients with cerebrovascular disease undergoing carotid endarterectomy has been the EEG and more recently, processed EEG and median nerve SSEP.^{15,16} Our patient did not have any changes in her EEG or SSEP during the brief periods of haemodynamic instability and she emerged with no change in her neurological status. Also, the use of intraoperative glucose containing fluids was avoided and blood sugar level monitored, as hyperglycaemia may increase post-ischaemic cerebral injury.¹⁷

The anaesthetic agents chosen reflected our concern

surrounding the presence of cerebrovascular disease and a phaeochromocytoma. The patient was premedicated with a benzodiazepine in an effort to prevent catecholamine surges produced by anxiety enroute to the operating room. A narcotic-based anaesthetic was chosen for its cardiovascular stability and vecuronium was selected for its lack of cardiovascular effects. Low concentration isoflurane was used for amnesia and anaesthesia. Higher concentrations were used for controlling blood pressure.

In summary, we have discussed the perioperative management of a young woman with cerebral vascular pathology and a phaeochromocytoma. The pharmacological management of these patients is difficult and needs to be tailored to the individual case. These concerns required special consideration of her preoperative pharmacological preparation, anaesthetic management, and intraoperative monitoring of haemodynamic and cerebral functions.

References

- 1 St. John Sutton MG, Sheps SG, Lie JT. Prevalence of clinically unsuspected phaeochromocytoma. *Mayo Clin Proc* 1981; 56: 354-60.
- 2 Thomas JE, Rooke ED, Kvale WF. The neurologist's experience with phaeochromocytoma. *JAMA* 1966; 197: 754-8.
- 3 Radtke WE, Kazmier FJ, Rutherford BD, Sheps SG. Cardiovascular complications of phaeochromocytoma crisis. *Am J Cardiol* 1975; 35: 701-5.
- 4 Scully RE, Mark EJ, McNeely WF, McNeely BU. Case Records of the Massachusetts General Hospital. Case 15. *N Engl J Med* 1988; 318: 970-81.
- 5 Knisely AS, Sweeney K, Ambler MW. Phaeochromocytoma and sudden death as a result of cerebral infarction in Turner's syndrome: report of a case. *J Forensic Sci* 1988; 33: 1497-502.
- 6 Remine WH, Chong GC, Van Heerden JA, Sheps SG, Harrison EG Jr. Current management of phaeochromocytoma. *Mayo Clin Proc* 1973; 179: 740-8.
- 7 Bravo EL, Gifford RW Jr. Phaeochromocytoma: diagnosis, localization and management. *N Engl J Med* 1984; 311: 1298-303.
- 8 Hull CJ. Phaeochromocytoma. Diagnosis, preoperative preparation and anaesthetic management. *Br J Anaesth* 1986; 58: 1453-68.
- 9 Sheps SG, Jiang N-S, Klee GG, Van Heerden JA. Recent developments in the diagnosis and treatment of phaeochromocytoma. *Mayo Clin Proc* 1990; 65: 88-95.
- 10 Armstrong FS, Hayes GJ. Segmental cerebral arterial constriction associated with phaeochromocytoma. *J Neurosurg* 1961; 18: 843-6.
- 11 Van Heerden JA, Sheps SG, Hamberger B, Sheedy PF, Poston JG, ReMine WH. Phaeochromocytoma: current status and changing trends. *Surgery* 1982; 91: 367-73.

- 12 *Mihm FG*. Pulmonary artery pressure monitoring in patients with phaeochromocytoma. *Anesth Analg* 1983; 62: 1129–33.
- 13 *Ehrenfeld WK, Hamilton FN, Larson CP et al*. Effect of CO₂ and systemic hypertension on down-stream cerebral arterial pressure during carotid endarterectomy. *Surgery* 1970; 67: 87–96.
- 14 *Michenfelder JD, Sundt TM Jr*. The effect of PaCO₂ on the metabolism of ischaemic brain in squirrel monkeys. *Anesthesiology* 1973; 38: 445–53.
- 15 *Rampil IJ, Holzer JA, Quest DO, Rosenbaum SH, Correll JW*. Prognostic value of computerized EEG analysis during carotid endarterectomy. *Anesth Analg* 1983; 62: 186–92.
- 16 *Markand ON, Dilley RS, Moorthy SS, Warren C Jr*. Monitoring of somatosensory evoked responses during carotid endarterectomy. *Arch Neurol* 1984; 41: 375–8.
- 17 *Lanier WL, Stangland KJ, Scheithauer BW, Milde JH, Michenfelder JD*. The effects of dextrose infusion and head position on neurologic outcome after complete cerebral ischaemia in primates: examination of a model. *Anesthesiology* 1987; 66: 39–48.