Perioperative management of a patient with a malignant pheochromocytoma

Donald Miller MD FRCP(C),
James A. Robblee MD FRCP(C)

A case report is presented of a patient with a known malignant pheochromocytoma, who was to undergo an orthopaedic procedure using methylmethacrylate bone cement. Preoperative preparation of the patient included the use of prazosin and metyrosine. Epidural blockade was chosen as the anaesthetic technique for intraoperative management. Surgical fixation with methylmethacrylate did not produce profound or prolonged hypotension despite sudden massive blood loss prior to its use. Epidural morphine was administered for postoperative pain control.

Key words

ANAESTHETIC TECHNIQUES: epidural; SURGERY: pheochromocytoma; DRUG INTERACTIONS: metyrosine, prazosin, methylmethacrylate.

The necessity for adequate preoperative preparation of patients with pheochromocytoma is well established. Such preparation is mandatory to prevent severe intraoperative cardiovascular complications.¹⁻² The mainstay of preparation continues to be alpha-adrenergic blockade with or without beta-blockade. A variety of agents may be used to achieve this goal.¹⁻³ Phenoxybenzamine has been the predominant alpha-blocking agent administered in the management of the cardiovascular effects of pheochromocytoma. Propranolol has been used to control the beta-effects of such tumors.³ Prazosin, a specific alpha-1-adrenergic blocking agent, has been used successfully in the management of pheo-

chromocytoma.³ Metyrosine, a tyrosine hydroxylase inhibitor, is a newer agent for the treatment of patients with pheochromocytoma.⁴

Orthopaedic procedures using methylmethacrylate bone cement are becoming increasingly common. In addition to total hip and knee prostheses, many techniques are employed which utilize methylmethacrylate as a solid medium in which internal fixation may be applied. Fixation of pathological or impending pathological fractures is a widely accepted technique. In most instances, no attempt is made to excise the tumour. Because of potential cardiovascular complications occurring as a result of tumour manipulation, it may be advisable to widely excise a pheochromocytoma metastasis prior to internal fixation.⁵ The cardiovascular effects of methylmethacrylate during anaesthesia are well described. Hypotension is the major problem encountered. Several mechanisms have been proposed to account for this effect.⁶⁻⁸

Epidural anaesthesia has been used safely for management of pheochromocytoma.⁹⁻¹⁰ The technique permits a final assessment of sympathetic blockage prior to surgery. Deafferentation attenuates the rise in blood pressure that otherwise may accompany mechanical tumour manipulation. Respiratory depression may be avoided and postoperative analgesia may be administered.

The following case report describes the perioperative management of a patient with a malignant pheochromocytoma who was to undergo an orthopaedic procedure which would include excision of tumour and the application of methylmethacrylate. Epidural anaesthesia was the technique selected for management of the case.

Case report

A 39-year-old male known to have a malignant pheochromocytoma was admitted to hospital with a

From the Department of Anaesthesia, Ottawa Civic Hospital and University of Ottawa.

Address correspondence to: Dr. James A. Robblee, Department of Anaesthesia, Ottawa Civic Hospital, 1053 Carling Avenue, Ottawa, Ontario, K1Y 4E9.

TABLE Perioperative haemodynamic measurement

<i>Time/event</i>	<i>BP</i> <i>torr</i>	<i>CVP</i> <i>torr</i>	<i>PCWP</i> <i>torr</i>	<i>C.O.</i> <i>l·min⁻¹</i>	<i>SVR</i> <i>Dynes·sec·cm⁻⁵</i>
12 hours preoperative	102/52	8	11	11.8	413
Following 650 cc saline	105/60	8	12	13.3	378
Pre-induction	92/36	10	11	11.3	316
Post-epidural	104/42	12	14	11.5	355
Skin incision	100/48	10	12	10.9	404
*Tumour manipulation	101/47	10	7	10.4	500
†Sudden blood loss	70/40	6	8	9.2	382
2 minutes following methylmethacrylate	105/55	4	7	10.1	538
‡5 minutes following methylmethacrylate	108/52	4	9	10.6	552
End of procedure	110/52	8	10	10.4	487
Day 1 postop	124/74	7	12	14.2	473
Following epidural morphine	109/65	8	14	14.9	387

*1 unit packed cells.

†1 unit packed cells.

‡2 units packed cells.

metastatic lesion in the left femur. Because of the extent and location of the lesion, prophylactic internal fixation using methylmethacrylate and an intramedullary rod was proposed to prevent pathological fracture at the site of the lesion.

The patient had presented three years prior to admission with a T-6 paraparesis caused by spinal cord compression. Emergency surgical decompression of the spinal cord and stabilization of the spinal column was undertaken. Clinical suspicion of pheochromocytoma was aroused because of uncontrollable hypertension during the procedure. Tumour excised from the thoracic spinal cord was found to be histologically consistent with a pheochromocytoma. Metastases were demonstrated to be present in the skull, ribs, cervical spine and pelvis. Cardiovascular effects of the pheochromocytoma were controlled initially with phenoxybenzamine.

In the interval between diagnosis and the current admission, a number of complications ensued. These included sustained severe hypertension, high output congestive heart failure, arm and leg weakness, atony of the bowel and bladder, and bone pain from multiple metastatic sites. Adjustments to the medication regime were made at regular intervals. Prior to the present admission, the patient was receiving prazosin 2 mg q.i.d., propranolol 10 mg q.i.d., digoxin 0.125 mg o.d., phenoxybenzamine 10 mg t.i.d., potassium supplements, pentazocine and laxatives.

At the time of admission, the patient was in congestive heart failure. Blood pressure was consistently elevated to 180/110 torr. A persistent resting tachycardia of 120/min was noted. Haemoglobin and electrolytes were normal. Chest x-ray revealed the presence of several metastatic lesions. Efforts were undertaken to stabilize the patient prior to surgery. Propranolol dosage was increased to 30 mg q.6.h. The phenoxybenzamine dose was increased to 50 mg/day in divided doses. Cardiovascular status was unchanged by these initial measures. Consequently, the patient was started on a tyrosine hydroxylase inhibitor, metyrosine which was administered in a dosage of 500 mg q.i.d. Furosemide 40 mg o.d. was started at the same time as the metyrosine. These measures produced a gradual reduction in blood pressure to 130/80 torr and heart rate to 80/min. He was in suitable condition for anaesthesia and surgery by the tenth day following admission.

The patient was admitted to the intensive care unit on the day prior to surgery for insertion of a Swan-Ganz catheter and an arterial catheter. Haemodynamic parameters were recorded in order to establish a base line. A fluid challenge of 650 mL normal saline was administered to assess possible effects that might ensue when filling pressures were elevated prior to application of methylmethacrylate (Table). Ringers Lactate 100 cc/hr was then administered overnight.

On the morning of surgery, the patient received his regular oral medications. He was premedicated with lorazepam 4 mg p.o. An epidural catheter was inserted in the intensive care unit and haemodynamic parameters were measured (Table). Upon arrival in the operating room, bupivacaine 0.5 per cent was administered until a T-8 blockade was achieved. Bupivacaine 0.5 per cent was added as required throughout the procedure. The initial dose was 14 cc and total dose, 19 cc. Diazepam was administered to maintain moderate sedation. The total dose of diazepam throughout the procedure was 7.5 mg. Haemodynamic measurements were made at various critical times throughout the procedure (Table). On manipulation of the tumour, no changes occurred in the haemodynamic status. In anticipation of the application of methylmethacrylate, a unit of packed red blood cells and 500 cc of Ringers Lactate were administered. Twelve hundred cc of blood loss suddenly occurred from the tumour site. An additional unit of packed red blood cells and 1000 cc of Ringers Lactate were administered. Because of the unexpectedly profuse bleeding and the greater than expected extent of the tumour, the incompletely excised metastatic site was packed with methylmethacrylate in an effort to control haemorrhage and to provide stability to the shaft of the femur. Insertion of an intramedullary rod was considered to be dangerous. The sudden blood loss produced a transient drop in blood pressure to 70/40 torr. Packing the tumour site with methylmethacrylate produced no further drop in blood pressure. Within two minutes of the application of cement, stabilization of haemodynamic parameters had occurred. Two additional units of packed red blood cells were transfused during the balance of the procedure. Total blood loss was estimated to be 2000 cc. Four units of packed red blood cells were transfused and 2200 mL of Ringers Lactate were administered. The patient was transferred to the intensive care unit in satisfactory condition.

On the first day following surgery, morphine 10 mg was administered through the epidural catheter for relief of pain. The patient was continued on epidural morphine in a pain-free state until discharge from the intensive care unit on the third postoperative day. Radiation was applied to the femur on the sixth postoperative day. He was allowed to ambulate on the eighth day following surgery, and was discharged on the eleventh day.

Discussion

Pheochromocytoma is a rare tumour, occurring in approximately two in 100,000 of the population and in 0.1 per cent of adult hypertensive patients. The tumour can be detected with accuracy because of its release of potent biogenic amines. The perioperative management of these patients is well established in the literature, and has improved in the past decade.¹ Improvement has occurred because of the development of new drugs to attenuate the effects of catecholamines. Intraoperative techniques have changed. New halogenated agents sensitize the myocardium to the effects of catecholamines to a lesser extent than does halothane, when general anaesthesia is selected.⁹⁻¹⁰ Epidural management has also been used successfully.¹¹⁻¹² Improved haemodynamic monitoring is possible through the use of the Swan-Ganz catheter.

Two major challenges were illustrated by this case. The first was the preoperative management of sustained, uncontrolled hypertension and congestive heart failure. The second challenge was the anticipation of significant haemodynamic alterations induced by the use of methylmethacrylate during the procedure.

Phenoxybenzamine alone was insufficient to control this patient's hypertension. Both prazosin and metyrosine were added to control blood pressure. Prazosin is a specific alpha-1 adrenergic blocking agent and acts to block norepinephrine receptor sites on the effector cell. This is a pharmacological advantage over a drug such as phenoxybenzamine which blocks both alpha-1 and alpha-2 receptors. Alpha-2 receptor stimulation normally inhibits presynaptic norepinephrine release.³

Metyrosine is a new agent available for treatment of patients with pheochromocytoma. It controls the rate-limiting step of catecholamine production by inhibiting tyrosine hydroxylase which catalyzes the conversion of tyrosine to dihydroxyphenylalanine (DOPA). This blockade results in decreased endogenous levels of catecholamines. Metyrosine is indicated in patients who are refractory to phenoxybenzamine therapy or those in whom beta-adrenergic blockade is contraindicated.⁴ An important side effect of metyrosine is sedation but this was not a problem in our patient.

The combination of drugs resulted in a sustained normal blood pressure and heart rate prior to surgery. Congestive heart failure was controlled.

The latter was demonstrated clinically and confirmed by haemodynamic monitoring. The patient had a normal left ventricular end diastolic pressure and the systemic vascular resistance was low. The cardiac output was 2 to 2.5 times normal. This high output state was thought to be due to two major factors. Circulating catecholamines continued to be elevated and produced a persisting effect. In addition, the low systemic vascular resistance achieved by pharmacological intervention resulted in a compensatory rise in cardiac output. Unfortunately, haemodynamic indices were not obtained prior to the onset of medical therapy.

In a report on the use of methylmethacrylate in a patient with a malignant pheochromocytoma, no mention was made of the haemodynamic changes that occurred, nor was the anaesthetic management described. The general effects of methylmethacrylate have been extensively reported, but controversy still remains about the mechanism of hypotension. Hypotension secondary to peripheral vasodilation caused by the monomer has been documented.⁸ A dose dependent depression of left ventricular dp/dt correlating with depression of heart rate has been demonstrated in experimental animals.¹³ Decreases in arterial oxygen tension (PaO_2) and increased shunt (QS/QT) also occur with acrylic cement insertion.⁶ Vascular hypotension resulting from bone marrow embolism has been described in patients undergoing hip prosthesis surgery.⁷

In anticipation of these factors, the choice of an epidural anaesthetic confirmed the adequacy of preoperative vasodilator therapy. Extensive sympathetic blockade and deafferentation was achieved. Respiratory complications in a patient with pulmonary metastases were avoided. Tumour manipulation which would have been expected to release catecholamines, caused neither hypertension nor cardiac dysrhythmias. Introduction of methylmethacrylate into the tumour site occurred at a time of sudden massive blood loss and did not result in increased hypotension. The patient's condition was rapidly stabilized with blood and fluid infusion.

Adequate preoperative preparation of patients with pheochromocytoma is still the mainstay of anaesthetic management. The use of prazosin and metyrosine are important advances in control of the difficult or refractory patient. Many anaesthetic techniques have been proposed to minimize intraoperative cardiovascular complications. No

technique satisfies all possible criticism. Epidural management produced stable anaesthesia and adequate surgical conditions in this patient. Hypotension, which occurred in our case because of sudden blood loss, was not worsened by the application of methylmethacrylate. Epidural morphine administered in the postoperative period resulted in a pain-free patient who was able to tolerate early ambulation.

References

- 1 *Pratila V, Pratila MG.* Management of pheochromocytoma. *Can Anaesth Soc J* 1979; 26: 253-9.
- 2 *Van Heerden JA, Sheps SG, Hamberger B, Sheedy II, PF, Poston JG, ReMine WH.* Pheochromocytoma: current status and changing trends. *Surgery* 1982; 91: 367-73.
- 3 *Cubbedu LX, Zarate NA, Rosales CB, Zschaek DW.* Prazosin and propranolol in preoperative management of pheochromocytoma. *Clin Pharmacol Ther* 1982; 32: 156-60.
- 4 *Lapierre G.* Evaluation of metyrosine. *Can J Hosp Pharmacy* 1982; 35: 132-4.
- 5 *Mickelson MR, Bonfiglio M.* Resection and Zickel device fixation for metastatic tumor. *Clin Orthop* 1982; 164: 261-4.
- 6 *Turnbull KW, Berezowsky JL, Poulsen JB, Roots LS.* General anaesthesia and total hip replacement. *Can Anaesth Soc J* 1974; 21: 546-56.
- 7 *Breed AL.* Experimental production of vascular hypotension, and bone marrow and fat embolism with methylmethacrylate cement. *Clin Orthop* 1974; 102: 227-44.
- 8 *Wong KC, Martin WE, Kennedy WF, Akamatsh TJ, Convery RF, Shaw CL.* Cardiovascular effects of total hip replacement in man with observations on the effects of methylmethacrylate on the isolated rabbit heart. *Clin Pharmacol Ther* 1977; 21: 709-14.
- 9 *Desmonts JM, LeHouelleur J, Remond P, Duvaldestin P.* Anaesthetic management of patients with pheochromocytoma. *Br J Anaesth* 1977; 49: 991-7.
- 10 *Conner JT, Miller JD, Katz R.* Isoflurane anaesthesia for pheochromocytoma - a case report. *Anesth Analg* 1975; 54: 419-21.
- 11 *Bromage PR, Millar RA.* Epidural blockade and circulating catecholamine levels in a child with pheochromocytoma. *Can Anaesth Soc J*; 5: 282-7.
- 12 *Cousins MJ, Rubin RB.* The intra-operative management of pheochromocytoma with total epidural sympathetic blockade. *Br J Anaesth* 1974; 46: 78.

- 13 Peebles DJ, Ellis RH, Stride SDK, Simpson BRJ.
Cardiovascular effects of methylmethacrylate cement. Br Med J 1972; 1: 349-51.

Résumé

Un compte-rendu est présenté d'un patient atteint de phéochromocytome malin devant subir une procédure orthopédique utilisant le méthylméthacrylate. La préparation pré-opératoire du patient a compris l'utilisation de la prozosin et de la métyrosine. Le bloc épidural a été choisi comme technique anesthésique pour la conduite per-opératoire de ce cas. La fixation chirurgicale avec le méthylméthacrylate n'a pas produit d'hypotension prolongée ou profonde malgré une perte sanguine massive et soudaine précédant son utilisation. L'administration de morphine par voie épidurale a été utilisée pour le contrôle de la douleur dans la période post-opératoire.