Clinical Reports

Recognition of an unsuspected phaeochromocytoma during elective coronary artery bypass surgery

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A patient with a longstanding history of mild hypertension undergoing elective coronary artery bypass grafting exhibited extreme and paroxysmal elevations of systemic blood pressure immediately after separation from cardiopulmonary bypass. Conventional antihypertensive therapy (nitroprusside, hydralazine, propranolol) was ineffective, whereas phentolamine infusion produced a decrease in systemic blood pressure. These observations led to the discovery of a predominantly norepinephrine-secreting phaeochromocytoma. This case is noteworthy in that cardiopulmonary bypass may have served as a stimulus for tumour secretion of catecholamine. Possible mechanisms for this effect are discussed.

Key words
SURGERY: phaeochromocytoma, cardiovascular, cardiopulmonary bypass; ANAESTHETIC, INTRAVENOUS: fentanyl.

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The presence of an unsuspected phaeochromocytoma in a patient undergoing elective coronary artery bypass grafting provides an unusual challenge for the anaesthetist. We report our detection and management of a phaeochromocytoma in an unprepared patient.

Case report

A 65-year-old male with recent onset of rest angina was scheduled for elective coronary artery bypass grafting. He had an eight-year history of mild essential hypertension, treated only with beta-blockade. He had sustained two uncomplicated myocardial infarctions, eight and seven years prior to admission. His medications included metoprolol 25 mg BID, sulfinpyrazine, ASA, and sublingual nitroglycerin. Angiography revealed 80–90 per cent proximal obstruction of all three major coronary arteries and an ejection fraction of 0.80.

Examination revealed a 72 kg male with a blood pressure of 150/90 mmHg and a heart rate of 60 beats·min^{-1}. Physical examination was unremarkable. The electrocardiogram showed sinus rhythm, evidence of an old infero-posterior infarction, and voltage criteria consistent with left ventricular hypertrophy. The chest *x*-ray, serum electrolytes, blood urea nitrogen, and creatinine were all normal. The haematocrit was 40 per cent. The fasting blood glucose was mildly elevated to 200 mg·dl^{-1} (normal 80 to 120).

The patient was premedicated with morphine 10 mg IM, scopolamine 0.4 mg IM, and metoprolol

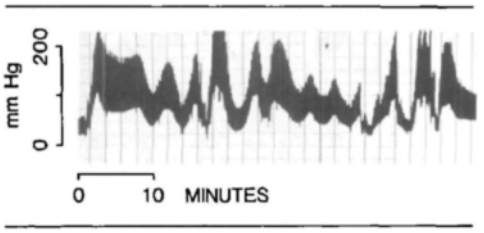

FIGURE Strip-chart recording showing frequent, paroxysmal elevations of systemic blood pressure appearing 2–3 minutes after separation from cardiopulmonry bypass.

25 mg PO. Prior to induction, the central venous pressure was found to be 0 mmHg, and one litre of lactated Ringer's solution was rapidly infused. After fluid administration, the central venous pressure was 2 mmHg. The blood pressure was 160/60 mmHg, with a mean arterial pressure (MAP) of 93 mmHg. Induction was accomplished with 10 mg diazepam, 1500 μg fentanyl, 1 mg propranolol and 10 mg pancuronium. During tracheal intubation, the MAP transiently rose to a peak of 150 mmHg while the heart rate remained stable at 60 beats·min^{-1}. With the addition of 500 μg fentanyl, 0.5 per cent enflurane, and 1–2 μg·kg^{-1}·min^{-1} nitroprusside, the MAP was maintained in the range of 80–100 mmHg until separation from cardiopulmonary bypass.

Immediately after separation from bypass, the MAP rose above 100 mmHg with frequent systolic peaks in excess of 200 mmHg (Figure). Enflurane was increased from 0.5 to 1.0 per cent, and nitroprusside was increased from 1–2 μg·kg^{-1}·min^{-1} to 5–10 μg·kg^{-1}·min^{-1}. Anaesthesia was supplemented with fentanyl 500 μg, morphine 20 mg, diazepam 35 mg, and droperidol 10 mg. Additional therapy for hypertension included hydralazine (70 mg) and propranolol (17 mg). Because of the extreme and refractory nature of the hypertension, the presence of a phaeochromocytoma was suspected and phentolamine was administered as a 5 mg bolus, followed by an infusion of 1–5 μg·kg^{-1}·min^{-1}. The addition of phentolamine resulted in a decrease in MAP to approximately 80 mmHg, although frequent peaks to 100–110 mmHg were still observed. Throughout this period, the heart rate was 80–100 beats·min^{-1}. Nine liters of lactated Ringer's solution and four units of whole blood were infused to maintain the central venous pressure in the range of 3–10 mmHg. The urine output ranged from 200–300 ml·hr^{-1}. Arterial blood gas values remained within the normal range. The haematocrit was 34 per cent at the completion of surgery.

Upon arrival in the intensive care unit, the MAP was 90 mmHg and the heart rate was 100 beats·min^{-1}. Because of the unusual intraoperative requirements for fluids and vasodilators, a pulmonary artery catheter was inserted. Initial measurements revealed: central venous pressure 6 mmHg, pulmonary artery pressure 20/10 mmHg, wedge pressure 10 mmHg, and cardiac index 3.5 L·min^{-1}·m^{-2}. With a constant infusion of phentolamine at a rate of 1–4 μg·kg^{-1}·min^{-1} the MAP remained below 90 mmHg for the first four hours. Shortly thereafter, a sudden increase in MAP to 120 mmHg was followed by brisk output of blood through the chest tubes. Coagulation studies did not suggest the presence of a coagulopathy. The patient was returned to the operating room where exploration revealed diffuse oozing from the sternum and serosal surfaces. No significant bleeding was observed from the anastomoses or cannulation sites.

Paroxysms of hypertension persisted for the next two days, despite the use of nitroprusside, phentolamine, hydralazine, trimethaphan, and alpha-methyldopa in various combinations. Transient supraventricular tachyarrhythmias occurred, and were treated with procainamide. Beginning with the third postoperative day, the blood pressure gradually declined to normal range and the infusion of vasodilators was discontinued.

Plasma and urinary catecholamine studies performed on the fifth postoperative day revealed marked elevations above the normal range (Table). An abdominal CT scan showed a 3 × 7 cm mass overlying the abdominal aorta at the origin of the superior mesenteric artery. Based upon these findings, treatment with oral phenoxybenzamine was begun at 10 mg/day and advanced to 60 mg/day. Mild postural hypotension was observed, but no further paroxysms of hypertension were noted. Vigorous hydration was maintained.

One month after the bypass surgery, an exploratory laparotomy was performed. The patient was induced with thiopentone and anaesthesia was maintained with 50 per cent nitrous oxide and 0.5–1.5 per cent isoflurane in oxygen. Vecuronium was used for muscle relaxation. An infusion of nitroprusside was required during surgical manipu-

TABLE Postoperative plasma and urinary catecholamines

Assay		*Normal range*	*Patient**
Epinephrine	(plasma)	0–70 pg·ml^{-1}	675
Norepinephrine	(plasma)	100–400 pg·ml^{-1}	14,575
Metanephrine	(urine)	0.3–0.9 mg/24 hr	32.2
Vanillylmandelic acid	(urine)	2–8 mg/24 hr	34

*Blood and 24-hr urine specimens were obtained on postoperative day 5.

lation of the tumour when the MAP rose to 130 mmHg, but the intraoperative course was otherwise uneventful. Surgical exploration revealed an invasive, nonresectable phaeochromocytoma at the origins of the superior mesenteric and adrenal arteries. Because the patient was not considered an appropriate candidate for radiation therapy or chemotherapy, chronic treatment was initiated with oral metrisone (an inhibitor of tyrosine oxidase). To date, blood pressure and symptoms have been successfully controlled with this drug.

Discussion

Phaeochromocytoma is a rare catecholamine-secreting tumour which is found in about one of 1000 routine autopsies and accounts for approximately 0.1 per cent of all cases of hypertension in the general population.[1] This tumour arises from neuroectodermal tissue and is usually found in the adrenal glands. Phaeochromocytomas can secrete both norepinephrine and epinephrine. When secretion of epinephrine predominates, symptoms of intense beta-adrenergic stimulation (tremor, nervousness, anxiety, pallor) may be present. When secretion of norepinephrine predominates, symptoms may be less dramatic and the overall clinical picture can mimic essential hypertension. An important clue to the presence of phaeochromocytoma is a history of paroxysmal headache, sweating, or palpitations. Hyperglycaemia is an associated finding in about 25 per cent of cases. The basic principles of diagnosis and management of patients with phaeochromocytoma have recently been reviewed by Bravo and Gifford.[2]

Surgery in the setting of an unsuspected phaeochromocytoma carries a poor prognosis. In a survey reported by Apgar[3] in 1951, approximately 50 per cent of patients with unsuspected phaeochromocytoma died during the early postoperative period. In another early series published by Scott *et al.*,[4] three of 11 patients with unsuspected tumours died in the postoperative period. The mode of death in most of these cases was cardiovascular collapse, attributable at least in part to hypovolemia. Other complicating factors included myocardial infarction, adrenal failure, acidosis, and cerebrovascular accidents. Several recent reports,[5–7] have emphasized the importance of severe cardiovascular instability as a clue to perioperative recognition of phaeochromocytoma. These reports also suggest that prompt termination of surgery and transfer to an intensive care unit for postoperative management may improve survival in patients with previously undiagnosed phaeochromocytomas.

Our case appears to be the first report of the use of high-dose fentanyl in an unprepared phaeochromocytoma patient undergoing cardiac surgery. Coronary artery bypass surgery in an unprepared patient has previously been reported,[8] but the diagnosis was not suspected until persistent hypertension was noted in the postoperative period and the details of the anaesthetic were not described. A possible advantage of high-dose fentanyl in the setting of phaeochromocytoma is the alpha-blocking effect that this drug produces in vascular smooth muscle.[9] Masuda *et al.* have reported the successful use of high-dose fentanyl for phaeochromocytoma resection in a previously diagnosed patient.[10]

A basic principle in the management of patients with phaeochromocytoma is that beta-blocking drugs should not be administered until alpha-blockade has been established.[1] The rationale for this principle is that beta-mediated vasodilation may attenuate the degree of hypertension produced by catecholamine release. If beta-mediated vasodilation is blocked, then the unopposed vasoconstriction produced by alpha-receptor stimulation may result in extreme elevations of the blood pressure. Our patient had been treated with metoprolol as an outpatient, and he also received propranolol during surgery. As soon as a diagnosis of unsuspected phaeochromocytoma was entertained, the intra-

operative use of propranolol was discontinued. It is interesting to note, however, that the pressor response to beta-blockade seems to depend upon the presence of epinephrine rather than norepinephrine.[11,12] The fact that our patient had a predominantly norepinephrine-secreting tumour may have fortuitously minimized the effects of preoperative and intraoperative beta-blockade.

The intraoperative use of phentolamine may have had a favourable bearing on outcome by permitting prompt and aggressive restoration of intravascular volume and perhaps by attenuating the potentially toxic effects of excess catecholamines on the heart.[13,14] The provisional intraoperative diagnosis of phaeochromocytoma also provided an impetus for postoperative investigation. This case thus illustrates the potential importance of the anaesthetist in the perioperative diagnosis and management of unsuspected phaeochromocytoma.

A curious feature of this case was that severe and paroxysmal hypertension began only after separation from bypass. Prior to separation from bypass, there was a single episode of marked hypetension during tracheal intubation. After bypass, however, the patient exhibited frequent episodes of severe hypertension that were not specifically related to noxious physical stimuli. Some of these episodes may have been related to drug effects. Droperidol, for example, was administered to our patient shortly after separation from bypass. Although this drug has been successfully used in patients with phaeochromocytoma,[15,16] Sumikawa and Amakata[17] reported one individual who exhibited acute and reproducible hypertension after intravenous administration of droperidol. Our patient also received morphine after bypass, and histamine release induced by this narcotic may have served as another stimulus for secretion of catecholamine by the tumour.[18] Finally, our patient received a large dose of propranolol prior to therapy with phenoxybenzamine. As previously discussed, the pressor response to catecholamine release may have been accentuated by giving a beta-blocking drug in advance of adequate alpha-blockade.

In addition to drug effects, cardiopulmonary bypass itself may have contributed to the severity of hypertension after bypass. Although high-dose fentanyl anaesthesia attenuates catecholamine and hormone release during induction of anaesthesia and surgical stimulation prior to cardiopulmonary bypass, large increases in catecholamines and hormones do occur during bypass.[19,20] These increases may have enhanced tumour secretion in the post-bypass period. Another stimulus for tumour secretion is exposure to cold.[21] The decrease in body temperature that was induced during cardiopulmonary bypass may have served as an equivalent stimulus.

In summary, a patient with unsuspected phaeochromocytoma survived elective coronary artery bypass grafting. The ultimate favourable outcome may be related to intraoperative suspicion of this tumour and initiation of appropriate therapy.

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Résumé

Un patient présentant une histoire d'hypertension modérée chronique devant subir un pontage aortocoronarien électif a présenté des élévations extrêmes de la tension artérielle immédiatement après la cessation de la CEC. Le traitement antihypertenseur conventionnel (nitroprussiate, hydralasine, propranolol) était inefficace, alors que la phentolamine en perfusion a produit une diminution de la tension artérielle systémique. Ces observations ont conduit à la découverte d'un phéochromocytome secrétant la norépinephrine. Ce cas est intéressant car la CEC peut avoir déclenché la sécrétion de catécholamine par la tumeur. Les mécanismes possibles de cet effet sont discutés.