Combined surgery for coronary artery disease and pheochromocytoma

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Purpose: To report a case of severe coronary artery disease complicating pheochromocytoma, managed with combined coronary artery bypass grafting (CABG) and adrenalectomy.

Clinical features: A 55-yr-old woman presented with poorly controlled hypertension and investigation revealed an active pheochromocytoma of her left adrenal gland. During medical preparation for adrenalectomy, she developed an acute myocardial infarct complicated with unstable angina. This required urgent CABG, and combined surgery for the triple vessels coronary artery disease and the pheochromocytoma was planned. We explain the details of medical preparation before surgery and the anesthetic considerations during the surgical procedure. Postoperative recovery was normal and no complication occurred. Even if the pheochromocytoma was malignant, her urinary catecholamines two months after the surgery were normal and remain normal after more than two years of follow-up.

Conclusion: We report a patient who underwent combined CABG and adrenalectomy for pheochromocytoma. The CABG was done first, followed by the adrenalectomy with invasive monitoring. The procedure was well tolerated with cure of the two underlying conditions. So we propose that combined procedure should be considered in this clinical setting.

Objectif : Citer un cas de phéochromocytome compliqué d'une cardiopathie ischémique, traité par un pontage aortocoronarien combiné à une surrénalectomie.

Éléments cliniques : L'examen d'une femme de 55 ans souffrant d'hypertension difficilement contrôlée a révélé un phéochromocytome actif de la glande surrénale gauche. Pendant la préparation médicale à la surrénalectomie, elle a subi un infarctus myocardique aigu accompagné d'angine instable qui exigeait donc un pontage aortocoronarien d'urgence. On a alors planifié une intervention combinée pour les trois vaisseaux touchés par la cardiopathie ischémique et pour le phéochromocytome. Nous avons expliqué les détails de la préparation médicale avant l'opération et les aspects anesthésiques de l'intervention. La récupération postopératoire a été normale et sans complication. Malgré un phéochromocytome malin, les catécholamines urinaires étaient normales deux mois après l'opération et sont demeurées telles après plus de deux ans de suivi.

Conclusion : Nous avons cité le cas d'une patiente qui a subi un pontage aortocoronarien combiné à une surrénalectomie pour l'ablation d'un phéochromocytome. Le pontage a été fait d'abord suivi par la surrénalectomie soutenue par un monitorage effractif. L'intervention, bien tolérée, a été suivie d'une guérison des deux conditions qui l'ont commandée. Nous suggérons que soit envisagée une intervention combinée dans ces circonstances.

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CONCOMITANT coronary artery disease (CAD) and pheochromocytoma are rare but may coexist since pheochromocytoma is associated with many risk factors of atherosclerosis. Pheochromocytomas are tumours which cause hypertension, glucose intolerance, dyslipidemia and enhanced coagulation.[1,2] Catecholamines can also damage the vasa-vasorum of small arteries inducing irreversible lesions of the intima. All these factors contribute to the development of CAD. A study of 40,078 autopsies at the Mayo clinic over 49 yr found 54 cases of undiagnosed pheochromocytoma, of which 11 patients (27%) had myocardial necrosis.[3]

The dramatic consequences of a hypertensive crisis caused by an uncovered pheochromocytoma during open-heart surgery are well known.[4–6] However, the management of a patient with both advanced CAD requiring coronary artery bypass grafting (CABG) and clinically active pheochromocytoma is challenging and not well established. One approach is to perform the adrenalectomy followed by the CABG a few days or weeks later.[7–8] In a case with more severe coronary artery disease, the CABG was done first and the adrenalectomy, six weeks later.[9] In this report, we describe a case of pheochromocytoma complicated by severe coronary artery disease and managed with simultaneous CABG and adrenalectomy.

Case Report

A 55-yr-old Caucasian woman presented with a history of hypertension complicated by an episode of malignant hypertension. She was also known for dyslipidemia and CAD with a myocardial infarct 13 yr ago. Several times a week she suffered episodes of trembling, palpitations and profuse sweating. She also noticed a weight loss of 13 kg in one year. At the time of admission, she weighed 45 kg, had a blood pressure (BP) of 190/100 mmHg and her ophthalmoscopic examination showed grade 3/4 hypertensive retinopathy. Her laboratory results showed anemia (Hb 100 $g \cdot L^{-1}$), normal electrolytes and serum creatinine, a normal phosphocalcic profile, a very high total cholesterol (7.89 $mmol \cdot L^{-1}$), and LDL-C (5.22 $mmol \cdot L^{-1}$), and high serum triglycerides (3.72 $mmol \cdot L^{-1}$).

Investigation revealed very high levels of urinary catecholamines (Table). Computed tomography showed a solid, nodular mass of 4.1 by 2.8 cm of her left adrenal gland, without extra-adrenal involvement (Figure 1). The meta-iodobenzylguanidine (^{131}I MIBG) scan was negative for any abnormal uptake. An echocardiogram showed the presence of concentric left ventricular hypertrophy with well preserved systolic function.

Thus, we planed an adrenalectomy and started 10 mg phenoxybenzamine *po* twice daily to achieve adequate α-blockade and optimal hydratation prior to surgery. The patient was also receiving 150 mg hydralazine and 5 mg quinapril per day. Phenoxybenzamine was progressively increased over five days, up to 20 mg three times daily, to achieve good BP control without orthostatic hypotension.

On the 6th day of phenoxybenzamine treatment, despite normal BP and heart rate, the patient presented an acute inferior and anterior myocardial infarct. Thrombolysis with rTPA was initiated and led to reperfusion with an increase in CPK levels. Metoprolol was added to the medication, and the usual post-infarct care was given. A few days later, the patient had recurrent angina, and cardiac catheterization showed severe triple-vessel disease: occlusion of the right and left anterior descending coronary arteries and severe stenosis of the circumflex artery. The post-infarct echocardiogram revealed akinesia of the septum and moderate hypokinesia of the anterior wall, LV ejection fraction was approximately 35%, and a septo-apical thrombus was found. Aggressive treatment for heart failure was instituted and phenoxybenzamine was reduced to 10 mg twice daily. Anticoagulation with intravenous heparin was started.

The cardiac condition of the patient required urgent CABG but we were concerned about the high risk of complications associated with an unresected pheochromocytoma during and after such surgery. So, we decided to perform combined surgery with adrenalectomy immediately following CABG. Two weeks before the surgery, we progressively resumed the phenoxybenzamine to 20 mg every eight hours and we weaned the diuretic to assure maximal α-blockade and optimal hydration. The patient already had adequate ß-blockade with 100 mg metoprolol per day. At that time, the other anti-hypertensive medications were 75 mg hydralazine and 20 mg quinapril per day, which were given for her reduced cardiac performance.

The day before surgery, the ECG showed normal sinus rhythm at 80bpm with subacute anteroseptal infarct. The Hb was 100 $g \cdot L^{-1}$ and serum electrolytes and creatinine were normal. Heparin infusion was ceased four hours before surgery. On the day of surgery,

TABLE Preoperative 24 hr urinary catecholamines

Catecholamines	*Patient Value*	*Normal Range*
Norepinephrine	12,133 $\mu mol \cdot d^{-1}$	89-473
Dopamine	1,062 $\mu mol \cdot d^{-1}$	424-2,012
Vanillylmandelic acid	189.2 $\mu mol \cdot d^{-1}$	3.0-60.0

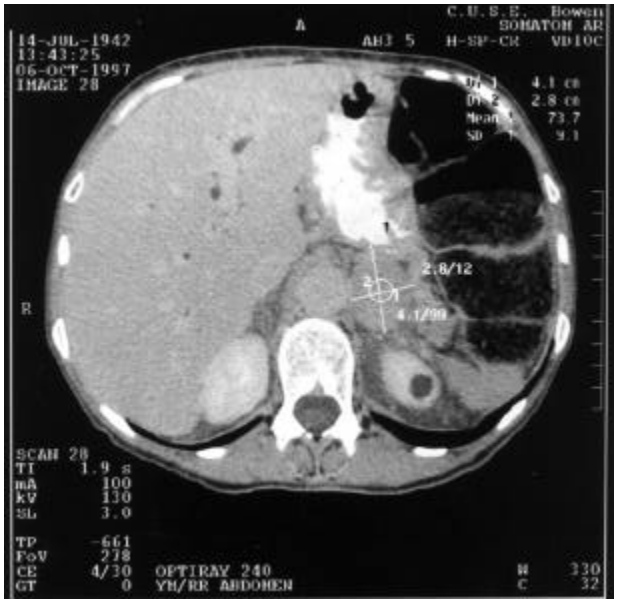

FIGURE 1 Abdominal computed tomography showing a well-defined nodular mass of the left adrenal gland. The mass measures 4.1 × 2.8 cm, shows solid density and doesn't spread.

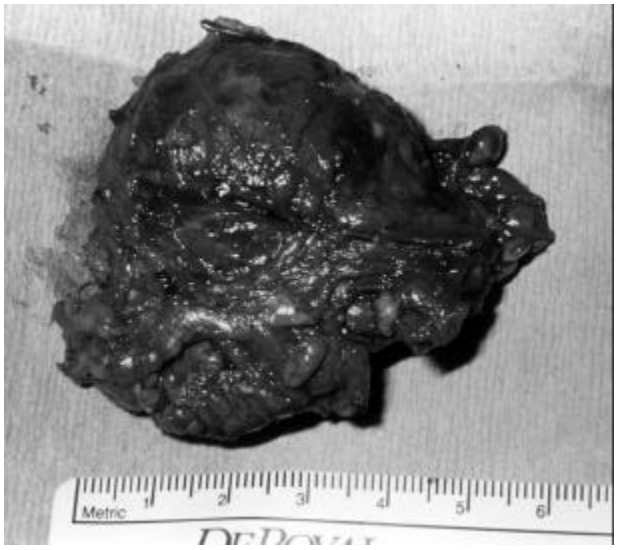

FIGURE 2 Macroscopic aspect of the left adrenal mass. The normal gland is replaced by a large tumour of 3.5 × 2.5 cm. There is no invasion of the surrounding tissue.

the patient received her usual antihypertensive medication and was premedicated with 0.15 mg·kg^{-1} diazepam and 0.15 mg·kg^{-1} morphine. After insertion of two large bore *iv* cannulas and right radial artery catheterization, anesthesia was induced with 5 μg·kg^{-1} sufentanil, 4 mg midazolam and 0.9 mg·kg^{-1} rocuronium. Her blood pressure decreased from 150/80 to 120/60 while her pulse diminished from 70 to 60 bpm. Insertion of the pulmonary artery catheter via the right jugular vein was uneventful. Central venous pressure (CVP) was 7 mmHg and the PCWP 14 mmHg. Indexed cardiac output was in normal range at 2,70 L·min^{-1}·m^{-2}. Systemic vascular resistance (SVR) was slightly above normal at 1400 dynes·sec^{-1}·cm^{-5}. Maintenance of anesthesia consisted of isoflurane 0.5% together with an infusion of 1 μg·kg^{-1}·hr^{-1} sufentanil, amnesic doses of midazolam and hourly boluses 2 mg doxacurium. Before CBP, she received a total of 1500 mL Lactate Ringer. To reduce preoperative bleeding, 20 mg·kg^{-1} tranexamic acid, an antifibrinolytic agent, were given before cardiopulmonary bypass (CPB).

The surgical procedure began with the CABG. Sternotomy, heart exposure and insertion of CPB cannulas were done without complication. However, during CPB, the patient needed 50 μg·min^{-1} neosynephrine and 5 μg·min^{-1} noradrenaline perfusions in order to maintain mean arterial blood pressure above 50 mmHg. Intermittent 10°C blood cardioplegia was given to achieve cardiac arrest during CPB and thereafter every 10 min during the 45 min of cross-clamp to perform the distal anastomosis. The left internal mammary artery was anastomosed to the left anterior descending artery and saphenous grafts were anastomosed to the first diagonal, the postero-lateral and right coronary arteries. After a "warm shot" of blood, the aorta was unclamped. The proximal anastomoses were performed with a partial aortic clamp. The patient was weaned from CPB after 80 min with 10 μg·min^{-1} adrenaline, 7 μg·min^{-1} noradrenaline and 20 μg·kg^{-1}·min^{-1} dopamine. These drugs were progressively withdrawn in the following hour. At that time, CVP was 12 mmHg, pulmonary artery pressure 36/14 mmHg, cardiac output 6.9 L·min^{-1}·m^{-2} and SVR 765 dynes·sec^{-1}·cm^{-5}. After decannulation of the CPB cannulas, the cannulating tourniquets were snared without being tied to permit an easy resumption of the CPB in case of extreme increase of blood pressure. 250 mg of protamine was then given slowly to reverse anticoagulation.

The second team of surgeons performed a left subcostal incision extending laterally. The inferior part of the pancreas was dissected and a voluminous vein draining the infero-medial aspect of the adrenal gland was found. The vein was suture-ligated without hemo-

dynamic change. The pheochromocytoma was easily removed. Throughout the adrenalectomy, the patient experienced no major change in blood pressure: mean arterial blood pressure was maintained around 70 mmHg.

General anesthesia lasted for six hours and five minutes and there was no excessive bleeding during the procedure. A total of 3.8 L of Ringer's lactate, two albumin units and four packed red blood cell units were given. The patient was then admitted to the recovery room in a stable hemodynamic state and transferred to the surgical intensive care unit. Because her SVR was low (585 dynes·sec^{-1}·cm^{-5}), she received neosynephrine (an average of 0.4 µg·kg^{-1}·min^{-1}) and low doses of adrenaline for the next 12 hr (an average of 6 µg·kg^{-1}·min^{-1}). Otherwise she maintained normal and stable pressure throughout the postoperative course. The trachea was extubated on the first postoperative day and she was released from the intensive care unit on day three. Her subsequent recovery was similar to the usual post-CABG evolution, except for a brief ileus.

Macroscopic examination of the mass revealed a 3.5 × 2.5 cm tumour (Figure 2), well delimited and encapsulated, originating from the adrenal gland. Microscopic examination showed that the tumour infiltrated locally the capsule, the adrenal cortex and the surrounding fat tissue. The tissue removed from the kidney hilus contained two infiltrated lymph nodes. Immunohistochemical binding of the tumour and lymph nodes was intense for chromogranine and moderate for synaptophysine in many cells. Thus, the final diagnosis was malignant pheochromocytoma with metastases to regional lymph nodes.

The patient was discharged from the hospital on postoperative day eight. Two months after surgery, her urinary catecholamines were normal and remain so after more then two years of follow-up.

Discussion

Patients with severe CAD requiring CABG and an actively secreting pheochromocytoma are challenging to the physicians in charge of them because they have to manage two conditions at risk for poor surgical outcome. Undiagnosed pheochromocytoma can cause extreme paroxysmal changes of blood pressure, malignant dysrhythmias, pulmonary edema, and shock during open heart surgery,[4–6] and carries a high mortality rate. The risk of severe hypertension after surgery is also a major concern because it submits the bypass anastomosis to intense shearing stress. On the other hand, adrenalectomy in a patient with severe coronary artery disease is associated with greater risk of adverse cardiac events by itself, and this risk is largely increased by the swings in blood pressure frequently seen during removal of pheochromocytoma.

There are few reports of the management of patients with both severe CAD and pheochromocytoma. Vacheron *et al.*[7] presented such a case and proposed the pheochromocytoma be removed first and then investigation of CAD should be considered and may lead to CABG. However, although the outcome of their patient was good, she did not have severe CAD (only the anterior descending coronary artery was affected) and she was not subjected to a recent infarct. Another group[9] reported the case of a man with severe CAD, but without recent infarct, and bilateral adrenal pheochromocytomas managed by CABG under thoracic epidural analgesia, followed by bilateral adrenalectomy six weeks later.

Our patient was more at risk of cardiac complication during and after adrenalectomy than previously published cases. She had triple vessel disease complicated by unstable angina following a recent myocardial infarct. According to the score of Detsky *et al.*,[10] unstable angina associated with recent myocardial infarct implies a risk ratio of 4.1 for peri-operative cardiac events, compared with 1.1 in unstable angina alone. Furthermore, the risk of a cardiac event after an adrenalectomy is probably higher for a pheochromocytoma than for other adrenal lesions.[1,2] This emphasizes the high risk of cardiac event or mortality if the adrenalectomy is planned before the CABG, in such cases.

Because of these risks, we were forced into doing the CABG before the adrenalectomy. We could have done the CABG under thoracic epidural analgesia as described in 1991 by Liem *et al.*,[9] but we decided to perform the adrenalectomy during the same procedure as the CABG. There are only two other case-reports, published by two different groups in 1995,[8,11] where CABG and adrenalectomy for a pheochromocytoma were combined in the same procedure. Each case was found to have triple vessels CAD and pheochromocytoma, but had no recent myocardial infarct. Surgeries were well tolerated, without perioperative adverse events. The good outcome of these two cases and the normal postoperative evolution of our patient with recent myocardial infarct and triple vessels CAD show that combined surgery is feasible, even in very high risk patients.

The patient must be well prepared with α- and ß-blockade, optimal hydration, invasive monitoring and CPB. In order to prevent hemodynamic instability during anesthesia, maintenance drugs known for their lack of histaminoliberation and minimal cardiovascular effects should be used: sufentanil, amnesic dose of midazolam and doxacurium, with small concentration

of isoflurane. Hemodynamic instability during certain phases of anesthesia and surgery may be expected. So, the anesthesiologist must be prepared with stand by solutions of vasodilatators (nitroglycerine and nitroprusside) and direct-acting catecholamines (adrenaline, noradrenaline and neosynephrine). Indirect catecholamines such as ephedrine are not recommended because of the unpredictable response that patients with pheochromocytoma may have. This response is caused by release of catecholamines from nerve endings that are loaded by the reuptake process.[12] We were also concerned by the possible release of catecholamines from the pheochromocytoma on rewarming and CPB weaning, but this did not happen in our case. Unfortunately, we did not measure plasma catecholamine concentration during specific phases.

The CABG was performed first to avoid retroperitoneal bleeding at the site of a fresh adrenalectomy during the anti-coagulated state needed for CPB. Then, the adrenalectomy could be performed with an open sternotomy, untied cannulating sites for CPB and back up extra-corporal circulation equipment in case of any adverse event. Invasive blood pressure and hemodynamic monitoring helped to detect and correct rapidly any BP increase during manipulation of the pheochromocytoma or decrease that is often seen postoperatively. Any decrease of blood pressure during CPB is more refractory to catecholamines because of the preoperative α- and ß-blockade. These patients have a better response to volume replacement. Another concern is the possible coagulopathy post-CPB that could make the fresh coronary bypass bleed or the dissection of the adrenal gland more difficult. The ACT, PT, PTT and platelets counts were all normal post-CPB and no abnormal bleeding was noticed.

With combined surgery, recovery may be more secure because the two conditions are treated. This alleviates considerably the risk of postoperative cardiovascular events due to CAD, or post-CABG hypertensive complications associated with secreting pheochromocytoma. When the patient is α-blocked preoperatively with phenoxybenzamine, hypotension can be expected postoperatively. To ensure optimal perfusion of the coronary bypasses, hypotension should be aggressively managed with optimal volume replacement and, if needed, high dose catecholamines.

Another particularity of our case was the malignant nature of the tumour based on the finding of local invasion or metastases. The most common metastatic sites are lymph nodes, bone, lung, and liver. In general, these are slow growing tumours. The five years survival rate is about 44%, but some patients have survived for 20 yr or longer.[1 3]

Conclusion

We report a patient who underwent combined surgery of CABG for severe coronary artery disease and adrenalectomy for pheochromocytoma with a good outcome. The risk of coronary event was probably reduced by performing the CABG first and the risk of hemodynamic instability during adrenalectomy was better controlled with invasive monitoring and standby CPB. However, particular anesthetic considerations should be taken into account as discussed. Surgical treatment of both of these high risk conditions makes the postoperative course more secure. The combined procedure might be considered in the future when CABG has to be done in a patient with actively secreting pheochromocytoma.

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