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Anesthetic management of simultaneous coronary artery bypass grafting and cardiac pheochromocytoma resection under cardiopulmonary bypass

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Abstract
We experienced simultaneous coronary artery bypass grafting and cardiac pheochromocytoma resection under cardiopulmonary bypass in a 79-year-old woman with atherosclerotic angina. During manipulation of the tumor under cardiopulmonary bypass, the serum norepinephrine concentration increased to over seventy times the normal limit, and there was a 25-mmHg rise in mean arterial pressure. Cardiopulmonary bypass has been recommended for the resection of cardiac pheochromocytoma to isolate the heart from the systemic circulation, and thus prevent massive catecholamine release when handling the tumor. However, the serum catecholamine concentration surged in our patient during tumor manipulation under cardiopulmonary bypass, probably because of the reperfused blood from the operating field. We suggest that cardiopulmonary bypass be performed for the anesthetic management of cardiac pheochromocytoma resection, because excessive hypertension can be avoided during cardiopulmonary bypass, even if the catecholamine concentration increases excessively when handling the tumor.

Key words Cardiac pheochromocytoma · Cardiopulmonary bypass · Norepinephrine

Case report

A 79-year-old woman, who had a 20-year history of hypertension and a 10-year history of exertional angina, presented at Suwa Red Cross Hospital with nocturnal chest pain. She weighed 61 kg and had a blood pressure of 180/100 mmHg, with normal blood counts, electrolytes, and blood chemistry. While undergoing coronary angiography, she developed hypertensive crisis, with a blood pressure of 275/116 mmHg, tachycardia (135 beats·min^{-1}), ventricular arrhythmia, diaphoresis, and palpitations. Coronary angiography showed 99% stenosis in the left anterior descending artery, 75% to 90% stenoses in the diagonal and posterolateral arteries, and a highly vascularized tumor in the left atrium, fed by the left circumflex artery. Pheochromocytoma was suspected, on the basis of increased serum and urinary norepinephrine (2988 pg·ml^{-1}; normal range, 100–450 pg·ml^{-1}, and 612 μg·day^{-1}; normal range, 26–121 μg·day^{-1}, respectively). Thoracic and abdominal magnetic resonance imaging (MRI) and ^{131}I-metaiodobenzylguanidine (MIBG) scintigraphy confirmed the diagnosis of solitary cardiac pheochromocytoma.

She was scheduled to undergo combined coronary artery bypass grafting (CABG) and cardiac pheochromocytoma resection on cardiopulmonary bypass (CPB). Doxazosin mesilate was started orally from 0.5 mg·day^{-1} and was gradually increased to 16 mg·day^{-1} before the operation.

Without premedication, she entered the operating room in the supine position, with blood pressure of 135/65 mmHg and heart rate of 55 beats·min^{-1}. Anesthesia was induced with midazolam (5 mg), fentanyl (0.05 mg), propofol (50 mg), and vecuronium bromide for tracheal intubation. Under controlled ventilation with end-tidal carbon dioxide at 33–35 mmHg, anesthesia was maintained with fentanyl (total, 1.1 mg), propofol (2.5–3 mg·kg^{-1}·h^{-1}), and vecuronium bromide (total, 30 mg). Nitroglycerine was continuously infused at 0.1 μg·kg^{-1}·min^{-1} throughout the operation.

Tracheal intubation, midline sternotomy, heart exposure, and the insertion of bicaval and aortic cannulas were performed without a hypertensive surge. Immediately after the start of CPB with heparinization, her mean arterial pressure dropped below 40 mmHg, and it recovered after a 0.025-mg norepinephrine injection.

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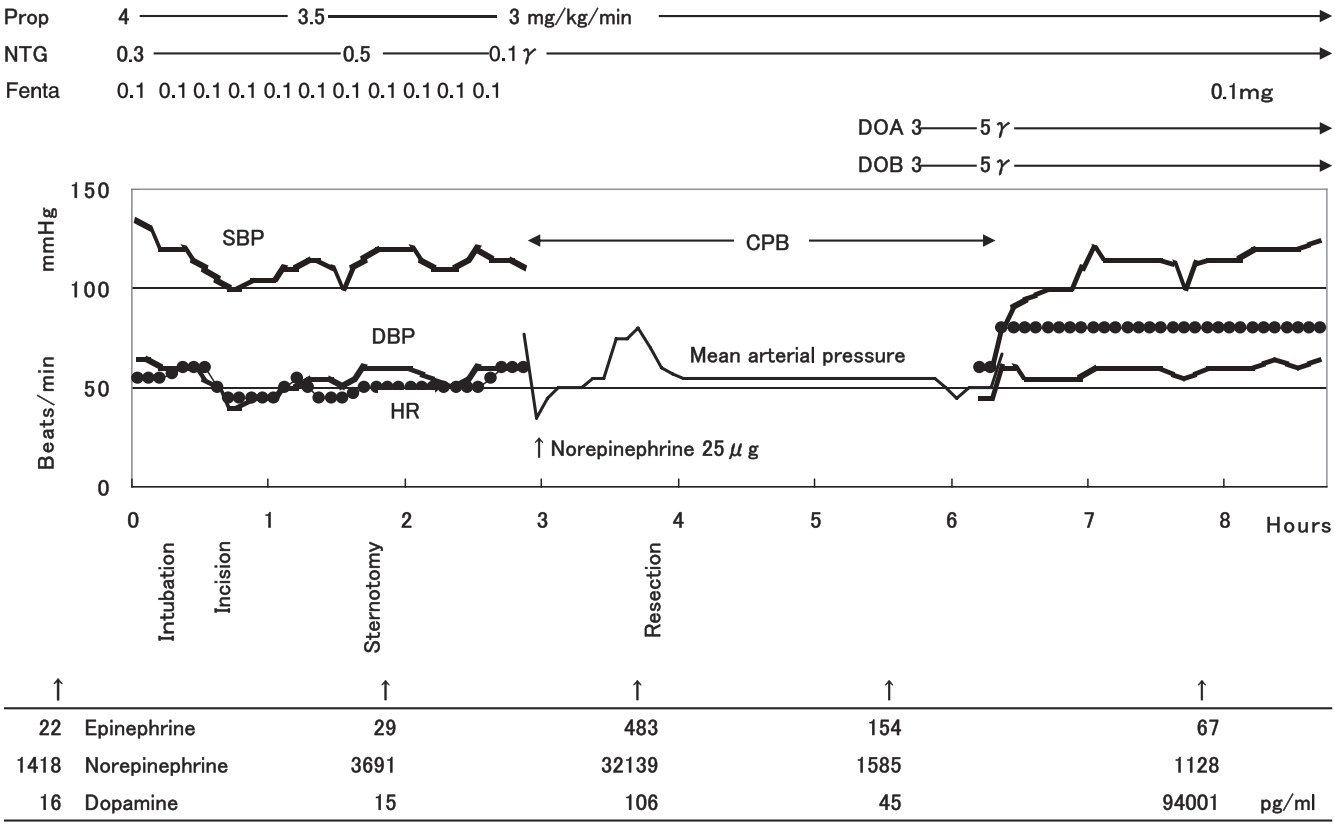

↑		↑	↑	↑	↑	
22	Epinephrine	29	483	154	67	
1418	Norepinephrine	3691	32139	1585	1128	
16	Dopamine	15	106	45	94001	pg/ml

Fig. 1. Hemodynamic changes and serum catecholamine concentrations during the operation. *Prop*, propofol; *NTG*, nitroglycerine; *Fenta*, fentanyl; *DOA*, dopamine hydrochloride; *DOB*, dobutamine hydrochloride; *CPB*, cardiopulmonary bypass; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *HR*, heart rate

The aorta was cross-clamped, and the heart was arrested with hypothermia of 32°C. A yellowish tumor was located behind the pulmonary artery, encapsulated in the left atrial wall. During tumor resection, the patient's mean arterial pressure increased to 80 mmHg, and it returned to 55 mmHg after the excision of the tumor at a constant pump flow of 3.48 l·min^{-1}. Bypass grafts to the left anterior descending artery, first and second diagonal branches (sequential), and posterolateral artery were performed, using the left internal thoracic artery and bilateral saphenous veins. The patient was on CPB for 218 min and was weaned with dopamine and dobutamine at 5 μg·kg^{-1}·min^{-1} each. At the end of the procedure, heparin was reversed with protamine. General anesthesia lasted for 8 h and 49 min. The total amount of fluid given during the operation was 2930 ml, including platelet cells and fresh-frozen plasma. Total bleeding was 754 ml and urine production was 1610 ml.

Fluctuations of the systolic and diastolic blood pressure and heart rate during surgery are presented, along with plasma epinephrine, norepinephrine, and dopamine concentrations, in Fig. 1.

Dopamine and dobutamine were progressively withdrawn and the trachea was extubated 6 h after the operation. She had an uneventful postoperative course, and was discharged from the hospital with prescriptions for aspirin, isosorbide mononitrate, metildigoxin, furosemide, and diltiazem hydrochloride. She has been free from symptoms with these drugs for a year.

The resected tumor, measuring 4.5 × 3.5 × 3 cm, was solid and yellowish, with intermingled melanin-like pigmentation on the cut surface. Histological examination showed sheets of polyhedral cells with basophilic cytoplasm, surrounded by a fibrous septum. Some of the tumor cells and fibrous septa contained brownish-black pigmented granules, histochemically suggestive of neuromelanin. Immunostaining showed that the tumor cells were positive for chromogranin A, with sustentacular cells positive for S-100, typical of pheochromocytoma.

Discussion

Cardiopulmonary bypass with cardioplegic arrest is recommended in the surgical resection of cardiac pheochromocytoma. The main reason for this recommendation is that, during the bypass, the cardiac tumor

is isolated from the systemic circulation; thus, the excessive release of catecholamines brought about by handling the tumor will not flow into the systemic circulation [1,2]. However, the serum norepinephrine level in our patient exceeded 32 ng·ml^{-1} (about seventy times the normal limit) during tumor manipulation under CPB. Because the circulating level of norepinephrine during an ordinary cardiopulmonary bypass increases to as much as twofold higher than the baseline [3], we assumed that this increase in norepinephrine was caused by suctioned blood from the operating field, which was reperfused to the circulation through the cardiopulmonary pump, based on a report of a high concentration of catecholamines in reperfused suctioned blood during pheochromotoma resection [4].

No previous report of cardiac pheochromocytoma resection has described hypertension during the manipulation of the tumor under CPB. Shibata et al. [5] reported hypertension of 210/120 mmHg during caval cannulation before CPB, with a serum norepinephrine level of over 30 ng·ml^{-1}, and no change in the arterial pressure, with a norepinephrine surge of over 20 ng·ml^{-1} in cardiac pheochromocytoma resection during CPB.

Contrary to that report, our patient showed no hypertension before CPB, but a 25-mmHg rise in mean arterial pressure was shown during CPB, with a nor epinephrine surge of 32 ng·ml^{-1}. Because the pump flow was constant, this rise was produced by increased peripheral vascular resistance. The mean arterial pressure during CPB is correlated with the sum of systemic vascular resistance and the CPB circuit. We speculate that the blood pressure would be caused to rise slightly by increased serum catecholamines when the CPB circuit resistance represents a considerable part of the total vascular resistance.

We suppose that, during CPB, the high concentration of norepinephrine did not cause significant hypertension in our patient, because the cardiac output was fixed, and the increased resistance brought about by systemic vascular constriction was partly negated by the fixed CPB circuit resistance and the preoperative administration of an alpha-adrenergic antagonist.

Lethal coronary artery disease is not uncommon among patients with pheochromocytoma [6,7]. In addition to the compromised myocardial oxygen demand and supply, pheochromocytoma is associated with risk factors of atherosclerosis, such as glucose intolerance, dyslipidemia, and enhanced coagulation [8]. However, CABG in cardiac pheochromocytoma has been limited to patients with coronary arteries involving the tumor itself [9,10], probably because of the tumor's rarity and the relatively young ages of the patients.

We found about 70 cases of cardiac pheochromocytoma reported worldwide, of which 59 patients, with a mean age of 36.2 years, were surgically treated (45 patients with CPB). Cardiac pheochromocytomas are being increasingly reported among older patients with the advent of CT, MRI, and MIBG, suggesting that these tumors are more common than suspected among patients with atherosclerotic coronary artery disease.

This is the first report of cardiac pheochromocytoma resection with CABG for atherosclerotic coronary artery disease. After pretreatment with an alpha-adrenergic antagonist, the anesthetic and surgical procedures were uneventful under propofol and fentanyl anesthesia with nitroglycerine infusion. When the tumor was manipulated during CPB, the serum norepinephrine level reached over 32 ng·ml^{-1}, possibly brought about by the reperfused blood from the operating field. However, this catecholamine surge caused only a 25-mmHg increase in the mean arterial pressure, suggesting that a high concentration of norepinephrine may not cause excessive hypertension under CPB.

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