Emergency Operation in a Patient with Asymptomatic Pheochromocytoma

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Intraoperative care of the patients with pheochromocytoma presents many difficult problems in anesthetic management[1]. There are some patients who show no definite clinical symptoms, so-called "asymptomatic pheochromocytoma"[2-8]. Recent advances in techniques of computed tomography (CT) and magnetic resonance imaging (MRI) have increased an opportunity of the incidental discovery of retroperitoneal tumors, in the absence of clinical symptoms. We experienced a case of asymptomatic pheochromocytoma associated with sudden hypertension and tachycardia following surgical manipulation.

Case Report

A 68-year-old man, weighing 37 kg and 150 cm tall, presented with appetite loss. Routine laboratory tests revealed hypercalcemia (13.1 $mg \cdot dl^{-1}$, normal range 9.1–10.6 $mg \cdot dl^{-1}$) and slight anemia (Hb 9.2 $g \cdot dl^{-1}$, normal range 13.3–17.0 $g \cdot dl^{-1}$). He was admitted to our hospital for further investigation of hypercalcemia. He had a medical history of acute subdural hematoma 4 years ago resulting in left hemiparesis. CT finding of the abdomen demonstrated a mass with necrosis at a left supraadrenal lesion. An aortic angiogram showed that the tumor was originated from the left adrenal gland artery. This suggested a possible case of pheochromocytoma but he presented no complaints of hypertension, palpitations, headache or sweating. Blood pressrue (BP) and heart rate (HR) were within the normal range. The functions of the thyroid, pancreatic islet cells, adrenal cortex and pituitary gland were also within the normal range. Electrocardiogram showed slight depressions of the ST-segment on V_1-V_5 leads.

Subsequent to admission, the patient was febrile to 38.5°C for several days. White cell counts were within the normal range, but monocytes increased. Blood and urine cultures were obtained, and intravenous broad-spectrum antibiotics were started. In view of the rapid deterioration of this patient, an emergency operation was planned to remove the mass, which was thought to include an infectious lesion. Serum and urinary catecholamines were examined, but the results had not been returned yet.

He was premedicated with scopo-

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lamine, 0.3 mg, intramuscularly. On arrival in the operating room, BP was 130/80 mmHg and HR was 92 beats·min^{-1}. Central venous pressure (CVP) was 6 cmH_2O. An epidural catheter was inserted at the Th 10/11 interspace and was placed cephalad. General anesthesia was then induced with thiamylal 200 mg followed by tracheal intubation with vecuronium 5 mg for muscle relaxation. An arterial catheter was inserted in the right radial artery to measure intra-arterial BP. The induction was hemodynamically uneventful. Anesthesia was maintained with 66% nitrous oxide in oxygen and 0.5–1.5% of isoflurane while muscle relaxation was maintained with vecuronium and intermittent epidural administration of 1.5% lidocaine.

Surgery went on uneventfully until mobilization of the tumor was attempted. During manipulation of the tumor, both BP and HR began to increase. We suspected the tumor might be pheochromocytoma. Phentolamine and trinitroglycerin (TNG) infusions were initiated and the doses were adjusted based on intra-arterial BP. Despite that BP was elevated up to 200/92 mmHg and HR increased to 125 beats·min^{-1}. Although the phentolamine infusion rate was increased to 10 μg·kg^{-1}·min^{-1}, this did not control the blood pressure change. Diltiazem, 10 mg, and propranolol, 1 mg, were added intravenously. BP gradually decreased and the doses of phentolamine and TNG were adjusted based on BP. Following excision of the tumor, BP suddenly decreased to 78/52 mmHg with the CVP value of 2 cmH_2O. We discontinued the infusion of phentolamine and TNG immediately. A noradrenaline infusion was started at a rate of 0.03 μg·kg^{-1}·min^{-1}, and we increased the rate of fluid infusion and blood transfusion. BP was stabilized at 100/50–120/62 mmHg by the noradrenaline infusion and fluid replacement. The operation was completed in 4 hrs 25 min and the blood loss measured 572g.

Postoperatively the patient was transferred to the intensive care unit. The noradrenaline infusion was weaned off within 24 hrs. A pheochromocytoma was confirmed by the histology. Seven days after surgery, we obtained results of the endocrine examinations which revealed elevations of serum adrenaline (1052 ng·ml^{-1}, normal ranges: 35–62 ng·ml^{-1}) and parathyroid hormone (PTH) related peptide (362.8 pmol·l^{-1}, normal ranges: 16.2–64.7 pmol·l^{-1}). These results confirmed that the tumor was an asymptomatic pheochromocytoma and PTH-related peptide secreting one. The postoperative course was stable and uneventful. The serum noradrenaline and PTH-related peptide values were normalized three weeks after the tumorectomy. The patient was discharged one month after the surgery.

Discussion

Pheochromocytom is a rare tumor found in less than 1% of the patients with secondary hypertension. The autopsy incidence of pheochromocytoma at Mayo Clinic was reported to be 0.3%[2]. Pheochromocytoma is classified into 3 types consisting of sustained, paroxysmal, and asymptomatic types according to the clinical manifestations. Although most patients are symptomatic, approximately 1 to 10% of patients are clinially silent and found at autopsy[3,4]. The diagnosis of pheochromocytoma without classical symptoms is difficult, especially in the emergency situations without the aid of biochemical tests.

Pheochromocytoma secretes noradrenaline and adrenaline which usually cause labile or sustained systemic hypertension. Only some patients have been reported to be normotensive[2–8]. The reasons of no hypertension in

some patients with pheochromocytoma have been described as follows[5,6]; 1) predominant secretion of adrenaline, 2) concomitant secretion of di-hydroxyphenyl-alanine (dopa), which has antiadrenergic action inhibiting the vasoconstrictive effect of other amines, 3) inactivation of the secretions within the tumor, 4) myocardial failure, and 5) tolerance or down regulation of tissue receptors to circulating catecholamines. These reasons may be responsible in this patient. Although the tolerance may be present in some patients with pheochromocytoma, the exact mechanism of maintaining normal BP in some patients is still controversial.

There have been only a few reports on the management of asymptomatic pheochromocytoma during anesthesia[4,6,8]. Although no cardiovascular changes during tumor mobilization in asymptomatic pheochromocytoma were reported[6], our case showed sudden increases of both BP and HR. This increase in BP and HR was thought to be caused by a sudden release of the catecholamines stored in the tumor during surgical manipulation.

Recently, the use of extradural block has been advocated as it interrupts the innervation of the adrenal gland and thus obtunds neurogenic stimulation of the tumor[9]. In our case, extradural block was unable to control or attenuate the hemodynamic changes during tumor mobilization. Isoflurane has been also recommended for pheochromocytoma resection[10]. During tumor manipulation, 2–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of phentolamine and 0.5–1.0 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of TNG were used as vasodilators. Because surgical maneuver might make plasma catecholamine concentrations significantly high, the elevation of BP and tachycardia could not be reduced by increasing inhaled isoflurane concentration, and rate of infusions of phentolamine and TNG. Additional use of diltiazem and propranolol injections were effective.

Patients of the pheochromocytoma rarely showed hypercalcemia. Recently elevation of serum PTH-related peptide was reported in some hypercalcemic patients with breast cancer[11]. The hypercalcemic effect of PTH-related peptide is due to both an increase in bone calcium resorption, as assessed by an increment in fasting urinary calcium, and an elevation in renal calcium reabsorption[12]. Further examinations are necessary when we suspect pheochromocytoma in case of adrenal tumor with hypercalcemia.

In summary, we described a case of an asymptomatic pheochromocytoma associated with sudden hypertension and tachycardia following surgical preparation. Asymptomatic pheochromocytoma detected incidentally should be managed as a functioning one, even in the absence of specific symptoms of pheochromocytoma.

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