Anesthesia for One-Stage Bilateral Pheochromocytoma Resection in a Patient with MEN Type IIa : Attenuation of Hypertensive Crisis by Magnesium Sulfate

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Abstract

Multiple endocrine neoplasia (MEN) type IIa, manifesting as an autosomal dominant trait, consists of medullary thyroid carcinoma, parathyroid adenoma or hyperplasia, and pheochromocytoma. We report our experience of a 42-year-old woman, MEN type IIa with a large bilateral pheochromocytoma, who underwent one-stage bilateral tumor resection under a combined continuous epidural technique with 0.25 per cent bupivacaine and general anesthesia using vecuronium, fentanyl, nitrous oxide, and isoflurane. An initial intra-operative hypertensive response was acceptably controlled by nitroprusside and a β-blocker but during tumor handling the hypertensive crisis worsened and she developed acute pulmonary edema despite a continuing high dose of nitroprusside infusion. After receiving intermittent IV $MgSO_4$ up to 3 g in 15 min, her condition gradually improved and the cardiovascular response was under control throughout the period of tumor handling. Hypotension encountered post-pheochromocytoma resection was treated by volume replacement, metaraminol, $cacl_2$, and dopamine infusion. The patient's post-operative course was uneventful.

Key word : Anesthesia, MEN Type IIa, Pheochromocytoma, Acute Pulmonary Edema, Magnesium Sulfate

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Multiple endocrine neoplasia (MEN) type IIa, or Sipple's syndrome includes medullary carcinoma of the thyroid, parathyroid adenoma or hyperplasia, and pheochromocytoma. This syndrome is inherited by an autosomal dominant pattern with the mutation in the RET proto-oncogene on chromosome 10. Bilateral pheochromocytoma occurs in approximately 75 per cent of cases but is rarely extraadrenal or malignant[1]. A case of MEN type IIa is presented complicated with diastolic left ventricular dysfunction in whom successful perioperative management for one-stage bilateral pheochromocytoma resection was performed.

CASE REPORT

A 42-year-old, 40 kg, 1.5 m woman was referred to the King Chulalongkorn Memorial Hospital for further management of a suspected pheochromocytoma. Her problems during a previous admission was congestive heart failure and uncontrolled severe hypertension which were partially improved by furosemide, digitalis, amlodipine, and enalapril. She had a past history of a 20 year enlargement of the thyroid gland and 5 years of type II DM which was poorly controlled by an oral hypoglycemic drug.

Upon the patient's arrival, neither dyspnea nor orthopnea was found. Physical examination revealed a heart rate of 110 bpm, arterial blood pressure of 140/90 mmHg, puffy eyelids, tremor of the hands, bilateral enlargement of the thyroid gland, cardiomegaly and basal coarse crepitation in both lung fields. Routine laboratory examination revealed a hemoglobin of 9.9 $g.dL^{-1}$ and hematocrit of 31 per cent. Electrocardiogram showed sinus tachycardia and left ventricular hypertrophy which was confirmed by chest radiograph. Two-dimensional echocardiogram revealed diastolic LV dysfunction with mild MR and AR, moderate TR, and severe pulmonary hypertension (PAP = 69/28 mmHg). Left ventricular ejection fraction was 0.68. Biochemical screening revealed urine VMA 24.2 $mg.24\ h^{-1}$ (normal 0.7-6.8 $mg.24\ h^{-1}$), serum parathyroid hormone 79.5 $ng.mL^{-1}$ (normal 10-65 $ng.mL^{-1}$), and serum calcium 12.1 $mg.dL^{-1}$ (normal 8.1-10.4 $mg.dL^{-1}$). Serum free T_3, free T_4, TSH, and cortisol were normal. Magnetic resonance imaging showed a bilateral adrenal mass. Focal uptake in the thyroid gland and bilateral suprarenal areas were shown by computed tomography (CT) with ^{131}I-labeled metaiodobenzylguanidine (mIBG). Thyroid tumors were histologically proved to contain abnormal cells by needle biopsy. Parathyroid scintigraphy showed hyperplastic parathyroid glands. No demonstrable metabolic bone disease was shown by bone scan. The patient was diagnosed as MEN type IIa with diastolic LV dysfunction and type II DM. Oral prazosin 2 mg every 6 hours and then metoprolol 100 mg twice daily were given to stabilize the cardiovascular system. Two weeks later, her blood pressure was maintained at 150/100-120/70 mmHg with orthostatic hypotension and a heart rate of 100-110 bpm. Hyperglycemia was controlled by 45 units of humulin 70/30 subcutaneously in the morning and 25 units in the evening.

The patient underwent one-stage bilateral pheochromocytoma resection under combined thoracic epidural and balanced general anesthesia. The usual doses of prazosin and metoprolol were given in the morning of the surgical day. An insulin infusion of 2 $u.h^{-1}$ together with a glucose and hydrocortisone infusion were started and continued throughout the procedure. In the operating room, an additional 40 mcg of fentanyl was given intravenously. The patient's monitoring consisted of a continuous electrocardiogram, right radial artery catheter for direct pressure measurement and blood sampling, and central venous pressure (CVP). The patient was carefully placed in a left lateral position to prevent pressure on her abdomen. A paramedian approach at T_{10-11} epidural interspace was used and correct positioning of the needle was ascertained by using the loss-of-resistance method with air and a test dose of 1.5 per cent lidocaine 3 ml. Five ml of 0.25 per cent bupivacaine was injected through the catheter intermittently with a total dose of 10 ml. Analgesic level tested by pin prick sensation was between T_6-T_{12} dermatome without cardiovascular changes. General anesthesia was then induced with IV thiopental 200 mg and vecuronium 6 mg. The trachea was intubated, and anesthesia was maintained with nitrous oxide 66 per cent in oxygen, intermittent fentanyl 40-50 mcg totally 170 mcg, and isoflurane up to 2 per cent. Additional monitoring included end tidal CO_2, temperature probe, and urine output. A bilateral subcostal incision was made to facilitate tumor removal. Significant hemodynamic variables and management are shown in Table 1. During tumor handling, the patient developed severe hypertension and tachycardia which could not be controlled well by nitroprusside (up to 3.5 $mcg.kg^{-1}.min^{-1}$), and labetalol 10 mg IV. Thirty minutes after

Table 1. Hemodynamic parameters and management of different perioperative intervals.

	Baseline	1	2	3	4	5	6
Heart rate (bpm)	104	120	110	132	122	96	108
SBP (mmHg)	148	200	180	240	140	82	118
DBP (mmHg)	96	120	108	160	96	44	69
CVP (cmH_2O)	1	1	1	1	2	3	6
Management		Esmolol	SNP Labetalol	SNP $MgSO_4$	SNP	Metaraminol Dopamine $CaCl_2$	Dopamine

1 = immediately following induction of anesthesia, 2 = 15 min after surgical incision,
3 = during maximal tumor handling and pulmonary edema, 4 = 5 min after 3 g of magnesium IV, 5 = 15 min after tumor removal,
6 = 12 h after surgery, SPN = sodium intropruside, SBP = systolic blood pressure, DBP = diastolic blood pressure,
CVP = central venous pressure.

tumor handling, she developed signs of acute pulmonary edema with a CVP of 1-2 cmH_2O. Ventilation was controlled with 100 per cent oxygen and positive end-expiratory pressure of 5-10 cmH_2O. An additional dose of 0.25 per cent bupivacaine 5 ml was given through the epidural catheter without improvement of the patient's cardiorespiratory status. Since the surgeon had to continue operation for bleeding control, it was decided to add magnesium sulfate to control the exaggerated cardiovascular response at that moment. After administering 3 g of magnesium sulfate intravenously within 15 min, the hypertensive crisis was satisfactorily controlled and clinical improvement of acute pulmonary edema was shown. One hour post-$MgSO_4$ injection, hypotension following total tumor devascularization was encountered and immediately treated by volume replacement, metaraminol, and a dopamine infusion (up to 8 $mcg.kg^{-1}.min^{-1}$). During tumor handling, hyperglycemia was controlled by insulin IV infusion 4 $u.h^{-1}$ which was tapered to 2 $u.h^{-1}$ after tumor removal. Isotonic saline solution 20 $mL.kg^{-1}.h^{-1}$ was infused during the first two hours, and 15 $mL.kg^{-1}.h^{-1}$ was infused until the completion of surgery. The estimated blood loss of 1,200 mL was replaced and urine output was maintained 2 $mL.kg^{-1}.h^{-1}$. At the end of the 3-hour operation, hypocalcemia was corrected by IV calcium replacement. The unextubated patient was transferred to the ICU for continuing resuscitation. Following overnight ventilation, tracheal extubation was performed early in the morning. Her blood pressure was normal on the third post-operative day without cardiovascular drugs. The patient's pain control was accomplished by continuous epidural infusion with 0.125 per cent bupivacaine and fentanyl 4 $\mu g.mL^{-1}$ during the first 72 h. Then morphine 3 mg was given epidurally once daily for 4 days. After that she received only insulin and steroid replacement therapy. Histopathological examination of the surgical specimens revealed a well circumscribed pheochromocytoma of the adrenals.

After bilateral pheochromocytoma resection, her cardiac functional class gradually improved. Screening of urine metanephrine was normal. Follow-up two-dimensional echocardiogram revealed improvement of diastolic LV dysfunction and decrease in pulmonary pressure (PAP = 38/12 mmHg). Three weeks later the patient underwent total thyroidectomy and parathyroidectomy with a small piece of parathyroid implantation in the left forearm without complications. Histopathological examination of the thyroid and parathyroid confirmed the diagnosis of MEN type IIa. At the time of discharge, the patient was receiving thyroid hormone, fludrocortisone acetate, calcitriol, prednisolone and oral hypoglycemic.

DISCUSSION

The anesthetic management of the surgical resection of a pheochromocytoma requires optimum pre-operative preparation, good communication between the surgeon and anesthesiologist, and knowledge on the part of the anesthesiologist about the pathophysiology of the pheochromocytoma[2]. The use of pre-operative alpha-adrenergic blockade can decrease the morbidity associated with cardiovascular instability and myocardial dysfunction[3]. This case of MEN type IIa with diastolic LV dysfunction and a history of congestive heart failure received

prazosin, a specific alpha$_1$-adrenergic antagonist, to gradually allow re-expansion of intravascular volume which was accompanied by decreased hematocrit. Tachycardia was then fairly well controlled by metoprolol. Although some authors have recommended using pulmonary artery pressure monitoring, especially in patients with cardiomyopathy, for accurate assessment of LV filling pressure and estimation of systemic vascular resistance[4,5], some institutes including ours do not use it routinely and have successfully managed most patients by central venous pressure monitoring[6-8]. Given the severity of pulmonary hypertension in these cases, concern arises about the risks of pulmonary artery rupture [9], cardiac arrest[10] and the accuracy of wedge pressure monitoring. Nevertheless, the acute pulmonary edema with low CVP in this patient may represent the discrepancy of CVP and pulmonary capillary wedge pressure from long-standing severe hypertension and persistently elevated catecholamine levels.

During anesthesia, any anesthetic, surgical, or pharmacological stimuli to catecholamine release, and drugs that release histamine must be avoided to prevent an intra-operative hypertensive crises[6, 11]. Sympathetic blockade by epidural anesthesia has been shown to inhibit sympathetic innervation in the adrenal medulla[12,13] but not the release of catecholamine in response to tumor handling[6,14, 15]. Also, epidural analgesia facilitates post-operative pain control and the patient's recovery.

James[8] described a series of 17 patients in whom hypertension was mainly controlled with a loading dose of magnesium sulfate (40-60 mg.kg^{-1}) followed by an infusion of 1-2 g.h^{-1}. However, all patients required additional doses of magnesium sulfate during tumor handling. In our case, the cardiovascular response during tumor handling was exaggerated leading to acute pulmonary edema which did not respond well to conventional treatment but improvement was shown after $MgSO_4$. Reports of the use of $MgSO_4$ in inhibition of catecholamine release, direct blockade of catecholamine receptors, vasodilation, antiarrhythmic effect, and myocardial protection during catecholamine stimulation[16] make it suitable for use in controlling cardiovascular disturbances and catecholamine release at induction and intubation and in association with other agents in controlling hypertension and arrhythmia during tumor handling[8,17-19].

In conclusion, the management of patients with surgical resection of pheochromocytoma is still a challenge for anesthesiologists. A consensus on the most suitable anesthetic technique has not been reached. Epidural blockade may be a useful adjunct to general anesthesia in the perioperative management of patients with pheochromacytoma who get adequate pre-operative alpha-adrenergic blockade and re-expansion of the circulating volume. The authors consider $MgSO_4$ to be an additional useful drug in the management of an intra-operative hypertensive crisis.

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การให้ยาระงับความรู้สึกสำหรับการผ่าตัดฟีโอโครโมซัยโตมาออกทั้งสองข้างในผู้ป่วยที่เป็น MEN type IIa : การรักษาวิกฤติความดันโลหิตสูงด้วยแมกนีเซียม-ซัลเฟต

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Multiple Endocrine Neoplasia (MEN) type IIa ประกอบด้วย medullary thyroid carcinoma, parathyroid adenoma หรือ hyperplasia และ pheochromocytoma เกี่ยวข้องกับลักษณะทางพันธุกรรมแบบ autosomal dominant trait ผู้รายงานให้การระงับความรู้สึกแก่ผู้ป่วยหญิงอายุ 42 ปี ที่เป็น MEN type IIa ร่วมกับ diastolic LV dysfunction และมารับการผ่าตัด pheochromocytoma ขนาดใหญ่ออกทั้ง 2 ข้าง โดยเทคนิค continuous epidural ด้วย 0.25% bupivacaine ร่วมกับการวางยาสลบทั่วไปด้วย vecuronium, fentanyl, nitrous oxide และ isoflurane ความดันโลหิตสูงระยะแรกในระหว่างการผ่าตัดควบคุมโดย nitroprusside และ β-blocker ขณะศัลยแพทย์ผ่าตัดก้อนเนื้องอกเกิดวิกฤติความดันโลหิตสูงและผู้ป่วยมีภาวะน้ำท่วมปอดเฉียบพลัน แม้จะยังคงให้ nitroprusside ในขนาดสูงหยดเข้าหลอดเลือดดำตลอดเวลา เมื่อผู้ป่วยได้รับแมกนีเซียมซัลเฟตฉีดเข้าหลอดเลือดดำเป็นระยะ ๆ รวม 3 กรัมในเวลา 15 นาที สามารถควบคุมความดันเลือดได้ในเกณฑ์ปกติ และภาวะน้ำท่วมปอดเฉียบพลันดีขึ้นตามลำดับ ความดันเลือดตกซึ่งเกิดขึ้นหลังตัดก้อน phechromocytoma ออก รักษาด้วยการให้สารน้ำ metaraminol และ dopamine ผู้ป่วยฟื้นตัวในระยะหลังผ่าตัดอย่างปลอดภัย

คำสำคัญ : การให้ยาระงับความรู้สึก, MEN type IIa, ฟีโอโครโมซัยโตมา, ภาวะน้ำท่วมปอดเฉียบพลัน, แมกนีเซียมซัลเฟต

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