Total Spinal Anesthesia for Resection of Pheochromocytoma

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(Key words: total spinal anesthesia, pheochromocytoma removal)

Anesthetic management during the surgical removal of adrenal pheochromocytoma emphasizes hemodynamic control of striking hypertension and tachycardia which frequently occur during manipulation of the adrenal tumor, as well as the sudden hypotension that may occur immediately after removal of the tumor[1].

There have been several reports of the use of inhaled anesthetics with halothane[2], enflurane[3], isoflurane[4], and seveflurane[5], and of epidural anesthesia[6]. However, with any of these anesthetic agents, the use of vasodilators[7] and beta blockers[8] may be mandatory. In order to provide hemodynamically stable and safe anesthesia for the resection of pheochromocytoma, we performed a total spinal block in combination with general anesthesia and report the following findings.

Case Reports

Patient 1: A 49-year-old woman, 156 cm tall and weighting 56 kg first experienced hypertension, headache, and severe general fatigue in 1985. During that time, her blood pressure elevated paroxysmally to 200/100 mmHg over a baseline of about 175/95 mmHg. In December 1987, she developed progressively worsening chest pain, orthostatic dizziness and cold sweating.

She was admitted to the Department of Internal Medicine in our hospital. Abdominal ultrasonography, angiography, and iodine ^{131}I-metaiodobenzyl guanidine (MIBG) scan revealed a pheochromocytoma of the right adrenal gland. She was admitted to the Department of Surgery for removal of the tumor. She had been taking nifedipine 30 mg·day^{-1} and trichlormethiazide 6 mg·day^{-1} since 1985. However, since the control of her hypertension was poor with this treatment, labetalol 30 mg·day^{-1} and prazosin hydrochloride 1.5 mg·day^{-1} were prescribed instead of the previous drugs after admission. Her blood pressure prior to surgery was 150/100 mmHg and her heart rate was 72 beats·min^{-1}.

Routine blood analysis revealed no abnormalities of liver and kidney functions. The plasma electrolyte levels were: Na^+=138 mEq·l^{-1}; K^+=3.8 mEq·l^{-1}; and Cl^-=107 mEq·l^{-1}. The fasting blood glucose level was 125 mg·dl^{-1}. Electrocardiography (ECG) revealed the presence of a U wave

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J Anesth 7:483–488, 1993

in the precordial leads and, immediately after exercise loading, a flat T wave in V4-6 and aVF. Plasma hormone levels included epinephrine (E)=1.6 $ng \cdot ml^{-1}$ (normal range: up to 0.15 $ng \cdot ml^{-1}$) and norepinephrine (NE)=0.28 $ng \cdot ml^{-1}$ (normal range: 0.07–0.31 $ng \cdot ml^{-1}$). Urinary excretion of catecholamines was: E=653 $\mu g \cdot day^{-1}$ (normal range: up to 12 $\mu g \cdot day^{-1}$), NE=278 $\mu g \cdot day^{-1}$ (normal range: 10–90 $\mu g \cdot day^{-1}$) and vanillyl mandelic acid (VMA)=13.3 $mg \cdot day^{-1}$ (normal range: 2.6–9.6 $mg \cdot day^{-1}$). Overall these findings indicated an E-secreting type of pheochromocytoma. Other pituitary, adrenal cortex and thyroid hormone levels were all within normal ranges.

Patient 2: A 44-year-old man, 174 cm tall, weighting 70 kg had occasional bouts of headaches and dizziness in 1984. Nose bleeds began to occur in 1985, but were left untreated. When donating blood in 1987, the patient was found to have hypertension and since that time, he has experienced severe headaches, palpitation, and a feeling of general fatigue. In April 1988, he underwent examinations at another hospital because of an aggravation of the symptoms, resulting in a diagnosis of essential hypertension.

In November of the same year, he was extensively examined in our hospital, and the result of these tests revealed the presence of a pheochromocytoma in the right adrenal gland. The patient was informed that surgical treatment was necessary, and in December, during a temporary discharge from our hospital, he suffered from a cerebral hemorrhage in the left lateral lobe after a bout of heavy alcohol drinking. Surgery to remove the cerebral hematoma and cranioplasty were performed at another hospital. During anesthesia, there were great fluctuations of blood pressure, but the surgery was concluded without any serious complications, although hemiplegia of the right side remained. In March 1989, the patient was readmitted to the Department of Surgery in our hospital for removal of the pheochromocytoma. While he was in our hospital, his hypertension was treated with labetalol 150 $mg \cdot day^{-1}$, nifedipine 60 $mg \cdot day^{-1}$, and enalapril maleate 10 $mg \cdot day^{-1}$, but his blood pressure fluctuated in the ranges of 140–220/80–140 mmHg, with heart rate variations between 56 and 84 beats per minute. Blood analysis showed neither liver nor kidney function abnormalities. The plasma electrolyte levels included: Na^{+}=138 $mEq \cdot l^{-1}$; K^{+}=4.4 $mEq \cdot l^{-1}$; and Cl^{-}=99 $mEq \cdot l^{-1}$. The fasting blood glucose level was 147 $mg \cdot dl^{-1}$. Apart from a left axis deviation, no ECG abnormality was observed.

Endocrinological findings included plasma catecholamine levels of E=0.06 $ng \cdot ml^{-1}$, and NE=1.1 $ng \cdot ml^{-1}$, and urinary catecholamine excretion of E-12.4 $\mu g \cdot day^{-1}$, NE=1040 $\mu g \cdot day^{-1}$, and VMA=28.4 $mg \cdot day^{-1}$. This case represented a NE-secreting type of pheochromocytoma.

Anesthetic Procedures

The protocol in anesthetic technique was approved by the Department of Anesthesiology and the Second Department of Surgery, Hyogo College of Medicine and informed consent was obtained from each patient.

In both cases, 100 $ml \cdot hr^{-1}$ of lactated Ringer's solution was administered continuously from the evening prior to surgery. After entering the operating room, the radial artery was catheterized under local anesthesia to enable continuous arterial blood pressure monitoring, and a Swan-Ganz catheter was inserted via the right internal jugular vein.

In case 1, the initial blood pressure in the operating room was 200/98 mmHg, and the pulse rate was 78/min.

The patient was placed in the left lateral decubitus position, and a mixture of 20 ml of 2% mepivacaine, 10 ml of 1% mepivacaine and 5 ml of 50% glucose was injected into the subarachnoid space between the second and third lumbar vertebrae. Following the spinal tap, the patient was immediately turned to a supine position, 20 mg of diazepam was then injected intravenously. After loss of consciousness, cessation of respiration, and dilation of the pupils, manual ventilation was performed with 100% oxygen through a face mask. Sudden hypotension of 90/55 mmHg required rapid infusion of 200 ml of lactated Ringer's solution, and the blood pressure then rose rapidly to 280/130 mmHg, with a pulse of 135/min. Immediately, 0.3 mg of propranolol and 3 mg of phentolamine were injected intravenously, and continuous intravenous infusion of sodium nitroprusside and nitroglycerine was initiated, stabilizing the blood pressure at 120/82 mmHg. Endotracheal intubation was performed without the administration of muscle relaxant, but no change in blood pressure or heart rate occurred.

During surgery, the patient was maintained with inhalation of 2 $l \cdot min^{-1}$ of oxygen and 4 $l \cdot min^{-1}$ of nitrous oxide. When the tumor was manipulated, the blood pressure increased to 205/101 mmHg and the heart rate accelerated to 128/min. The patient was treated with low concentration of enflurane (0.2–0.5%) and a total of 19 mg of phentolamine, and was also given 2 mg of acebutolol. For muscle relaxation, only 4 mg of pancuronium was required near the end of surgery. Following surgery, the patient's consciousness was clear after cessation of nitrous oxide inhalation and reversal of the muscle relaxant with 1.5 mg of atropine sulfate and 3.0 mg of neostigmine. The endotracheal tube was removed. The total volume of infused fluid was 2400 ml, and the volume of transfused blood was 900 ml. The blood loss was 450g, and the urine output was 785 ml.

In case 2, the initial blood pressure in the operating room was 120/60 mmHg and the pulse rate was 80/min, preoperatively. In the right decubitus position, 20 ml of 2% mepivacaine was injected into the subarachnoid space between the 7th cervical vertebrae and 1st thoracic vertebrae. Following this, he was immediately turned to a supine position and a 20 mg bolus of diazepam was injected intravenously. After loss of consciousness, his pupils became widely dilated and unresponsive to light. Endotracheal intubation was performed without muscle relaxant. Blood pressure after intubation fell transiently to 98/50 mmHg, but recovered promptly after rapid infusion of 100 ml of lactated Ringer's solution. Two $l \cdot min^{-1}$ of oxygen and 3 $l \cdot min^{-1}$ of nitrous oxide were administered concurrently, and stabilized blood pressure was obtained. However, when the tumor was manipulated, hypertension was transient and mild, and treated with a single dose of 2 mg of phenotolamine. Four mg of pancuronium was administered intraoperatively, and after surgery the muscle relaxant was reversed easily, and the endotracheal tube was removed. The volume of infused fluid and transfused blood were 2500 ml and 1100 ml, respectively. The blood loss was 900g, and the urine output was 430 ml.

Unintentional hypotension which occurred immediately after tumor resection in both cases was treated by rapid infusion of lactated Ringer's solution or blood transfusion as the first-choice. However, since this was inadequate, exogenous epinephrine and norepinephrine were intravenously administered for a short period in case 1, and 3 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of dopamine was administered continuously in case 2. The postoperative courses in both cases were unremarkable. Table 1 shows the changes of hemodynamics, plasma hormonal levels (catecholamine, ACTH, cortisol), and plasma mepivacaine concentrations in these two cases.

Discussion

In case of pheochromocytoma, a marked reduction in circulating blood volume resulting from elevation of peripheral vascular resistance induced by high plasma catecholamine concentrations is usually noted. For this reason, the primary aim of preoperative management should be the recovery of a normal circulating blood volume using alpha- and beta-blockers, with adequate fluid and blood replacement.

Although total spinal anesthesia performed in the treatment of traumatic cervical disk syndrome has caused considerable peripheral vasodilation, reported blood pressure and heart rate variations are minor because sympathomimetic and vagal nerves participating in cardiac function and peripheral vascular tone were blocked simultaneously and completely at the brain and spinal regions by a total spinal block[9]. Thus, this technique of anesthesia appears ideal for the patient with pheochromocytoma, which involves an excessive contraction of the peripheral vessels. Until now, we have found that the inhaled anesthetic method is to be successful, although, the anesthetic treatment requires many drugs for complete control of hemodynamic status. However, in the removal of pheochromocytoma with total spinal sympathetic block combined with general anesthesia, it was easy to control blood pressure, with less medication. Our experience with anesthesia in these two cases, however, raises the following questions.

First, total spinal anesthesia performed with the cervical approach afforded very stable hemodynamics during surgery, especially during manipulation of the pheochromocytoma (case 2). However, case 1 with the lumbar approach was associated with blood pressure elevation probably as a baroreceptor reflex, following a sudden hypotention immediately after the injection of local anesthetic into the subarachnoid space. In addition, the intraoperative blood pressure fluctuated greatly with the lumbar approach (case 1). Hemodynamic reactions during induction of anesthesia and surgery varied with the two approaches. Were these differences due to the disparity between catecholamine secreting type of pheochromocytomas, or to the dissimilarity in the manner in which the neural blockade spread – that from the lumbar approach started from the lumbar region and that from the cervical approach started from the brain stem region –?

When the block is initiated from the lumbar region, a fall in blood pressure occurs as the result of sudden peripheral vasodilation before complete blockade of the central autonomic nervous system, which activates the sympatho-adrenomedullary system through the upper baroreceptors, resulting in a sudden rise in blood pressure. We presumed that in case 1, with the lumbar approach, the abrupt changes in blood pressure immediately after local anesthetic injection into subarachnoid space, occurred because this mechanism is particularly accentuated in the patient with the pheochromocytoma. Also, the sharp rises in plasma catecholamine concentrations that occurred about the same time indicated a strong activation of the sympatho-adrenomedullary system, supporting this hypothesis.

In case 2, in which the cervical approach was employed, the above series of events did not take place. Neither immediately after the block was performed nor at the time of intubation

Table 1. The changes of plasma hormonal responses and hemodynamics during surgery

		pre anesthesia	post-TS	post-intubation	op. 10 min	manipu-lation	removal of tumor	end of op.
NE	case 1	0.43	2.95	0.63	1.90	6.68	2.57	0.21
($ng \cdot ml^{-1}$)	case 2	4.44	7.58	8.75	13.94	16.66	1.75	2.100
E	case 1	0.90	12.58	2.02	9.86	36.32	2.59	0.48
($ng \cdot ml^{-1}$)	case 2	0.32	0.19	0.18	0.21	0.27	0.36	0.33
Cortisol	case 1	5.9	4.0	6.1	22.8	20.1	14.7	18.9
($\mu g \cdot dl^{-1}$)	case 2	6.1	4.2	3.5	5.4	4.6	7.7	13.1
ACTH	case 1	38	43	63	110	40	77	606
($pg \cdot ml^{-1}$)	case 2	26	3	29	1	7	20	63
Mepivacaine	case 1	0	1.55	2.81	3.67	3.41	2.54	2.23
($\mu g \cdot ml^{-1}$)	case 2	0	0.08	0.73	2.43	2.19	1.98	1.15
mABP	case 1	141	138	58	86	127	106	143
(mmHg)	case 2	93	79	72	86	89	82	71
HR	case 1	67	120	73	71	110	72	80
($beats \cdot min^{-1}$)	case 2	74	82	83	87	89	82	71
CI	case 1	3.08	2.95	2.83	2.49	5.64	3.6	4.43
($\ell \cdot min^{-1} \cdot m^2$)	case 2	3.85	2.18	2.20	4.09	4.04	3.04	2.88
SVRI	case 1	3305	3277	1214	2250	1576	1868	2313
(dyne.s./cm5.m2)	case 2	1923	1845	1979	2446	2050	691	952

Abbreviations;
NE: Norepinephrine, E: Epinephrine, mABP: mean Arterial Blood Pressure, HR: Heart Rate, CI: Cardiac Index, SVRI: Systemic Vascular Resistance Index, TS: Total Spinal Block

did changes in blood pressure or heart rate occur. This effect was probably due to the rapid and direct action of the local anesthetic on the brain stem, and to complete blockade of the autonomic nerves in the medulla oblongata, the hypothalamus, and the cerebral cortex and the autonomic nerve plexusus located in the upper cervical region. The changes of plasma ACTH and cortisol concentrations in case 2 were very little in comparison with case 1 (table 1). Total spinal block via the cervical approach is effective and suppresses the autonomic function of the brain completely.

Second, although the plasma catecholamine levels increased makedly in both cases (table 1), the blood pressure changes in case 2 were small. The reason for this is unclear, but if blockade of the central sympathomimetic nervous system and vagal nerves including the areas supplied by the cranial nerve, had been more complete, would the reactivity of the myocardium and the smooth muscle of the blood vessels be weakened, and would there be an effect on catecholamine receptors (desensitization)?

However, the authors suppose that even if the blockade of the autonomic and vagal nervous system by total spinal anesthesia was complete, it would be difficult to completely prevent hypertension and increses in plasma catecholamine levels released from the pheochromocytoma at the time of tumor manipulation.

In conclusion, based on our cases studied, a combination of total spinal blockade using the cervical approach and general anesthesia has been proven successful for the removal of pheochromocytoma because of the total loss of afferents from surgical stimulus. Although, there have not been enough cases to ascertain, total spinal block using cervical approach might be a recommended anesthetic procedure in comparison with that using lumbar approach. Further studies are necessary to understand the difference and mechanism of the hemodyamic changes between the cervical and the lumbar approaches.

Acknowledgement: The authors wish to thank Daniel M. Philbin, M.D., Professor in the Department of Anesthesia, Harvard Medical School and Massachusetts General Hospital, for making this case report.

(Received Sep. 9, 1992, accepted for publication Jan. 19, 1993)

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