Hypertensive Crisis during the Resection of an Adrenal Tumor in Primary Aldosteronism

Hiroshi OTSUKA, Makoto IMAI and Osamu KEMMOTSU

Primary aldosteronism is one of the few causes of hypertension which is subject to total surgical treatment, but a hypertensive crisis can occur during the resection of the adrenal tumor. We undertook this study to evaluate the relationship between hormonal factors and a hypertensive crisis during surgery. Sixteen patients with primary aldosteronism who were scheduled for the resection of an adrenal tumor were participated in this investigation. Hormonal factors and hemodynamic variables were evaluated before induction of anesthesia, after induction of anesthesia, 30 minutes after the incision, during tumor manipulation, during resection, and immediately after surgery. During tumor manipulation, a hypertensive crisis occured in six patients (hypertensive group; HG) but not in any others (non-hypertensive group; NHG). There were no differences in hormonal levels, except epinephrine, during tumor manipulation between HG and NHG. Hemodynamic evaluations revealed an increase of systemic vascular resistance during the hypertensive crisis. We conclude that the hypertensive crisis during the manipulation of an adrenal tumor is caused by the rapid release of epinephrine from the manipulated adrenal gland. (Key words: the resection of an adrenal tumor, primary aldosteronism, hypertension)

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Primary aldosteronism, caused by an adrenal tumor, is associated with hypertension, hypokalemia, and sodium retension[1]. Primary aldosteronism is one of the few causes of hypertension which can be treated surgically and extreme variances of blood pressure and hypertensive crisis during tumor manipulation can occur[2]. One previous report described increased aldosterone or norepinephrine levels during a hypertensive crisis[3]. However, few data are available correlating the hormonal changes with the hemodynamic variables. To evaluate which hormonal factors may provoke a hypertensive crisis, we compared the changes in the concentrations of hormonal factors between hypertensive and non-hypertensive patients during surgical adrenalectomy.

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Materials and Methods

We studied sixteen patients with primary aldosteronism, aged 21–71 yr,

Table 1. Demographic Data

	HG	NHG
Number	6	10
Age (yr)	40 ± 14	46 ± 14
Sex (MF)	2/4	4/6
Combined Anesthetic Techniques (%)		
Epidural block	50	60
Use of Nitroglycerine	100	80

HG = Hypertensive group;
NHG = Non-hypertensive group.

undergoing resection of an adrenal tumor. Anesthesia was induced with thiamylal 5–6 mg·kg^{-1} iv. Tracheal intubation was facilitated with succinylcholine 1 mg·kg^{-1} iv. Anesthesia was maintained with nitrous oxide 60% in oxygen and 1–2% inspired enflurane. Neuromuscular blockade was achieved with pancuronium. A cannula was inserted into a radial artery for blood pressure monitoring and blood sampling. A 7.5Fr pulmonary artery catheter was placed via the right jugular vein in eight patients. Arterial blood gas analysis was performed immediately after induction of anesthesia to exclude abnormally ventilated patients.

Assessed hemodynamic variables and hormonal values were as follows: heart rate, systolic blood pressure, diastolic blood pressure, pulmonary artery pressure, pulmonary capillary wedge pressure (PCWP), cardiac index, systemic vascular resistance, pulmonary vascular resistance, renin activity, aldosterone, angiotensin I, angiotensin II, epinephrine, norepinephrine, bradykinin, adrenocorticotropic hormone (ACTH), cortisol. Hormonal factors were assayed using radioimmunoassay, except epinephrine and norepinephrine, which were measured by high performance liquid chromatography.

These variables were assessed at six times: before induction of anesthesia, after induction of anesthesia, 30 min after the incision, during manipulation of the tumor, during resection, and after surgery.

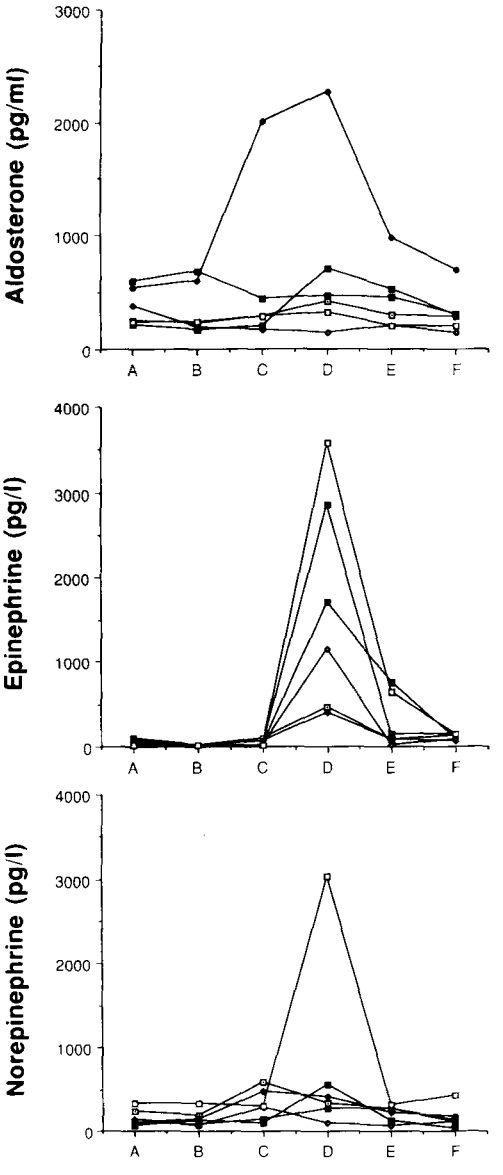

Fig. 1. Changes of aldosterone, epinephrine, and norepinephrine in the HG group. A: before induction of anesthesia; B: after induction of anesthesia; C: 30 min after the incision; D: during manipulation of the tumor; E: during resection; F: after surgery.

Table 2. Hormonal Values during Adrenal Manipulation

		HG	n	NHG	n	p-Value
Renin	($ng \cdot ml^{-1} \cdot hr^{-1}$)	1.5 ± 1.9	5	0.8 ± 1.1	9	NS
Aldosterone	($pg \cdot ml^{-1}$)	723 ± 782	6	602 ± 498	10	NS
Angiotensin I	($pg \cdot ml^{-1}$)	143 ± 201	5	43 ± 23	7	NS
Angiotensin II	($pg \cdot ml^{-1}$)	15 ± 9	6	15 ± 10	7	NS
Epinephrine	($pg \cdot l^{-1}$)	1690 ± 1295	6	80 ± 32	10	$P < 0.05$
Norepinephrine	($pg \cdot l^{-1}$)	783 ± 1112	6	200 ± 85	10	NS
ACTH	($pg \cdot ml^{-1}$)	198 ± 103	5	200 ± 127	5	NS
Cortisol	($\mu g \cdot dl^{-1}$)	27.1 ± 18.1	6	23.4 ± 7.2	7	NS
Bradykinin	($pg \cdot ml^{-1}$)	19.9 ± 9.1	2	20.5 ± 16.6	4	NS

HG = Hypertensive group; NHG = Non-hypertensive group. mean ± SD

Patients whose systolic blood pressure increased rapidly by more than 40 mmHg and exceeded 150 mmHg during adrenal manipulation were enrolled in the hypertensive group (HG) and all others were assigned to the non-hypertensive group (NHG). Anesthetic management was supervised by the same anesthesiologist.

Values were expressed as mean ± SD. A Mann-Whitney U analysis was used to compare the hormonal values between the two groups. Demographic data were compared by Fisher's exact test. A P value less than 0.05 was considered significant.

Results

Demographic data for the patients are summarized in table 1. Nitroglycerine was employed intravenously as an anti-hypertensive agent. Six patients were enrolled in the HG and ten patients in the NHG. There were no differences in the distribution of ages, gender, or combined anesthetic technique between the two groups.

Hormonal values during manipulation of the tumor are shown in table 2. There was a significant difference in the epinephrine level between the HG (1690 ± 1295 $pg \cdot l^{-1}$) and the NHG (80 ± 32 $pg \cdot l^{-1}$). Neither aldosteronenor norepinephrine levels differed between the two groups. There were no differences in renin, angiotensin I, angiotensin II, ACTH, cortisol, bradykinin between the two groups.

Systolic blood pressure before induction of anesthesia was 179 ± 24 mmHg in the HG and 177 ± 21 mmHg in the NHG (table 3). Abnormally high aldosterone levels (normal level; 28–136 $pg \cdot ml^{-1}$) were also revealed in both groups; 373 ± 161 $pg \cdot ml^{-1}$ (HG), 285 ± 223 $pg \cdot ml^{-1}$ (NHG). These values before induction of anesthesia were not related to the intraoperative hypertensive crisis. There were significant differences in systolic blood pressure, diastolic blood pressure, and epinephrine levels between the two groups during tumor manipulation.

Changes of aldosterone, epinephrine, and norepinephrine are shown in figure 1. Epinephrine levels elevated during tumor manipulation in all cases. The striking elevation of norepinephrine in one patient and aldosterone in another patient was observed.

Hemodynamic changes with pulmonary catheters are obtained in three patients in the HG. (fig. 2) A el-

Table 3. SBP, DBP, HR, Epinephrine, and Aldosterone Level in HG and NHG Over Time.

		A	B	C	D	E	F
HG (n=6)	Systolic blood pressure (mmHg)	179 ± 24	126 ± 15	130 ± 36	189 ± 30*	154 ± 28	149 ± 39
	Diastolic blood pressure (mmHg)	111 ± 25	81 ± 17	84 ± 25	113 ± 14*	102 ± 13*	90 ± 23
	Heart rate (beat·min^{-1})	107 ± 11	100 ± 7	109 ± 31	105 ± 20	110 ± 13*	99 ± 23
	Epinephrine (pg·l^{-1})	40 ± 34	13 ± 5	37 ± 37	1690 ± 1295*	284 ± 321	114 ± 36
	Aldosterone (pg·ml^{-1})	373 ± 161	351 ± 227	559 ± 718	723 ± 782	447 ± 294	322 ± 192
NHG (n=10)	Systolic blood pressure(mmHg)	177 ± 21	131 ± 25	143 ± 22	139 ± 18	136 ± 24	140 ± 20
	Diastolic blood pressure (mmHg)	108 ± 12	82 ± 15	92 ± 19	88 ± 12	83 ± 16	82 ± 14
	Heart rate (beat·min^{-1})	100 ± 24	94 ± 11	93 ± 17	89 ± 17	88 ± 16	88 ± 17
	Epinephrine (pg·l^{-1})	142 ± 300	28 ± 28	38 ± 35	80 ± 32	258 ± 408	82 ± 75
	Aldosterone (pg·ml^{-1})	285 ± 223	294 ± 259	792 ± 891	602 ± 498	392 ± 288	272 ± 198

HG = Hypertensive group; NHG = Non-hypertensive group. A: before induction of anesthesia; B: after induction of anesthesia; C: 30 min after the incision, D: during manipulation of the tumor; E: during resection; F: after surgery. mean ± SD

*Significantly different from NHG value ($P < 0.05$)

evation of systolic blood pressure was accompanied by increases of systemic vascular resistance. PCWP or cardiac index did not appear to play a major role in the hypertensive crisis.

Discussion

Primary aldosteronism is associated with hypertension that is often resistant to medications. An increase of aldosterone secretion is believed to play a role in the hypertenson[4]. Nevertheless, the etiology of intraoperative hypertensive crisis remains uncertain. It has been thought that the striking hypertension results from the release of aldosterone during adrenal manipulation.

In this study, the hypertensive crisis was highly associated with an increase in plasma epinephrine level. It is known that the epinephrine level can be easily elevated by surgical stress. However, the epinephrine level at each of the other periods did not support this hypothesis. There is no doubt that epinephrine was released from the adrenal gland by manipulation. These results imply that any anesthetic method, including epidural anesthesia[5], may not prevent this hypertensive crisis. It is possible that the relatively hgih level of aldosterone might promote the crisis.

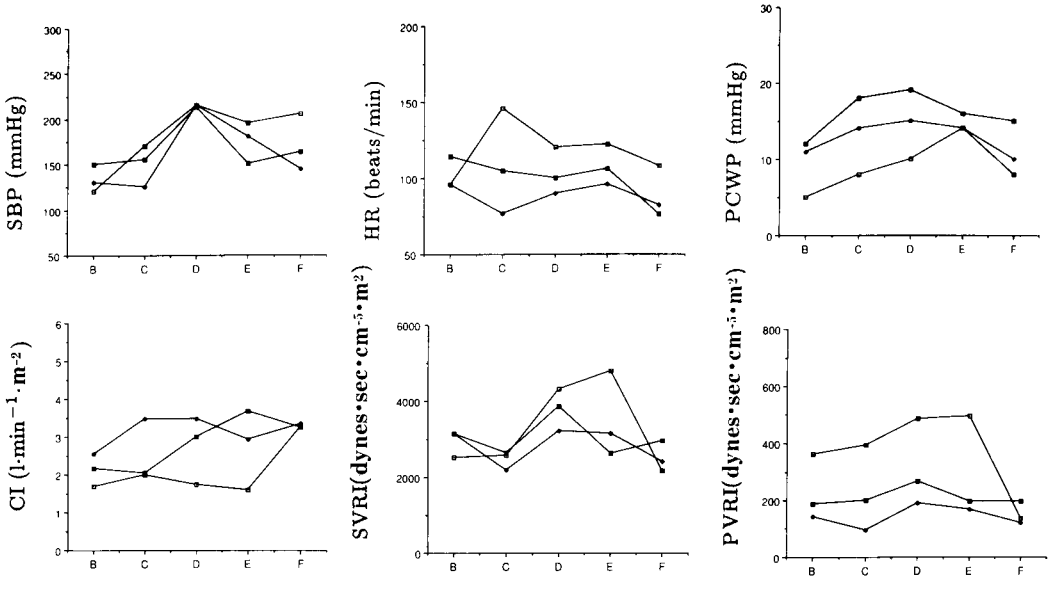

Fig. 2. Changes of hemodynamic values in HG patients with a PA catheter. B: after induction of anesthesia; C: 30 min after the incison; D: during manipulation of the tumor; E: during resection; F: after surgery.

SBP: systolic blood pressure; HR: heart rate; PCWP: pulmonary capillary wedge pressure; CI: cardiac index; SVRI: systemic vascular resistance Index; PVRI: pulmonary vascular resistance Index.

It has been thought that the cause of hypertension in primary aldosteronism is the increase of extracellular fluid volume. Purdy et al. suggested the vasoconstrictor effects of aldosterone[6]. Furthermore, sustained hypertension may facilitate the gradual elevation of systemic vascular resistance. These two factors, a volume factor and a vasoconstrictive factor, induce severe hypertension secondarily, which often become resistant to antialdosterone agents. In essential hypertension patients, the resistant arteries are sensitive to a vasoconstrictive stimulation[7]. We frequently observe that blood pressure is easily elevated by slight stimulation, such as intubation, light anesthesia, and surgical pain. Vasosensitivity in primary aldosteronism remains unclear.

Our findings differ from those of Shirasaki et al.,[3] who suggested that norepinephrine caused the striking elevation of blood pressure during tumor manipulation. Coincidental essential hypertension might influence the results. Further studies are needed to attempt to isolate the possible influence of primary aldosteronism from that of essential hypertension[8].

In summary, the present results suggest that the intraoperative hypertensive crisis in primary aldosteronism patients is highly associated with the epinephrine release from the adrenal gland caused by surgical manipulation. The hypertensive crisis is also accompanied by the elevation of systemic vascular resistance. Intravenously administered nitroglycerine was not sufficient to prevent the crisis. More potent vasodilators would be essential for the treatment of the hypertensive crisis.

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