—Report on Experiments and Clinical Cases—

Primary Aldosteronism in Pregnancy

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Abstract

Aldosteronism is a rare complication of pregnancy. We report a case of a 26-year-old woman who became pregnant soon after a diagnosis of primary aldosteronism due to left adrenal adenoma was made. Only oral potassium supplementation was required in addition to routine prenatal care until 36 weeks' gestation. Subsequently, antihypertensive medication was needed to control elevated blood pressure. A healthy male infant was delivered by cesarean section because of abruptio placentae. The postoperative course was uneventful. Left adrenalectomy was conducted eight months after delivery under laparoscopic visualization. In this case report, we discuss management of aldosteronism in pregnancy and review the literature. (J Nippon Med Sch 2000; 67: 275—279)

Key words: aldosteronism, pregnancy

Introduction

Primary aldosteronism is present in approximately 1 percent of unselected hypertensive patients[1], and is rarely associated with pregnancy. About 20 cases have been reported in the English language literature[2-19], which we have reviewed here (**Table 1**). Cases have also been reported in the Japanese literature, but these are not included in the present report.

Based on earlier reports dealing with such patients, several authors have suggested that adrenalectomy should be strongly considered in patients with primary aldosteronism during early pregnancy[15-17]. We report a case of primary aldosteronism during pregnancy in which the patient declined adrenalectomy because hypertension was not initially marked, and in whom cesarean section was indicated because of abruptio placentae.

Case Report

A 25-year-old Japanese woman had enjoyed good health other than a history of bronchial asthma during childhood until hypertension was pointed out while donating blood. She presented to the Department of Internal Medicine at Nippon Medical School, and a diagnosis of primary aldosteronism was made, upon which basis she was admitted for further evaluation. On admission, her height was 160 cm, weight 58 kg and blood pressure 150/100 mmHg. Plasma aldosterone level was 310 pg/m*l* (normal range 29.9～159 supine), plasma renin activity was 0.1 ng/m*l*/hr (0.3～2.9 supine), urinary 17 KS was 8.8 mg/day (2.4～11.0), urinary 17 OHCS was 4.9 mg/day (2.2～7.3), plasma cortisol was 11 μg/d*l* (4.0～18.3), plasma angiotensin converting enzyme was 11.4 IU/*l* (8.3～21.4), plasma epinephrine was 57 pg/m*l* (＜100), plasma norepinephrine was 248 pg/m*l* (100～450) and plasma dopamine was less than 5 pg/m*l* (＜20). Serum sodium was 146 mEq/m*l*, potassium was 2.6 mEq/m*l*

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Table 1 Review of reported cases

Reference	Age	Cause	Outcome
Crane et al[2], 1964	17	Not available	HT: refractory, IUFD at 32wk, abruptio placentae, vaginal delivery, pp: renal failure
Gordon et al[4], 1967	19	Adenoma	Adrenalectomy during pregnancy, delivery: not mentioned
Biglieri et al[5], 1967	32	Not available	HT: improved during pregnancy, vaginal delivery
Levy et al[6], 1971	25	Not available	HT: refractory, c/s at term
Aoi et al[7], 1978	30	Adenoma	Lower BP during pregnancy, vaginal delivery pp: elevated BP
	28	Adenoma	Same as above
Hammond et al[8], 1982	37	Adrenal mass	Vaginal delivery at term
Shimizu et al[9], 1983	34	Adenoma	Accelerated HT, induced vaginal delivery at 8 mo, maternal death 2yr after delivery
Elterman et al[10], 1983	39	Adrenal mass	Vaginal delivery at 36wk, virilized infant pp: heart failure
Merrill et al[11], 1984	24	Adenoma	HT refractory, c/s at 31wk
Lotgering et al[13], 1986	28	Adrenal mass	Fetal distress at 36wk, c/s
Neerhof et al[14], 1991	27	No adenoma	Fetal distress at 26wk, c/s, abruptio placentae
Baron et al[15], 1995	17	Adenoma	Adrenalectomy at 17wk, vaginal delivery at term
Aboud et al[16], 1995	29	Adenoma	Adrenalectomy in the 2nd trimester, vaginal delivery at term
Solomon et al[17], 1996	31	Adenoma	HT: refractory, adrenalectomy at 15wk, c/s at term after failed inductoin of labor
Webb et al[18], 1997	32	No adenoma	BP: well controlled, vaginal delivery at term
Fujiyama et al[19], 1999	30	Adenoma	Pulmonary congestion, fetal distress, c/s at 31wk

Two cases in which pregnancy was terminated in the early stages were excluded
HT: hypertension; c/s: cesarean section; BP: blood pressure; pp: the postpartum period.

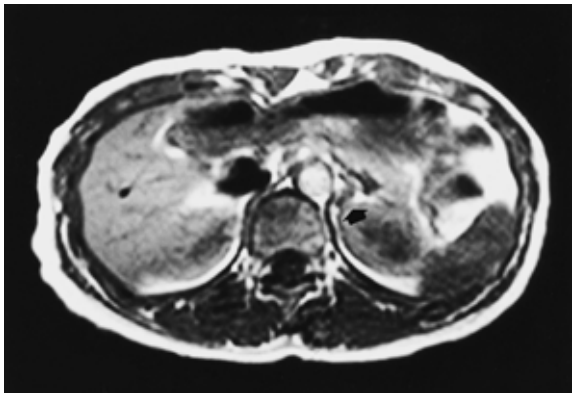

Fig. 1 MRI of the adrenal gland. A T 1-weighted image demonstrates an adenoma (arrow).

and chloride was 102 mEq/m*l*. The size and location of the aldosterone producing adenoma were determined by CT scan and MRI (**Fig. 1**). Percutaneous transfemoral adrenal vein catheterization was performed and adrenal venography demonstrated a left adrenal tumor of about 1 cm in diameter. Adrenal vein sampling demonstrated an increase in the plasma aldosterone level on the left side compared with that of the right side (greater than 4000 pg/m*l* vs. 510 pg/m*l*). Primary aldosteronism secondary to left adrenal adenoma was confirmed. Spironolactone was prescribed, but was subsequently stopped because of the appearance of skin eruption. Shortly after this point in time, the patient married a healthy 20 year-old Japanese man.

She was first seen in the Ob/Gyn outpatient clinic at age of 26 for ammenorrhea 4 months after the diagnosis of primary aldosteronism, which up to this point had not been treated with medication. At this time, she was found to be pregnant at 4 weeks' gestation. At 6 weeks' gestation, the heart beat of the embryo could be detected. Her blood pressure was 112/64 mm Hg. The values for plasma aldosterone level, renin activity, angiotensinI, angiotensinII, atrial natriuretic peptide, and serum potassium are shown in **Table 2**. The aldosterone level was elevated and gradually rose further as pregnancy advanced. The level of angiotensinII remained low. The level of atrial natriuretic peptide rose with the progress of pregnancy and further increased after delivery. The course of pregnancy was uncomplicated with only potassium supple-

Table 2 Levels of plasma aldosterone, renin activity, angiotensin Ⅰ, angiotensin Ⅱ, atrial natriuretic peptide and serum potassium.

Gestational age	Aldosterone pg/ml	Renin activity ng/ml/hr	Potassium mEq/ml	Angiotensin Ⅰ pg/ml	Angiotensin Ⅱ pg/ml	Atrial natriuretic peptide pg/ml	Blood pressure mmHg
4 weeks	370	0.2	4				
							153/92
13 weeks	370		4.2				
21 weeks	710(S)	3	3.8	77	3	< 10	126/75
31 weeks	880	1.7	3.7	39	6	31	147/71
	1,100(S)	1.7(S)					
33 weeks	910	1.2	3.8				137/72
	1,100(S)	1.7(S)					
37 weeks	1,100	1.5	4.3	55	17	52	158/106
10 days after delivery	410	0.2	3.9	< 30	< 3	110	138/90 *

Normal range: aldosterone 29.9—159 pg/ml(supine), renin activity 0.3—2.9ng/ml/hr(supine), angiotensin Ⅰ < 110pg/ml, angiotensin Ⅱ < 22pg/ml, atrial natriuretic peptide < 40pg/ml.
(S): sitting. * on antihypertensive drugs.

mentation administration (potassium L-aspartate 900 mg/day) until 29 weeks' gestation. At 31 weeks' gestation, the patient's blood pressure rose to 155/79 mm Hg, at which time she was admitted for 8 days of bed rest. Her blood pressure rose again at 35 weeks' gestation, at which time proteinuria was noted, and the patient was subsequently admitted at 36 weeks' gestation. The admission blood pressure was 172/98 mm Hg. Her weight was 67 kg at that time and no edema was evident. Salt and calorie intake were restricted to 3 g and 1600 Cal a day, respectively. Funduscopy showed diffuse narrowing of arterioles (Scheie (S) 0-I, (H) I), 24 hour creatinine clearance was 83.1 l/day and serum potassium was 3 mEq/ml. Fetal weight was estimated at 2479 g, the amniotic fluid volume was normal (AFI 14.8) and non-stress test was reactive. Pulse Doppler showed RI of the fetal mid-cerebral artery and umbilical artery, at 0.62 and 0.72, respectively. Twenty four-hour blood pressure measurements revealed that systolic pressure rose to 210 mm Hg and diastolic pressure to 150. She was asymptomatic, but antihypertensive drugs were started (hydralazine chrolide 90 mg/day and nifedipine 40 mg/day). Her blood pressure was around 140/90 mm Hg. Plasma human placental lactogen level was 6.4 μg/ml (3.0～9.9) and plasma free estriol was 25 ng/ml (5.6～29). An attempt to induce delivery was made by mechanical dilatation of the cervix, and at 38 weeks 1 day, the cervix was dilatated to 6 cm with oxytocin infusion. At this time, the patient complained of persistent low abdominal pain and vaginal bleeding was noticed. Abruptio placentae was suspected, after which a male infant was delivered by cesarean section under epidural anesthesia. Abruptio placentae was confirmed. Blood pressure during labor was within normal limits. Birth weight was 2,492 g and Apgar score were 9 at 1 min. and 10 at 5 min. Microscopic examination of the placenta was compatible with abruptio placentae.

The postoperative course was uneventful. Twenty-four-hour creatinine clearance was 120.6 l/day. On the 14 th day after delivery, the antihypertensive medication was changed to amurozipine. She was discharged on the 18 th day of puerprium. Eight months after delivery, the left adrenal gland was removed laparoscopically and adenoma of the left adrenal gland was histologically confirmed. Blood pressure and plasma aldosterone and renin activity returned to normal values.

Discussion

A diagnosis of primary aldosteronism can be made in the face of three criteria: a) diastolic hypertension without edema; b) diminished renin secretion with failure to increase appropriately following volume depletion; and c) excessive secretion of aldosterone with failure to suppress appropriately in response to vol-

ume expansion[20]. It is well known that plasma renin activity and aldosterone levels are all increased in normal pregnancy[21]. However, most reported cases of pregnancy complicated with primary aldosteronism have showed elevated plasma aldosterone and suppressed renin activity. Consequently, the usual criteria for diagnosis of primary aldosteronism based on the basal levels of aldosterone and renin activity can be relied on in pregnant patients. Provocative tests of renin stimulation or aldosterone suppressibility help to confirm the diagnosis of primary aldosteronism in nonpregnant patients. In pregnant patients, provocative tests should be limited to sodium restriction and maintaining an upright position for fear of potential risks to the fetus.

Aldosterone-producing adenomas are found in approximately 60～85% of patients with primary aldosteronism, whereas hyperplasia is found in about 20～40%[8,13,22]. The distinction between these two pathological findings as pertaining to the cause of the disorder presents significantly important therapeutic implications. That is, surgical intervention is more likely to cure hypertension in the case of adenoma, whereas with hyperplasia, surgery is seldom of value in terms of therapeutic outcome. Consequently, imaging studies of the adrenal glands are a required component in the evaluation of this disorder.

Pregnancy complicated by primary aldosteronism follows a variable course during both the prenatal and the postpartum periods. In one case, metabolic and blood pressure abnormalities improved over the course of the pregnancy[5]. Most cases reported in the literature have indicated significant risks associated with this disease. In some cases, cesarean section was indicated because of refractory hypertension[6,11] or fetal distress[13,14,19]. Some cases become more severe after delivery[7,10]. Adrenalectomy during pregnancy is proposed as the treatment of choice for this reason, provided that a localized adenoma is involved[15–17]. As for timing for an adrenalectomy, surgery early in the second trimester is recommended as with other surgeries during pregnancy[23]. However, in nonpregnant patients, it has been reported that a surgical procedure alone does not always correct the problem in cases of adenoma[24].

Conservative medical management with antihypertensive medication and potassium supplementation is the treatment in many patients with primary aldosteronism, especially among those with adrenal hyperplasia. In pregnant patients, medical options remain limited. Spironolactone is relatively contraindicated during pregnancy because of the potential for adverse effects on the fetus[10]. Angiotensin converting enzyme inhibitors should be considered as only a last resort because of the fear of risks to the fetus[25]. Calcium channel blockers may be the first choice for the treatment of patients with primary aldosteronism, both for controlling blood pressure and reducing aldosterone levels[26]. In conservative medical management, termination of pregnancy may occasionally be indicated to prevent the onset of damage to maternal vital organs.

In addition, special consideration of abruptio placenta is required. Of 20 reported cases including the present case, pregnancy was terminated in early pregnancy in 2 cases and adrenalectomy was performed during pregnancy in 4 cases. Of the remaining 14 cases abruptio placentae was present in 3 cases. Abruptio placentae is not a common condition, but can develop even when the blood pressure is in an acceptable range during delivery, as was seen in the present case.

We explained to the patient in this case that a better outcome could be expected with surgical intervention, but the patient remained opposed to adrenalectomy. Her concern were based on fear of surgery, and the fact that her blood pressure was within normal limits at that time. Webb et al.[18] proposed that except for those pregnant patients with adenoma that fail to respond to medical therapy, surgical intervention should be avoided or delayed until after completion of pregnancy. Four cases reported had a satisfactory course after adrenalectomy during pregnancy[4,15,16,17], although there is no description about the delivery in one case. It is difficult to draw conclusions because of the small number of reported cases, however it appears that a favorable outcome can be expected with adrenalectomy based on the literature published to date. We recommend adrenalectomy be considered for primary aldosteronism during pregnancy when a localized adenoma has been identified.

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