Laparoscopic Adrenalectomy on a Patient with Primary Aldosteronism during Pregnancy

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Abstract. A pregnant 26-year-old woman was referred for evaluation and management of progressive hypertension and hypokalemia at 14 weeks of gestation. Her plasma aldosterone level was markedly elevated and magnetic resonance imaging showed a right adrenal tumor. Primary aldosteronism due to an aldosterone producing-adenoma was diagnosed. Because of progressive severe hypertension, a laparoscopic adrenalectomy was performed at 17 weeks of gestation. The procedure was completed without complication, and plasma aldosterone and potassium levels rapidly improved post-operatively. However, her hypertension persisted and the growth retardation of the fetus was found. Regrettably, intrauterine fetal death was confirmed at 26 weeks of gestation. Histological examination of the placenta revealed that the placental artery had very thick walls which had apparently caused a critical failure in fetal blood flow. The optimal timing of laparoscopic surgery during pregnancy and perioperative management were subsequently discussed.

Key words: Primary aldosteronism, Pregnancy, Laparoscopic adrenalectomy

PRIMARY aldosteronism is not a rare cause of hypertension [1], and its association with pregnancy has been reported. However, we found that only 23 cases have been described in the literature published in English since the first report of primary aldosteronism in pregnancy described by Crane et al. in 1964 [2].

A recent evolution in adrenal surgery, including minimally invasive laparoscopic surgery, has largely improved modality and QOL of patients with primary aldosteronism. As of yet, however, there has been little discussion of performing laparoscopic adrenalectomy on a pregnant woman. We report a case of primary aldosteronism during pregnancy that was treated by a laparoscopic adrenalectomy and discuss the feasibility of this procedure on pregnant women.

Case Report

A 26-year-old Japanese woman was hypertensive when she registered for prenatal care at 14 weeks and 4 days of gestation. She had been healthy before becoming pregnant; however, the initial laboratory assessment revealed low potassium and high plasma aldosterone levels. She was told three years ago that she had mild hypertension that could be controlled
without medication. On admission, she was 158 cm tall, weighed 48 kg and of 16 weeks of gestation. Her blood pressure measured as high as 220/120 mmHg, and her pulse was 84 beats per minute with the administration of hydralazine hydrochloride 90 mg daily. Her clinical course is summarized in Figure 1. Results from fundoscopic and cardiovascular examinations were all within normal range. Ultrasonography showed fetal size within average range, although moderate-grade impairment of blood flow in the uterine artery was recognized. Maternal blood potassium level was 2.1 mEq/L, plasma aldosterone level was 613.4 ng/dl (normal range was reported as 7.8–74.3 (average 30.3) ng/dl in pregnant women [3]), and plasma renin activity was suppressed to 1.09 ng/ml/hr (normal range 6.75–10.5 (average 8.7) ng/ml/hr in pregnant women [3]). All other variables in blood and urine tests, including catecholamine, cortisol and adrenocorticotropic hormone (ACTH) tested in normal range. Magnetic resonance imaging revealed a round mass on the right adrenal gland clearly bordered from adjacent structures without showing any sign of malignant tumor. The tumor showed low intensity in T1-image and slightly high in T2-image displaying similar intensities as kidney. No abnormal findings were recognized in the contralateral gland (Fig. 2). Oral administration of nifedipine (20 mg/day) and potassium chloride (1.8 g/day) was initiated in addition to hydralazine and her blood pressure fell to 180/100. Further descent of her blood pressure was not intended in order to maintain uterine blood flow. Although nifedipine and potassium supplements were increased to 40 mg/day and 6 g/day, respectively, the patient’s hypertension (182/96 mmHg) and low potassium level (2.3 mEq/L) did not improve further. Moreover, massive ascites became obvious along with the potassium supplementation by drip infusion (40 mEq/500 ml/day), and her blood pressure rose again to 210–220/120–130 mmHg. Consequently, an operation was performed under general anesthesia on the seventh day after admission, which was at 17 weeks of gestation.

A laparoscopic right adrenalectomy was performed by the transperitoneal anterior approach. Pneumoperitoneum was achieved with carbon dioxide insufflation to approximately 8 mmHg of pressure. In the abdominal cavity, massive clear yellow ascites was recognized. A yellowish round tumor was easily found on the right adrenal gland. Dissection and homeostasis around the adrenal gland were accomplished by clipping and an ultrasonically activated scalpel. The tumor with lateral part of the adrenal gland was dissected with a surgical anastomosing device. Because the tumor...
was big and clearly bordered from normal adrenal gland, partial adrenalectomy was chosen in order to shorten the operation time and minimize the blood loss in this case. The total operating time was 110 minutes and blood loss was 20 grams. The excised round tumor was 25 mm in diameter, golden yellow on the cut surface and surrounded by a thin fibrous capsule (Fig. 3a). Pathological examination revealed adrenal adenoma with neither cell atypia nor invasive growth. Histological examination showed that the tumor contained a heterogeneous cell population, with large and lipid rich cells (resembling the cells of zone fasciculata) found in the center, and smaller cells with eosinophilic cytoplasm (resembling the cells of zone glomerulosa) recognized on the edge of the tumor. The non-tumoral adrenal cortex was not atrophic (Fig. 3b).

Plasma aldosterone level (7.3 ng/dL on the 1st postoperative day (POD)), and potassium level (4.1 mEq/L on the 3rd POD) rapidly improved postoperatively. Her blood pressure measured 180/110 mmHg immediately after operation and nicaldipine 2 µg/kg/hr was initiated. Because the blood pressure fell to 160/100 on the 3rd POD, nicaldipine was terminated. No further improvement in the blood pressure was observed thereafter, thus nifedipine 40 mg/day was initiated on the 8th POD and was gradually decreased to 20 mg/day to avoid insufficient uterine blood flow. No remarkable change of fetal blood flow or reduction in the amount of amniotic fluid was found in the fetus during the patient’s stay; however the estimated fetal body weight did not
increase well after operation and a significant growth retardation was recognized when she was discharged uneventfully on the 30th POD. She was followed-up on a weekly basis after discharge, with blood pressure maintained at 160–180/90–110 mmHg with 20 mg of nifedipine daily. However, the fetal growth did not improve and intrauterine growth restriction was found along with the reflux of umbilical artery flow at 21 weeks of gestation. Intrauterine fetal death was confirmed at 26 weeks. On histological examination, the placental artery had a very thick wall with marked increase in elastic fiber (Fig. 4), which appeared to have caused failure in placental blood flow.

**Discussion**

Since 1964, when Crane et al. [2] first described a case of primary aldosteronism in pregnancy, there have been 23 cases reported in the English literature. In most cases, hypertension and hypokalemia became more difficult to control as the pregnancy progressed. Often, fetal and neonatal complications have attended these pregnancies, including intrauterine growth retardation and placental abruption. As these complications likely were the result of chronic severe maternal hypertension, intensive fetal surveillance is warranted. Of 24 reported cases, including this one, vaginal delivery at term was only accomplished in 10 cases (41.7%); cesarean section was performed in 7 cases (29.2%); pregnancy was terminated early in 2 cases (8.3%); abruptio placentae was present in 3 cases (12.5%); and fetal distress was present in 3 cases (12.5%), which included a lethal case of congestive heart failure and a case of dissection aortic aneurysm.

Conservative medical management with antihypertensive medication and potassium supplementation is the initial preoperative treatment for the patients with primary aldosteronism; however, these medical options are limited during pregnancy. Spironolactone is relatively contraindicated during pregnancy because of the potential adverse effects on the fetus. Likewise, angiotensin converting enzyme inhibitors are considered only as a last resort because of potential risks to the fetus. Calcium channel blockers may be the treatment of choice for pregnant patients with primary aldosteronism. For aldosterone producing adrenal adenoma, surgical removal of the tumor is the treatment of choice. After unilateral adrenalectomy, an excellent response in blood pressure has been reported; 70–89% of patients became normotensive, and the remainder showed improvement after surgery. In five cases [4–8] an adrenalectomy was performed during pregnancy (Table 1). All cases reported a satisfactory course after the adrenalectomy in reducing hypertension. Thus, it would seem reasonable to consider proceeding directly with surgery in the late first or early second trimester, rather than to attempt medical management given the extreme risk of hypertension to the fetus. In addition, we would like to emphasize the importance of early diagnosis and treatment of hypertension during first trimester in order to avoid irreversible pathological change in the placental vessels, as found in our case.

Recently, laparoscopic adrenalectomy has become a standard operative procedure to manage adrenal tumors because it is less invasive than alternative operative treatments and equally efficacious. Here at Osaka City University Graduate School of Medicine, we have performed laparoscopic adrenalectomy in more than 150 cases in the last 10 years and found it useful and safe as compared to the conventional open surgery [9]. Operation time is not any longer compared with open surgery, and it is even shorter now after applying this technique as a routine procedure. Furthermore, it is obvious that minimal invasiveness and rapid improvement after operation would result in lower intra-abdominal pressure in cases in which laparoscopic surgery was applied rather than in cases where open surgery was not possible.
surgery was applied. The present case was the first occasion that we performed laparoscopic adrenalectomy on a pregnant woman. Prior to this case, we did have experience successfully applying laparoscopic surgery (cholecystectomy) during pregnancy. Gouldman et al. [10] reported eight laparoscopic cholecystectomies performed in pregnant patients and observed no postoperative complications to mother or fetus. Furthermore, laparoscopic adrenalectomies have also been undertaken to treat pheochromocytoma [11] and Cushing’s syndrome [12] during pregnancy. Thus, we believed that laparoscopic adrenalectomy could be performed safely during pregnancy. Still to our knowledge only a case report by Shalhav et al. [7] describes the application of this minimally invasive technique to aldosterone producing adenoma of the adrenal gland in pregnancy that concluded in a live birth. They concluded that laparoscopic adrenalectomy is safe and reasonable to apply during pregnancy when it was performed 1) during the early second trimester, 2) with open pneumoperitoneum creation, 3) with less than 12 mmHg pressure of pneumoperitoneum, and 4) fetal monitoring throughout the procedure. In our case, as Shalhav had reported, laparoscopic adrenalectomy was performed at 17 weeks of gestation because of refractory hypertension and difficulty in continuing pregnancy. There was no trouble during the operation. Although hypertension persisted after operation, the potassium level rapidly improved postoperatively and she was discharged uneventfully. Regrettably, however, intrauterine fetal death was confirmed at 9 weeks after the operation. At that time, a marked thickening of the placental artery was found. We assumed that the extremely high blood pressure of the mother had already affected the placental vessel causing irreversible change that resulted in insufficient blood flow to the fetus, because the uterine blood flow had already been impaired before operation. Although it might be difficult to predict the fetal outcome, Okawa et al. [13] suggested that PRA level might be an important factor. They proposed, from the review of 27 reported cases, that PRA level higher than 1.0 ng/ml/hr indicated poor fetal outcome, as in the present case.

In conclusion, laparoscopic adrenalectomy can be performed safely on a patient with primary aldosteronism in pregnancy, but strict preoperative blood pressure control from the initial stage before complete placental formation and a gradual lowering of blood pressure with fluid compensation after operation are advised to minimize the risks to the fetus as well as the mother.

<table>
<thead>
<tr>
<th>Reporter (year)</th>
<th>Age</th>
<th>Operation timing</th>
<th>Blood pressure Before ope.</th>
<th>After ope.</th>
<th>Plasma aldosterone concentration</th>
<th>Plasma renin activity</th>
<th>Potassium level (mEq/l)</th>
<th>Outcome</th>
<th>Pathological Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gordon et al. (1964)</td>
<td>19</td>
<td>18W</td>
<td>170/110</td>
<td>120/80</td>
<td>8420 µg/day&lt;sup&gt;a&lt;/sup&gt;</td>
<td>130 ng/100 ml&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.8</td>
<td>not mentioned</td>
<td>left adrenaoma 4 × 3 cm</td>
</tr>
<tr>
<td>Baron et al. (1995)</td>
<td>17</td>
<td>17W</td>
<td>150/90</td>
<td>Normalized</td>
<td>90 ng/dl</td>
<td>1.0 ng/ml/hr</td>
<td>2.1</td>
<td>vaginal delivery at term</td>
<td>right adrenaoma 2 × 3 cm</td>
</tr>
<tr>
<td>Aboud et al. (1995)</td>
<td>29</td>
<td>2nd trimester</td>
<td>130/90</td>
<td>130/80</td>
<td>3700 pmol/l&lt;sup&gt;c&lt;/sup&gt;</td>
<td>0.2 nmol/l/hr&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.4</td>
<td>vaginal delivery at term</td>
<td>left adrenaoma 1.2 × 1 cm</td>
</tr>
<tr>
<td>Solomon et al. (1996)</td>
<td>31</td>
<td>15W</td>
<td>180/120</td>
<td>130/86</td>
<td>44.3 ng/dl</td>
<td>0.33 ng/dl/hr</td>
<td>2.3</td>
<td>Cesarean at term</td>
<td>left adrenaoma 1.6 cm</td>
</tr>
<tr>
<td>Shalhav et al. (2000)</td>
<td>23</td>
<td>2nd trimester laparoscopic</td>
<td>254/154</td>
<td>Improved</td>
<td>25 ng/dl</td>
<td>&lt;0.2 ng/dl&lt;sup&gt;e&lt;/sup&gt;</td>
<td>3.3</td>
<td>vaginal delivery at 34W</td>
<td>left adrenaoma 2 × 2 cm</td>
</tr>
<tr>
<td>Our case (2005)</td>
<td>26</td>
<td>17W laparoscopic</td>
<td>230/142</td>
<td>160/100&lt;sup&gt;f&lt;/sup&gt;</td>
<td>613.8 ng/dl</td>
<td>1.09 ng/ml/hr</td>
<td>2.1</td>
<td>intrauterine fetal death at 26W</td>
<td>right adrenaoma 2.5 × 2.6 cm</td>
</tr>
</tbody>
</table>

Normal range for plasma aldosterone level was reported as 7.8–74.3 (average 30.3) ng/dl, and for plasma renin activity was 6.75–10.5 (average 8.7) ng/ml/hr in pregnant women [3]. Also normal ranges were described individually as: a) 307–2912 µg/day, b) 860–1515 ng/100 ml, c) and d) not mentioned, e) 2.9–24 ng/dl, in each report, f) with nifedipine 20 mg/day.
References


