Cushing’s syndrome during pregnancy caused by adrenal cortical adenoma: a case report and literature review

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Abstract Cushing’s syndrome (CS) during pregnancy is a rare condition with significant maternal and fetal complications. A case of CS during the third trimester of pregnancy secondary to adrenocortical adenoma was reported. Literature review revealed the disadvantages of different treatments in this period. Besides the conservative treatment, surgery is recommended for CS during the third trimester of pregnancy secondary to adrenal adenoma, if an experienced surgeon is available.

Keywords Cushing’s syndrome; pregnancy; adrenocortical adenoma

Introduction

Cushing’s syndrome (CS) during pregnancy is a rare condition with significant maternal and fetal complications. The most common cause of CS during pregnancy is adrenal adenoma, followed by pituitary etiology, and adrenal carcinoma [1]. Surgical treatment of CS in pregnancy is recommended, except during the third trimester. If surgical therapy is contraindicated, then medical therapy may be considered.

In this article, we report a case of CS during the third trimester of pregnancy secondary to adrenocortical adenoma. Literature review revealed the outcome of different treatments in this period.

Case

A 24-year-old female G2 P1 patient presented with striae and leg swelling at 32 weeks of gestation. Physical examination revealed blood pressure of 127/79 mmHg, body mass index of 29.93 kg/m², buffalo hump, face and back acne, as well as striae of armpits, abdomen, and legs, and lower extremity edema. Laboratory data (Table 1) showed increased 24 h urine cortisol, elevated plasma cortisol, loss of diurnal cortisol rhythm, and total suppression of adrenocorticotropic hormone (ACTH), which are consistent with CS caused by primary adrenal hypercortisolemia. In addition, low-dose and high-dose dexamethasone suppression tests showed abnormal results. A low level of serum potassium and a negative 24 h urine microalbumin were detected. Result of the 75 g oral glucose tolerance test was abnormal (fasting glucose 92 mg/dl, 172 mg/dl after 1 h, and 161 mg/dl after 2 h). Hyperglycemia was diagnosed and a low glucose diet was instituted.

Table 1 Results of serum and urine chemical tests of patient

<table>
<thead>
<tr>
<th>Test</th>
<th>Results</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 AM serum cortisol (μg/dl)</td>
<td>31.35</td>
<td>8.7–22.4</td>
</tr>
<tr>
<td>4 AM serum cortisol (μg/dl)</td>
<td>24.76</td>
<td></td>
</tr>
<tr>
<td>0 AM serum cortisol (μg/dl)</td>
<td>25.59</td>
<td></td>
</tr>
<tr>
<td>24 h urine cortisol (μg)</td>
<td>2131.38</td>
<td>39–348</td>
</tr>
<tr>
<td>8 AM serum ACTH (pg/ml)</td>
<td>&lt;1</td>
<td>7.2–63.3</td>
</tr>
<tr>
<td>Low-dose dexamethasone midnight suppression test</td>
<td>8.72% &gt;50%</td>
<td></td>
</tr>
<tr>
<td>High-dose dexamethasone suppression test</td>
<td>8.16%</td>
<td></td>
</tr>
</tbody>
</table>

Fetal ultrasonography revealed a single fetus with single umbilical artery. Magnetic resonance imaging confirmed the presence of a 25 mm × 24 mm × 20 mm left adrenal mass.

The patient was treated with potassium supplements. At 36 weeks and 5 days of gestation, she spontaneously delivered a 3460 g male baby with an Apgar score of 10 at both 1 and 5 min. After delivery, hypertension was
detected in the patient, with the highest blood pressure at 140/100 mmHg. Nifedipine controlled-release tablets 30 mg qd was prescribed to control the blood pressure for three weeks.

A month after delivery, the patient underwent left adrenalectomy via laparoscopy without complication. Histology confirmed a benign adenoma. Glucocorticoid replacement with prednisone (5 mg/d) was begun after the operation.

**Literature review**

To determine the better option between surgical and conservative treatment for CS during the third trimester of pregnancy, we identified all cases reported in English by using MEDLINE, together with the references in each publication. A total of 42 patients (44 pregnancies) with CS caused by adrenocortical adenoma during the third trimester were identified in the period between 1961 and 2014. The current case was included. Unilateral adrenalectomy was performed before delivery in nine [2–9] of these patients (Group B). Conservative management was adopted in the remaining 35 pregnancies (Group A) [10–17].

Here, we summarized the results without comparing the difference between the two groups.

**Perinatal outcome (Table 2)**

Among the 35 pregnancies in Group A, 19 patients ended in preterm birth (54.3%), whereas 9 patients ended in term birth (25.7%). The number of cases of spontaneous abortion, stillbirth, neonatal death, and intrauterine growth retardation was 3 (8.6%), 4 (11.4%), 3 (8.6%), and 4 (11.4%), respectively. In Group B, the term birth rate was 66.6% (6 patients), whereas the preterm birth rate was 33.3% (3 patients). No other perinatal outcome was mentioned.

**Maternal outcome (Table 3)**

Hypertension is the most common maternal outcome both in Groups A (94.3%) and B (55.6%), followed by diabetes mellitus (42.9% and 11.1%, respectively). No other maternal outcome was mentioned for Group B. For Group A, the rate of pre-eclampsia and pulmonary edema were both 17.1%, which account for the main reason of emergency cesarean. In Group A, 3 (8.6%) patients suffered from wound complication, and no maternal death.

**Surgical timing**

The latest gestation age of surgery was 32 weeks in Group B. The time of adrenocortical adenoma surgery in Group A ranged from 0.25 to 72 months after delivery.

**Surgical complication**

Only one case in Group B reported signs of fetal distress 12 h after adrenalectomy (case 13).

**Discussion**

The first description of CS during pregnancy was reported by Hunt and McConahey in 1953 [18]. Since then, at least 166 pregnancies have been reported involving 149 patients as individual cases and small case series [8,9,11–14,16,19–36]. The etiology of CS in pregnant women is different from that in general population. Adrenal adenomas account for approximately 40%–50% of CS during pregnancy. Cushing’s disease appears to be less common during pregnancy, 33% of 122 pregnant women [20].

The diagnosis of CS during pregnancy is difficult because not only the clinical presentation, but also the laboratory result changed in pregnancy. Clinically, striae, hypertension, and gestational diabetes are common features in normal pregnancies; however, hypertension and diabetes are also the most common signs of CS in pregnant women (70% and 30% of all cases, respectively). Furthermore, biochemically normal pregnancy is associated with a threefold increase in plasma cortisol because of increased production of cortisol and cortisol-binding globulin. The urinary free cortisol (UFC) concentration also increases, and dexamethasone does not suppress
plasma cortisol to the same degree as that during a non-pregnant state [37].

Current data suggest that a combination of UFC concentrations greater than 3 times the upper normal limit and elevated midnight plasma or salivary cortisol concentrations could be the best strategies for screening and diagnosis of CS during pregnancy [38].

Treatment for pregnant patients with CS tends to be implemented sporadically, generally late in the course of the pregnancy. As a result, prevention of adverse outcomes is not well-established [39]. In the third trimester, conservative treatment and early delivery are preferred [40]. Meanwhile, the risk of surgery becomes more obvious as the pregnancy progresses, given that technical difficulties are encountered in the third trimester because of enlarged uterus, increased intra-abdominal pressure on uterine blood flow, and potential acidosis caused by carbon dioxide absorption.

In general, the perinatal and maternal outcomes of Group B were better than that of Group A. This difference could be mainly explained by the fact that, unlike the conservative treatment (i.e., cesarean delivery), surgical treatment of adrenocortical adenoma is selective. Further evidence is necessary to determine which option is better. A strict clinical research based on paired subjects is needed to provide convincing results. The data in Tables 2 and 3 showed that surgery did not increase the rate of perinatal and maternal outcomes. Thus, surgery seems to be a safe choice, particularly before 32 weeks of gestation.

In the current case, the patient did not receive surgery nor medication for CS. She eventually gave birth to a full-term healthy infant via vaginal delivery. The treatment plan for each case should be based on the clinician’s experience and the patient’s general condition.

When adrenocortical adenoma is suspected as the underlying cause of CS in the third trimester, surgery could be an alternative to conservative treatment given that an experienced surgeon is available.

Compliance with ethics guidelines

Wei Wang, Fengyi Yuan, Dan Xu declare that they have no conflict of interest. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). Informed consent was obtained from the patient included in this study.

References