

## A Case of Cushing's Syndrome in Pregnancy Secondary to an Adrenal Cortical Adenoma

Cushing's syndrome in pregnant women is rare and difficult to be diagnosed because of the syndrome's association with oligomenorrhea or amenorrhea and the changes in cortisol metabolism during normal pregnancy. Cushing syndrome in pregnancy is usually confused with complicated pregnancy, such as preeclampsia or gestational diabetes, and its rarity leads to a low degree of clinical suspicion, often delaying diagnosis. We experienced a case of Cushing's syndrome in pregnancy, which had been considered as the severe preeclampsia and gestational diabetes due to uncontrolled hypertension and hyperglycemia. The pregnancy was terminated with an emergency cesarean operation at 30 weeks of gestation because of severe preeclampsia. In consequence of the evaluation about the Cushing's syndrome after delivery, the adrenal cortical adenoma of right adrenal gland was diagnosed and laparoscopic adrenalectomy was performed.

**Key Words :** Cushing's Syndrome; Pregnancy; Adenoma, Adrenal Cortical

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Received : 18 March 2002  
Accepted : 8 July 2002

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### INTRODUCTION

Pregnancy rarely occurs in women with Cushing's syndrome (CS), because both excessive cortisol and androgen levels suppress gonadotropin secretion and impair ovarian and endometrial functions. CS usually presents with hypertension and diabetes, so it may give rise to increase maternal and fetal morbidity, including high rates of miscarriage or premature delivery. Here we report a case of CS in pregnancy secondary to an adrenal cortical adenoma, which was diagnosed after delivery and treated with laparoscopic adrenalectomy.

### CASE REPORT

A 30-yr-old pregnant woman gravida two para one at 30 weeks of gestation was referred and admitted in March 31 2001, because of the difficulty of controlling hypertension and cushingoid features. She had been diagnosed the gestational diabetes at 27 weeks' gestation by the 100-gram oral glucose tolerance test, and had been controlled through the diet control. She experienced preeclampsia in her previous pregnancy and was delivered by cesarean operation.

Physical examination revealed with some features of CS, including moon face, truncal obesity, muscular atrophy, purple striae on the abdomen, hyperpigmentation over pressure areas and acne. Her blood pressure in hospital ranged

from 150/100 to 190/120 mmHg. She was administered with intravenous hydralazine, but her blood pressure was not controlled.

Her blood sugar level after admission was 106 mg/dL due to diet control. Urinary dipstick test revealed significant proteinuria (+++). Except for mild increased serum GOT/GPT (57/100 U/L), other laboratory abnormalities were not found.

Fetal ultrasonography revealed a single viable fetus with normal morphology and parameters. Diastolic pressure of umbilical artery was nearly absent and RI was checked at 0.97. The fetal heart rate monitoring disclosed a loss of variability. Because of severe preeclampsia and compromised fetal status, emergency cesarean operation was performed. A 1,220-gram female baby with Apgar scores of 6 at 1 min and 8 at 5 min was delivered. The neonatal course was complicated by a moderate respiratory distress syndrome requiring artificial surfactant. The baby was discharged 3 months later in a good condition.

A provisional diagnosis of CS in pregnancy with gestational diabetes was made after delivery because of some clinical features of CS above described, and plasma cortisol, 24-hr urinary free cortisol and plasma ACTH, the plasma cortisol response to low- and high-dose dexamethasone suppression tests was measured. Her morning and evening plasma cortisol levels were 26.3  $\mu$ g/dL (normal: 5-25  $\mu$ g/dL) and 34.6  $\mu$ g/dL (normal: half of the morning level), respectively. 24 hr urinary free cortisol were 409.5 nmol/day (normal: 55-248 nmol/day), and were not suppressed with low-dose or

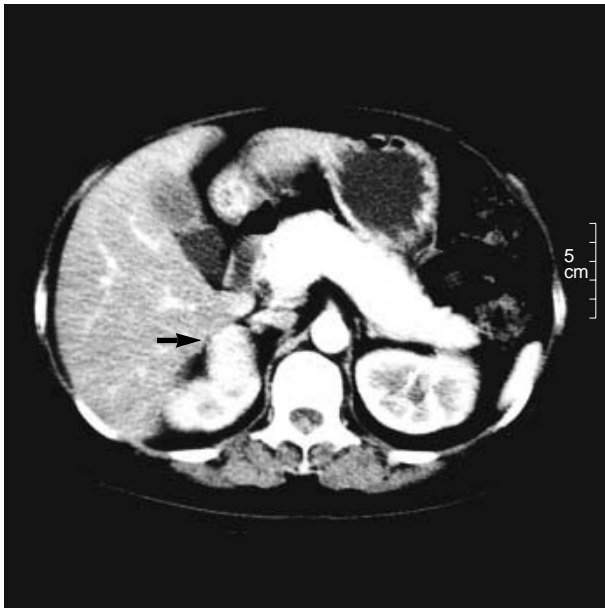


Fig. 1. Abdominal CT showing a right adrenal mass (arrow).

high-dose dexamethasone loading. ACTH level was 2-14 pg/mL (normal: 10-60 pg/mL). Abdominal CT detected a 3-cm sized right adrenal mass (Fig. 1). The final diagnosis was CS in pregnancy secondary to an adrenal tumor. The patient underwent a laparoscopic right adrenalectomy. Pathologic examination showed a benign adrenocortical adenoma.

Maintenance steroid replacement was continued postoperatively until now because of impaired adrenal function.

## DISCUSSION

The occurrence of pregnancy in the face of untreated CS is rare because of the high incidence of ovulatory disturbances experienced by patients with the disorder. In 1953, Hunt and McConahey (1) first reported several cases of pregnancy associated with untreated Cushing syndrome. Since then Buescher et al. (2) reviewed a total of 58 patients with 65 pregnancies associated with CS in the world literature and found that 50% of these cases were caused by adrenal adenoma, in contrast to 15.7% in nonpregnant women. In 1998, Murakami et al. (3) showed similar results that the benign adrenocortical adenoma was found in about half of pregnancy with CS, but the most common cause of CS in nonpregnant women was pituitary-dependent adrenal hyperplasia. This difference may be related to the mechanism of ovulation suppression. In other words, the patient with pituitary-dependent CS could due mainly to a disturbed gonadotropic axis, such as cosecretion of prolactin, but the patients with an adrenal adenoma are more likely to be purely cortisol-producing, allowing women to retain more often their ovulatory function (2-4).

CS is a disease associated with high mortality rates, estimated at 50% at 5 yr when the disease is untreated. CS in pregnancy follows a hazardous course with an increased incidence of abortion, premature labor, hypertension, gestational diabetes, cardiac failure and even pulmonary edema (2, 3, 5). It is therefore not surprising that the maternal morbidity in CS is excessive.

Hypertension and glucose intolerance are common maternal complications. Their incidences are reported as high as 58.8% and 25.0%, respectively (3). In this case, blood pressure was also very high and was not controlled by intravenous hydralazine administration. Although the maternal glucose level in this patient was not so high at the time of admission, postpartum blood glucose level ranged from 110 mg/dL to 240 mg/dL. This may be owing to the patient's strict diet control during antepartum period.

Fetal complications are also severe. Preterm deliveries, between 22 and 36 gestational weeks, were associated with half of pregnancies. Intrauterine growth retardation (IUGR) occurred in 13.2% and perinatal deaths were 8.8% of the pregnancies (3). Fetal weight in this case was 1,220-gram, so IUGR was not marked, considering that the gestational age was 30 weeks.

If the etiology of CS is adrenal adenoma, the therapeutic alternatives are unilateral adrenalectomy during pregnancy or medical treatment with operation performed after delivery (6, 7). The ideal timing for an adrenalectomy is not known, but most obstetricians and surgeons consider the second trimester to be suitable as the pregnancy is relatively more stable during this period (8). This patient was treated with laparoscopic adrenalectomy after delivery because the diagnosis was made after cesarean operation. Successful medical treatment of hypercortisolism secondary to an adrenal adenoma during pregnancy with metyrapone or ketoconazole has also been reported (9). However, metyrapone crosses the placenta and may affect fetal adrenal steroid synthesis, and ketoconazole is teratogenic and embryotoxic in animals (10). This treatment could be an alternative for poor surgical candidates or be used to stabilize patients prior to operation.

We believe that CS complicating pregnancy is a high-risk obstetric condition. Definitive treatment during pregnancy may not alter the perinatal outcome except for a reduction in the prematurity rates. During the third trimester, early delivery of the fetus, with delay of definite therapy until after delivery, may be the most prudent course. Vaginal delivery is preferable to cesarean operation because of the problems with poor tissue healing and wound breakdown. Therapy must be individualized between a definitive surgical approach versus alleviation of hypercortisolism using chemotherapy. There is no logical phase for supportive therapy alone because maternal and perinatal outcomes are unacceptably poor in the face of untreated Cushing syndrome.

Conclusively, CS in pregnancy requires a high index of suspicion because of its rarity, therefore CS is worthy of being

considered when a pregnant woman develops high blood pressure and/or hyperglycemia. Otherwise, both mother and fetus may have poor outcomes, since the diagnosis is delayed and treatment is not instituted in a timely manner.

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