CASE REPORT

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Cushing's Syndrome during Pregnancy: Post Delivery Adrenalectomy Consequent to Medical Management without Adrenal Enzyme Inhibitors

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Abstract

A 32-year-old female, gravid two, para one, with Cushing's syndrome (CS) was admitted to our hospital at 25 week of gestation with severe hypercortisolism. Basal urinary free cortisol (UFC) was elevated about 10 times above the upper limit of normal in two separate times and plasma cortisol failed to suppress after an overnight 1mg dexamethasone suppression test but Adrenocorticotropic hormone (ACTH) level was suppressed. An abdominal non-contrast magnetic resonance imaging (MRI) disclosed a 3-cm right adrenal mass (Fig. 1). Due to her critical general condition, the adrenalectomy was not performed. At 30 week of gestation, by the diagnosis of severe preeclampsia she underwent an emergent cesarean section. Two weeks later, right adrenalectomy was performed via laparotomy. Pathologic examination of the gland showed a benign adrenocortical adenoma. The newborn was a healthy male who weighed 1850 gram. There was no clinical or biochemical suppression of adrenocortical function in child and they were discharged after 40 days.**[GMJ. 2012;1(1):38-41]**

Keywords: Adrenalectomy - Cushing's syndrome – Preeclampsia - Pregnancy

Introduction

Cushing's syndrome (CS) occurs rarely during pregnancy and is difficult to be diagnosed (1). The diagnosis of Cushing's syndrome during pregnancy (CSP) needs a high index of clinical suspicion (2), because it is confounded by normal hormonal changes of pregnancy and it is easily obscured with complications of pregnancy, such as gestational hypertension (GHTN), preeclampsia and gestational diabetes mellitus (GDM) (3). Furthermore, management of CSP is an arduous work in presence of deleterious effects of several factors redounded to maternal and fetal morbidity. These deleterious effects are due to hypercortisolism, the side effects of medications and the problems of surgical resections of adrenal pathology and the potential risk of laparascopy during pregnancy including fetal acidosis or decreased uterine blood flow (4).

We represent a rare case of CSP who could not undergo surgical treatment of adrenal adenoma during pregnancy, as a consequence of her poor general condition.

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Case Report

A 32-year-old multiparous woman was referred to our center at 25 week of gestation with symptoms and signs of severe hypercortisolism. Initially she was formerly admitted to another hospital at 10 week of gestation with GHTN and GDM based on (100gr) OGTT. After 15 weeks, she was hospitalized in our hospital with dyspnea, resistant HTN, aggravation of GDM and symptoms and signs of CS including, moon face, buffalo hump, proximal muscle weakness and edema especially on the lower limbs, easy bruising, wide purple striae on the abdomen and calves and hypokalemia. Our case had no signs or symptoms of CS before pregnancy.

Her blood pressure was 195/90 mm Hg. The serum sodium level was 139 mmol/l, serum potassium was 3.5 mmol/l and spot sugar level was 95 mgr/dL on insulin therapy. She was assessed for her shortness of breathing during her hospitalization.

The diagnosis of CS was confirmed by:a high plasma cortisol level of 40 µg/dL (normal range: 5.5-26.1 µg/dL), which was not suppressed by (1mg) dexamethasone.a high 24-hour urinary free cortisol (UFC) level of 732 µg/24h (normal range: 13-75 µg/24h),and a low ACTH level of less than 1 pmol/l (normal range: 2.0-11.6 pmol/1).

An abdominal non-contrast magnetic resonance imaging (MRI) subsequently disclosed a 3-cm right adrenal mass (Fig. 1). Based on these findings, a diagnosis of CS caused by a right adrenal tumor was made. Color Doppler sonography of lower extremities showed no evidence of deep vein thrombosis. According to dyspnea, echocardiography was done and confirmed heart failure. The fetus condition had been under fetal heart rate monitoring and repeated sonography.

The patient was treated with antihypertensive therapy (i.e. hydralazine and methyldopa) and insulin twice daily (42 u/24h NPH, 30 u/24h regular); however, her hypertension responded poorly to these treatments. According to surgeons' consultation, she was not a good candidate for surgical treatment and also medical treatment of hypercortisolism was not possible, as we had not had any access to metyrapone and ketoconazole is teratogenic in pregnancy.

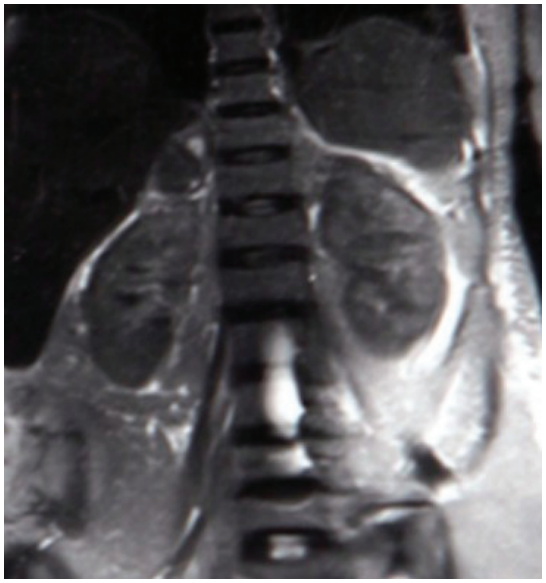

Figure 1.MRI showing a well margined heterogeneous 43*35*20 mm mass in the right adrenal gland (Arrow).

Pregnancy was uneventful until 30 week of gestation with hydralazine and methyldopa, when she presented with severe dyspnea, aggravation of proteinuria (295 mg/24 hr) and refractory hypertension (more than195/100) and headache, but without thrombocytopenia or abnormality in liver enzymes, with the diagnosis of severe preeclampsia, she underwent an emergency lower-segment cesarean section at 30 week of gestation. The newborn was a healthy boy who weighed 1850 gr with Apgar scores of 7-8 at 1st min and 7 at 5th min. Hypokalemia, hypertension, hyperglycemia and other manifestations of crushing's syndrome continued in mother, after delivery with no amelioration. Medical treatment of hypercortisolism began with ketoconazole, immediately after delivery. Due to critical general condition of mother, the adrenalectomy was postponed 2 weeks and right adrenalectomy was performed after two weeks of cesarean section. Pathologic examination of the gland showed a benign adrenocortical adenoma with no evidence of malignancy. Both postoperative periods were uneventful; although, the patient was kept in ICU for 3 days. She had no problem with wound healing.

Maintenance steroid replacement was continued postoperatively until now because of

impaired adrenal function. There was no congenital abnormalities and no clinical or biochemical suppression of adrenocortical function in the newborn. The neonatal course was complicated with mild respiratory distress syndrome required NICU admission. The baby was discharged home in good condition after 40 days.

Discussion

CS is associated with infertility in approximately 71% of female patients who have the disease so it is rare during pregnancy (1). However, some of the patients remains fertile, although pregnancy is uncommon and is associated with fetal morbidity includes prematurity (43%), intrauterine growth restriction (21%), and stillbirth (6%) (5). These patients are prone to GDM, severe GHTN and preeclampsia, wound complications, muscle weakness, profound depression, congestive cardiac failure, pulmonary edema or even death (6).

We present a case in this report who demonstrates the safety and utility of delayed surgical treatment after stabilization of the patient with CSP secondary to adrenal adenoma. Although this patient, had typical features of CS, including weight gain, wide striae, fatigue, plethora, proximal weakness, spontaneous ecchymosis and mood changes. These features are similar to those of normal pregnancy, and they are nonspecific. The single finding that appropriately prompted an evaluation of this patient for CS was unexplained hypokalemia.

The biochemical diagnosis of hypercortisolemia in pregnancy is accompanied by two confounding factors. First, cortisol production rates markedly increase during pregnancy, thus UFC levels in the second and third trimesters may overlap with levels seen in CS (7). Second, levels of corticotropin rise despite increasing cortisol levels which are consistent with the occurrence of decreased feedback on corticotropin secretion. Therefore, unless cortisol levels are markedly elevated, the results of these tests may be difficult to interpret. Regarding low-dose dexamethasone suppression test was suggested to be used to diagnose CS (8). We used low-dose dexamethasone suppression test besides UFC levels which were more than 600μg above the upper limit of the normal range during two 24-hour periods in the absence of glucocorticoid therapy. These findings established the diagnosis of CS clearly. Undetectable corticotropin level is considered to be suggestive of corticotropin-independent CS (9). We used a non-contrast MRI for evaluation of adrenal which have been recently cited by investigators (10).

If the etiology is adrenal adenoma as in our case, the therapeutic alternatives are unilateral adrenalectomy during pregnancy (6, 11-12) or medical treatment with operation performed after delivery (13-15). The presented case was not surgically treated as a consequence of her poor general condition, and the adrenalectomy postponed 2 weeks after CS. It has delineated which surgical treatment during pregnancy is associated with better fetal outcomes, although the difference did not reach statistical significance (16).

However, immediate surgical treatment for adrenal adenoma during pregnancy was recommended, as it seemed to be the preferred treatment option which is likely to improve fetal outcomes (17), we think it must be applied with caution. Care should be taken while assessing the benefits of various treatment options individually. In the present case, the risk of surgery was high due to her heart failure. So we preferred to wait until she became more stable and so it was eventually done two weeks later. Then in the choice of optimal time and method of treatment, factors such as age, parity, past obstetric history, gestation at diagnosis and severity of disease should have been taken into consideration.

This report shows that, choosing the method of treatment should be weighted for every case individually. Treatment is effective even by controlling hypertension of hypercortisolism during pregnancy by medical managment (hydralazine and methyldopa) without adrenal enzyme inhibitors therapy (ketoconazole or metyrapone) and by performing adrenalectomy with laparotomy after delivery.

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