

A Case of Cushing's Syndrome in Pregnancy

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What's Known

- Pregnancy is rare in women with Cushing's syndrome because hypercortisolism and hyperandrogenism suppress gonadotropin secretion.
- Decision on treating Cushing's syndrome during pregnancy and choice of treatment method are difficult since they must be approached on a case-by-case basis. They also depend on the disease's etiology and severity and gestation time.

What's New

- Novelty of this case is Cushing's syndrome and its presentations in pregnancy.

Abstract

Cushing's syndrome (CS) occurs rarely during pregnancy. CS can be caused by prolonged abnormal exposure to excess glucocorticoids leading to special and significant signs and symptoms. It is often difficult to diagnose pathological hypercortisolism in pregnant women since some symptoms of the disease might be due to a complicated pregnancy, including preeclampsia or gestational diabetes. In this study, we report the case of a 29-year-old female who referred to our institution with hypertension, weakness, striae, and truncal obesity. Physical examination revealed cushingoid characteristic. She was also found to be 27 weeks pregnant. CS was diagnosed on the basis of abnormal serum cortisol and adrenocorticotropic hormone (ACTH) levels, as well as radiologic findings. She eventually gave birth to a preterm infant via vaginal delivery. A right adrenal adenoma was diagnosed and was subsequently treated with surgical resection. The patient's condition remained stable after the surgery.

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Introduction

There are some maternal and fetal complications during pregnancy, such as hypertension, diabetes, heart failure, preterm labor, and growth retardation. However, Cushing's syndrome is rare in pregnant women because hypercortisolism and hyperandrogenism suppress gonadotropin secretion and leads to amenorrhea or oligomenorrhea in most cases.¹

Hypercortisolism leads to serious complications for the mother and fetus, including premature labor and high fetal mortality.² Long-term medical therapy for CS is ineffective and definitive therapy is the resection of pituitary or adrenal adenoma or bilateral adrenalectomy for hyperplasia.³ In this study, we report the case of a pregnant woman with Cushing's syndrome due to adrenal cortical adenoma. Cushing's syndrome was diagnosed early in pregnancy and treated with surgery.

Case Presentation

A 29-year-old, who was in the 27th week of her second pregnancy, complained of edema, weakness, and hypertension referred to us in April 2016 in Ghaem Hospital clinic (Mashhad, Iran). Edema started in the 16th week of her pregnancy and exacerbated for 4 weeks. She was first hospitalized with suspected preeclampsia, which was later excluded. Her medical history revealed that she has an abortion in the 16th week of her first pregnancy 2 years

earlier. In her first visit, we found several symptoms such as truncal obesity, moon facies, purple stria on her upper and lower limbs and abdomen, excessive edema, echimotic patches of limbs with suppurative lesions (due to superimposed bacterial infections), and wet skin (figures 1 and 2).

She was also found to have psychiatric disturbance such as obsessive thinking. No menstrual disorders were reported by her before the pregnancy. Physical examination indicated that her blood pressure ranged between 130-140/80-90 with antihypertensive therapy (methyldopa 250 mg every 6 hours). Her basic preeclampsia biochemical examinations were normal. Total 24 hours proteinuria was normal (130 mg/day) and preeclampsia ruled out. Hormonal profiles showed a high level of 24-hour urine cortisol (621 mcg/24 hours, normal range 10-100 mcg/24 hours) and a low level of adrenocorticotropin hormone (ACTH)



Figure 1: Purple stria on patient's chest, which is indicative of Cushing's syndrome.



Figure 2: Echimotic patches of limbs with suppurative lesions (due to superimposed bacterial infections) and wet skin.

(1.7 pg/mL). Due to asymmetric lower limbs edema, color Doppler ultrasonography was performed to rule out deep vein thrombosis and lymphatic insufficiency. Echocardiographic findings revealed a mild tricuspid regurgitation with minimal pericardial effusion and 55% ejection fraction. Abdominal ultrasonography showed a 30×30 mm round well-defined hypoecho right adrenal mass. To reassess, serum cortisol level in the morning and at night was checked because of the sonographic findings. The cortisol level was 30 (normal range 0.3-22.4 mcg/dL) at 8 a.m. and 40.2 (normal range 0.3-22.4 mcg/dL) at 12 p.m.

During hospitalization, the patient experienced an episode of generalized tonic-clonic seizure with 2 times crisis of blood pressure (maximum 180/120 mmHg). Although we earlier ruled out preeclampsia with normal amount of 24-hour proteinuria; however, we found no other differential diagnosis more plausible than eclampsia for this patient. Based on a high suspicion of eclampsia, pregnancy was terminated at the 28th week of gestational age with misoprostol. A male infant weighing 880 grams with Apgar score of 5 at one-minute and 7 at five-minute was delivered. Ketoconazole (150 mg/twice daily) was prescribed.

Considering the results obtained from ultrasonography and laboratory, computed tomography (CT) scan was performed 2 days postpartum. After the examination, a round isodense mass measuring 30×38mm diameters in the right adrenal glands with hemogenic enhancement was revealed (figure 3).

The patient underwent a laparoscopic right adrenalectomy after one week of delivery. After the surgery, the patient's blood pressure normalized and the serum cortisol level was below the normal range. Written informed consent was obtained from the patient prior to publication of this manuscript.

Discussion

Cushing's syndrome during pregnancy is a rare condition.¹ Cushing's syndrome is associated with (i) ingestion of prescribed glycocorticoids, (ii) a pituitary ACTH-secreting corticotroph adenoma (Cushing disease account for most cases), (iii) cortisol secreting adrenal adenomas and carcinomas, and (v) ectopic corticotrophin-releasing hormone (CRH) or ACTH secretion by bronchial carcinoids and other rare tumors. According to Murkami, adrenal adenoma is the most important cause of Cushing's syndrome in pregnancy.² Additionally, Sakakura et al.



Figure 3: Adrenal adenoma in abdominal CT-scan with double contrast.

stated that high levels of androgens, which can suppress reproductive functions, are commonly encountered in Cushing's syndrome. This might lead to anovulation and infertility.⁴

A typical cushingoid body habitus is reached by adipose tissue deposition that characteristically results in moon facies, a buffalo hump, and truncal obesity. Moreover, 75-85% of non-pregnant patients encounter fatigability and weakness, hypertension, hirsutism, and amenorrhea. The other common symptoms include personality changes, easy bruisability, and cutaneous striae. Up to 60% might have impaired glucose tolerance. Maternal and fetal complications frequently occur in these pregnancies. High complication rates such as hypertension, diabetes, heart failure, as well as maternal deaths were reported in some cases. Heart failure is common during pregnancy and it is considered as a major cause of maternal mortality. Additionally, wound healing delay may occur in some pregnancies complicated with hypercortisolism. Perinatal complications include fetal growth restriction, preterm delivery, stillbirth, and neonatal death.

Verification of the diagnosis is through elevated plasma cortisol levels that cannot be suppressed by dexamethasone or by elevated 24h urine free cortisol excretion. However, due to elevated levels of plasma cortisol, corticotrophin, and corticotropin-releasing factor during pregnancy, this is not the method of choice in pregnancy. The effective way to diagnose such problem is through utilizing imaging techniques such as magnetic resonance imaging (MRI), CT-scan, and ultrasonography.

The decision on treating Cushing' syndrome during pregnancy and choice of treatment method are difficult since they must be approached on a case-by-case basis. It also depends on the etiology and severity of disease and the time of gestation.

Successful medical treatment using metyrapone or ketoconazol has been reported during pregnancy.⁵ These could be an alternative treatment for poor surgical candidates or stabilized patients prior to surgery. James et al. reported the case of a pregnant woman with Cushing's syndrome in the 29th week of gestation. After treatment with metyrapone, the adrenalectomy was performed in the 31st week of gestation and finally in the 36th week of gestation the vaginal delivery was carried out.⁶ Woo et al. reported a 29-year-old woman with previous Cushing disease and a history of failed pituitary surgery. She was treated with cabergolin and the treatment continued during pregnancy. Eventually, she delivered a healthy female neonate.⁷

Long-term medical therapy for Cushing's syndrome is not usually effective. Thus, definitive therapy is the resection of pituitary or adrenal adenoma or bilateral adrenalectomy for hyperplasia. Abbassy et al. reported that surgery was beneficial in a 38-year-old pregnant woman with Cushing's disease recurrence. In her 18th week of pregnancy, she had endoscopic transsphenoidal of her pituitary adenoma with a good outcome for her and the fetus.³

Nassi et al. reported a case of 26-year-old female at the 19th week of pregnancy with a diagnosis of ACTH-independent CS, which was treated at the 21st week of gestation by robotic laparoscopic adrenalectomy.⁸

The best time for adrenalectomy during pregnancy is not yet identified. However, most surgeons consider the second trimester as the suitable time for surgical approaches.⁹ The patient in our case study was treated with laparoscopic adrenalectomy after the delivery.

Conclusion

Cushing's syndrome should be considered in hypertensive pregnant patients with remarkable signs of hypercortisolism. The best results would be achieved through a collaboration between obstetricians, endocrinologists, and surgeons.

Conflict of Interest: None declared.

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