CASE REPORT

Cushing's Syndrome During Pregnancy Secondary to Adrenal Adenoma

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Received: 4 Mar. 2011; Received in revised form: 14 Jul. 2011; Accepted: 27 Sep. 2011

Abstract- Pregnancy rarely occurs in untreated cases of Cushing's syndrome (CS) , because most of them are infertile due to significant maternal and fetal complications during pregnancy. Diagnosis of CS may be difficult during pregnancy. Since physiological changes of pregnancy are overlapped by classical presentation and biological confirmation of CS. Therefore the high clinical suspicious is needed for diagnosis. We present a 33 years old pregnant woman with a history of chronic hypertension from 10 years ago that referred to Imam Khomeini hospital for uncontrolled hypertension, gestational diabetes and fetal tachycardia at the 30 weeks of gestation. After initial studies abdominal MRI detected a 43 x 35 x 29 mm right adrenal mass. She was treated by anti-hypertensive drugs. But at 31.5 weeks of gestational age cesarean section was performed due to sever preeclampsia. Then two weeks after delivery open right adrenalectomy was carried out without any complications and in the histopathological evaluation benign adrenocortical adenoma was reported. CS is associated with considerable fetal and maternal morbidity and mortality. Selection of treatment method is variable and it depends on gestational age. Medical and surgical approaches have been used in managing CS in pregnancy. Surgical treatment is the first choice for CS which is recommended at the second trimester and in the late pregnancy medical treatment is preferred.

Acta Medica Iranica, 2012; 50(1): 76-78.

Keywords: Cushing's syndrome; Adrenal adenoma; Pregnancy

Introduction

Cushing's syndrome (CS) occurs in about 2/1,000,000 of general population (1). CS during pregnancy is a rare condition with fewer than 150 cases reported in the literature (2). Since CS is associated with a high incidence of ovulatory failure due to hypercortisolism and hyperandrogenism, most of these patients are infertile. There are significant maternal and fetal complications during pregnancy such as hypertension, gestational diabetes, heart failure, pulmonary edema, spontaneous abortion, preterm labor and fetal growth retardation. Therefore thes patiens suffer from high risk pregnancies.

Diagnosis of CS is often difficult because it is confused with complicated pregnancy such as preeclampsia and gestational diabetes. A high degree of clinical suspicion is required for early identification and appropriate management to avoid miscarriage or premature delivery.

Case Presentation

A 33 year old woman was referred to our institution (August 2010) at 30 weeks of gestation with hypertension, gestational diabetes and fetal tachycardia.

Physical examination revealed Cushingoid features, truncal obesity, striae on the abdomen, bruising over pressure areas and blood pressure 200/120 mmHg. Except for trace proteinuria other laboratory abnormalities were not found for diagnosis of preeclampsia. The biochemical screening was largely consistent with CS (Table 1).

Fetal ultrasonography revealed a single fetus in cephalic presentation and normal amniotic fluid. Fetal heart rate was about 200 beats/min. After these initial studies abdominal MRI detected a 43 x 35 x 29 mm right adrenal mass. The paraclinical diagnosis of this patient was based on the increasing of 24 hours urinary cortisol and serum cortisol level, low level of serum ACTH and the low level of serum potassium. MRI confirmed the diagnosis of CS.

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Table 1. Results of serum and urine chemical tests of patient.

Test	Patient	Normal
Cortisol (24 hours urine)	1251	13-75 (µg/day)
Cortisol (Serum)	40	5.5-26 (µg/dl)
ACTH * (Serum)	<1	7.2-64(pg/ml)
VMA** (24 hours urine)	9.8	2-12 (mg/day)
Metanephrine (24 hours urine)	89	0-350 (µg/day)
Normetanephrine (24 hours urine)	94	0-600 (µg/day)
Protein (24 hours urine)	115	20-150 (mg/day)
Cr*** (24 hours urine)	520	600-1800 (mg/day)
K****(Serum)	2.6	3.5-5(mmol/l)
FBS***** (Serum)	140	75-110 (mg/dl)

* AdrenoCorticoTropin Hormone
** Vanillylmandelic Acid
*** Creatinine
****Potassium
***** Fasting Blood Sugar

The patient was treated with methyldopa (metyrapone was unavailable) and insulin. Finally at 31.5 weeks of gestation a diagnosis of severe preeclampsia (blood pressure=180/110, 2+ proteinuria and headache) was made and she was delivered by emergency caesarean section. A 1500 g male baby with Apgar score 7 at both 1 and 5 minute was delivered. The neonatal course was complicated with moderate respiratory distress syndrome required neonatal intensive care. The baby was discharged 10 days later in good condition.

Two weeks after delivery the patient underwent right adrenalectomy via laparatomy without complication. Histology confirmed a benign adenoma. After operation glucocorticoid replacement with hydrocortisone (20 mg/day) was begun. Ten days later the patient was discharged with good general condition and blood pressure 140/80.

Discussion

There is an extensive spectrum of manifestation from subclinical to overt syndrome depending on the severity or duration of excess steroid production. Severity of symptoms or signs depends on some factors such as the reason of hypercortisolism, severity or duration of hypercortisolism and presence or loss of production of androgen.

Murkami reported that benign adrenal adenoma was the most common cause of CS in pregnancy, in contrast to non pregnant women where pituitary-depended hyperplasia is the most common cause of CS (3).

There are physiological changes during pregnancy that could confuse the diagnostic tests of CS. Estrogen-induced increases in cortisol binding globulin (CBG) coupled with increases in placental ACTH and corticotrophin releasing hormone (CRH) can lead to increases in free cortisol levels in plasma and urine, sometimes as high as two to three folds (4).

The increase of serum cortisol, CBG and urinary free cortisol are seen especially in the second and the third trimester of pregnancy (5,6). Serum ACTH increases during pregnancy due to synthesis and releasing of CRH and ACTH from placenta (7). Linsay *et al.*, reported urinary free cortisol levels greater than 3 times the upper normal limit should be taken as a credible primary indication of CS (8).

Imaging technologies such as MRI, CT scan and also ultrasonography could be useful for diagnosis of CS. There are some limitations of using MRI and CT scan during pregnancy. Although any harmful side effects of using MRI on fetus hasn't been reported yet,

Medical and surgical approaches have been used in managing CS in pregnancy. Surgical treatment is the first choice for CS which is recommended at the second trimester (5) and in the late pregnancy medical treatment being a second choice. Metyrapone (inhibitor of steroid genesis) is well tolerated in pregnancy and no congenital abnormalities have been reported yet.

A provisional diagnosis of this patient was made base on urinary free cortisol plasma cortisol and ACTH levels. Since the patient was in the third trimester medical treatment was preferred.

James *et al.*, reported in 2001 that a pregnant woman with CS at 29 weeks of gestation and after treatment by metyrapone, the adrenalectomy was performed at 31 weeks of gestation. And finally at the 36 weeks of gestation the spontaneous vaginal delivery was done (9).

In another case which was reported by Blanco *et al.*, in 2006, adrenal adenoma was diagnosed before pregnancy and the patient became pregnant during the consideration process (10). From 8-16 weeks of gestation the patient was treated by metyrapone and in this time laparoscopic adrenalectomy was done and adrenal deficiency was treated by cortisone 20 mg/day. Finally at 30 weeks of gestation spontaneous vaginal delivery was happened due to rapture of membrane and start of labor (10).

A similar case was reported, which considered as the severe preeclampsia and gestational diabetes. The pregnancy was terminated with an emergency caesarean section at 30 weeks and after delivery adrenal adenoma was diagnosed and laparoscopies adrenalectomy was done (11). Therefore, the treatment plan in each case is depended on the gestational age, clinician's experience and the patient's general condition.

Overall outcome may be further improved by medical treatment in late pregnancy. And finally, the best result would be acquired when a team consisting of obstetricians, endocrinologists, anesthesiologists, and surgeons evaluate and treat the patient (12).

References

1. Lo KW, Lau TK. Cushing's syndrome in pregnancy secondary to adrenal adenoma. A case report and literature review. Gynecol Obstet Invest 1998;45(3):209-12.
2. Vilar L, Freitas Mda C, Lima LH, Lyra R, Kater CE. Cushing's syndrome in pregnancy: an overview. Arq Bras Endocrinol Metabol 2007;51(8):1293-302.
3. Kita M, Sakalidou M, Saratzis A, Ioannis S, Avramidis A. Cushing's syndrome in pregnancy: report of a case and review of the literature. Hormones (Athens) 2007;6(3):242-6.
4. Terhune KP, Jagasia S, Blevins LS Jr, Phay JE. Diagnostic and therapeutic dilemmas of hypercortisolemia during pregnancy: a case report. Am Surg 2009;75(3):232-4.
5. Lindsay JR, Nieman LK. The hypothalamic-pituitary-adrenal axis in pregnancy: challenges in disease detection and treatment. Endocr Rev 2005;26(6):775-99.
6. Delibasi T, Ustun I, Aydin Y, Berker D, Erol HK, Gul K, Unal M, Guler S. Early severe pre-eclamptic findings in a patient with Cushing's syndrome. Gynecol Endocrinol 2006;22(12):710-2.
7. Magiakou MA, Mastorakos G, Rabin D, Margioris AN, Dubbert B, Calogero AE, Tsigos C, Munson PJ, Chrousos GP. The maternal hypothalamic-pituitary-adrenal axis in the third trimester of human pregnancy. Clin Endocrinol (Oxf) 1996;44(4):419-28.
8. Lindsay JR, Jonklaas J, Oldfield EH, Nieman LK. Cushing's syndrome during pregnancy: personal experience and review of the literature. J Clin Endocrinol Metab 2005;90(5):3077-83.
9. Shaw JA, Pearson DW, Krukowski ZH, Fisher PM, Bevan JS. Cushing's syndrome during pregnancy: curative adrenalectomy at 31 weeks gestation. Eur J Obstet Gynecol Reprod Biol 2002;105(2):189-91.
10. Blanco C, Maqueda E, Rubio JA, Rodriguez A. Cushing's syndrome during pregnancy secondary to adrenal adenoma: metyrapone treatment and laparoscopic adrenalectomy. J Endocrinol Invest 2006;29(2):164-7.
11. Kim HG, Lee KH, Je GH, Han MS. A case of Cushing s syndrome in pregnancy secondary to an adrenal cortical denoma. J Korean Med Sci 2003;18(3):444-6.
12. Sam S, Molitch ME. Timing and special concerns regarding endocrine surgery during pregnancy. Endocrinol Metab Clin North Am 2003;32(2):337-54.