

Successful pregnancy outcome in a case of Cushing's disease

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Abstract

Cushing's Syndrome is difficult to diagnose during pregnancy.¹ It could be mistaken for preeclampsia or gestational diabetes.¹ Early recognition and treatment ensures smooth course of pregnancy and improves maternal and fetal outcome.²

Keywords: Cushing's syndrome, Cushing's disease, plasma cortisol.

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Quick Response Code:	Website: www.innovativepublication.com
	DOI: 10.5958/2394-2754.2016.00029.1

Introduction

Cushing's Syndrome with pregnancy is a rare occurrence because of inhibition of ovulation and normal follicular development by hypercortisolism.^{2,3} There are fewer than 150 cases reported in literature¹ with the first description reported by Hunt and Mc Conahey, in 1953.⁴ Adrenal adenomas were found to be the commonest cause, with Cushing's disease being second.¹

Case Report

A 26 year old woman, presented with history of headache, blurring of vision, oligomenorrhea and primary infertility. She had no history of any medical or surgical co-morbidities. On examination, Pulse- 90/min, BP- 120/80 mm of Hg, no pallor, no icterus, no hirsutism, no evidence of easy bruisability or striae; respiratory and cardiovascular system were normal, abdomen was soft with no guarding or rigidity, local examination of genitalia were normal, cervix and vagina were normal on per speculum examination; on per vaginal examination, uterus was normal size, anteverted, smooth, firm and mobile and bilateral fornices were free. She was evaluated for infertility and it was found that midnight Cortisol was 13 µml/dl (Normal: 2.9-13 µml/dl)⁹. MRI was suggestive of a pituitary microadenoma of 6mm. She was started on Tab. Cabergoline 0.25mg once a week which was gradually stepped up to 0.5mg twice a week along with Tab. Metformin 500mg thrice a day. Serum cortisol level gradually reduced. A year after treatment, she conceived and followed up regularly in a tertiary care centre where Emergency Lower Segment Caesarean Section was done

at term in view of non progress of labour and she delivered a male child of 2.2kg with APGAR score of 9/10. There were no maternal or neonatal complications. However, 6 months postpartum there was persistence of a microadenoma of 7 x 6 mm on the right side. Trans-sphenoid pituitary surgery was done in a tertiary care centre. Post-operative serum cortisol was normal. She was started on Tab. Prednisolone 5mg once daily. Thyroid functions were normal and 3 month post-operative MRI showed no residual lesion. After 6 months, serum cortisol was well within normal limits and prednisolone was gradually weaned off. The following year she conceived spontaneously. She received oral progesterone daily in the first trimester. Her regular antenatal visits were managed in joint collaboration by an obstetrician and endocrinologist. There were no medical co-morbidities during the course of pregnancy. At 36 weeks of gestation, an emergency Lower Segment Caesarean Section was done in view of previous lower segment Caesarean section with premature rupture of membranes with poor Bishop's score. A female child of 2.8kg was born with APGAR score of 9/10. Post operative period was uneventful. The serum cortisol levels of both mother and baby were within normal limits.

Discussion

Clinical features in pregnant and non-pregnant women are similar- weight gain, hypertension, easy bruising, and hirsutism. It is often detected after 26 weeks of gestation, partially due to attribution of changes in physical appearance to normal pregnancy rather than pathological conditions.² There are manifestations of Cushing's Syndrome which may be attributed to complications of pregnancy (gestational diabetes, preeclampsia, etc.), and hence delaying the diagnosis.^{2,3,16}

Due to the delay in diagnosis of Cushing's Syndrome, the rate of early spontaneous abortions may be underestimated.^{2,7,15} Preterm labour is a common complication in around 60% of pregnancies². Other fetal

complications include intrauterine growth restriction and stillbirths.¹

There is significant maternal morbidity and mortality in approximately 70% of patients with Cushing's Syndrome.¹ Complications known to occur include hypertension and diabetes or impaired glucose tolerance.^{2,10,11} Poor wound healing, osteoporosis and fractures, maternal cardiac failure, psychiatric illness and death have also been reported.^{2,12,13,14}

The normal gestational changes in the HPA axis alter all hormonal parameters and complicate the diagnosis of Cushing's Syndrome.² This includes an increase in plasma cortisol and ACTH, cortisol binding globulin (CBG, and comparatively higher increases in plasma free cortisol and unfractionated cortisol (UFC)². The three most useful tools in diagnosis are the measurement of 24-hour UFC levels, low-dose dexamethasone-suppression tests, and determination of midnight serum cortisol or late-night salivary cortisol.^{6,17,18} ACTH levels are not suppressed in adrenal causes of Cushing's Syndrome, which may be identified by the 8mg dexamethasone suppression test.² Moreover, a blunted response of ACTH and cortisol to exogenous CRH may also occur.¹ Though it was initially the optimal diagnostic test and treatment for non-pregnant patients with pituitary-dependent Cushing's syndrome, inferior petrosal sinus sampling and trans-sphenoidal pituitary surgery now also safely facilitate the management of pregnant patients.² All of these tests vary in sensitivity and specificity, thus limiting their diagnostic accuracy¹⁹. Pituitary MRI must be performed in all patients with apparent ACTH-dependent Cushing's Syndrome, while chest and abdominal MRI could be considered for those with suspected ectopic ACTH secretion.¹ Pituitary MRI showing adenomas of more than 6mm can help clinch the diagnosis in conjunction with biochemical tests¹⁷.

The treatment preferred for Cushing's Syndrome in pregnancy is surgery (except in the late third trimester) which may help achieve remission, but the prognosis for the fetus remains guarded.² Medical therapy is considered second. Ketoconazole is the drug of choice in the medical treatment for Cushing's syndrome; however, it entails the theoretical risk of interfering with the development of external genitalia in a male fetus.²⁰

Conclusion

Cushing's disease in pregnancy is a rare entity and there is a need for development of criteria for interpretation of diagnostic tests and increased consideration of Cushing's Syndrome in pregnancy.² A multidisciplinary approach is best suited in order to reduce fetomaternal morbidity.

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