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Cushing's Syndrome and Pregnancy: A Report of Three Cases and Literature Review

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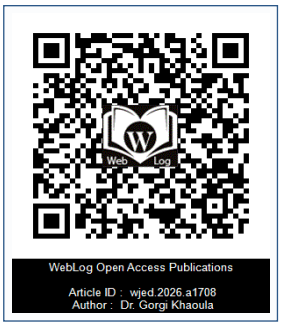

Abstract

Introduction: Cushing's syndrome (CS) during pregnancy is a rare and complex condition due to the overlap of symptoms with normal physiological changes during pregnancy and the associated maternal and fetal risks.

Objective: To describe three cases of Cushing's syndrome diagnosed during or shortly after pregnancy, detailing clinical characteristics, diagnostics, management, and outcomes, alongside a review of recent literature.

Methods: A retrospective analysis of three cases managed in a university endocrinology department, complemented by a review of current data on CS and pregnancy.

Results: The three patients presented clinical and biochemical signs of hypercortisolism. Two cases were due to adrenal adenomas confirmed by imaging and pathology, while one case corresponded to a recurrence of pituitary adenoma managed conservatively during pregnancy. Treatments included surgery and monitoring depending on disease activity and gestational age. Maternal and fetal outcomes varied, illustrating the diagnostic and therapeutic challenges.

Conclusion: Early diagnosis of CS during pregnancy is essential. Multidisciplinary tailored management optimizes maternal and fetal outcomes. Further studies are necessary to standardize care.

Keywords: Cushing's Syndrome; Pregnancy; Adrenal Adenoma; Pituitary Adenoma; Hypercortisolism

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Introduction

Cushing's syndrome (CS) during pregnancy is a rare endocrine pathology with an estimated incidence of about 1 case per 200,000 pregnancies [1]. It results from chronic exposure to excessive cortisol levels, leading to serious complications for both mother and fetus. Diagnosis is often delayed due to the similarity of symptoms with normal physiological changes during pregnancy (weight gain, hypertension, glucose intolerance) [2].

CS may originate from pituitary causes (Cushing's disease), adrenal causes (adenoma, carcinoma), or more rarely, ectopic ACTH secretion. In pregnant women, adrenal causes are more frequent compared to the general population [3]. Biochemical diagnosis is complicated by the changes in glucocorticoid metabolism induced by pregnancy [4]. Management should be adapted according to gestational age and symptom severity.

Here, we report a series of three cases illustrating different presentations and management of CS during pregnancy, followed by a critical literature review.

Patients and Methods

We conducted a retrospective descriptive study of three patients managed for CS related to pregnancy between 2018 and 2024 in our center. Clinical data, biochemical results (24-hour urinary free cortisol), radiological findings (CT scan, MRI), therapeutic modalities, and outcomes were analyzed.

CS diagnosis was based on clinical suspicion supported by biochemical confirmation of hypercortisolism and identification of the causative lesion via imaging. Follow-up included clinical and biochemical assessment after treatment.

Table 1: Summary of Patient Characteristics, Diagnosis, Treatment, and Outcomes.

Patient	Age (years)	Timing of Diagnosis	Clinical Presentation	Biochemical Findings	Imaging	Treatment	Outcome
1	29	2nd trimester (postpartum diagnosis)	Headaches, hypertension, acne, striae	Elevated 24-hour urinary cortisol	Right adrenal adenoma	Surgery after delivery	Good evolution
2	28	16 weeks gestation	Recurrence with elevated urinary free cortisol	Elevated 24-hour urinary cortisol	Pituitary microadenoma	Surgery after delivery	Good evolution
3	20	Late diagnosis (2 years postpartum)	Severe hypertension onset at 37 weeks, persistent abdominal pain postpartum	Very elevated 24-hour urinary cortisol	Right adrenal adenoma	Surgery after delivery	Good evolution

Case Descriptions

Case 1

A 29-year-old woman with no significant medical history presented in the second trimester of pregnancy with headaches and abdominal pain. Blood pressure was elevated (170/100 mmHg), initially suspected as preeclampsia, but biological tests, including proteinuria, were normal. She was started on antihypertensive treatment, lost to follow-up, and delivered vaginally a newborn weighing 3800 g. One month postpartum, she consulted a dermatologist for facial acne, who noted grade 1 obesity, persistent hypertension, and extensive purple striae. Clinical diagnosis of CS was made based on faciotroncular obesity, moon face, buffalo hump, and characteristic striae. Twenty-four-hour urinary free cortisol was elevated. Adrenal CT scan showed a right adrenal adenoma. She was referred for surgical management.

Case 2

A 28-year-old woman followed for pituitary Cushing's disease, operated previously, presented with recurrence. Surgical reintervention was planned for a pituitary microadenoma. Pregnancy was discovered at 16 weeks gestation, and surgery was deferred. Absence of clinical and biochemical activity allowed surveillance. Pregnancy progressed without complications.

Case 3

A 20-year-old woman was hospitalized at 37 weeks gestation for abdominopelvic pain and uterine contractions, with severe hypertension (200/120 mmHg). She was started on antihypertensives and underwent cesarean section, delivering a 4 kg infant. Lost to follow-up, she returned two years later with symptoms of CS and markedly elevated urinary free cortisol. CT scan revealed a right adrenal mass confirmed as adenoma post-surgery.

Results

See Table 1 and Figure 1.

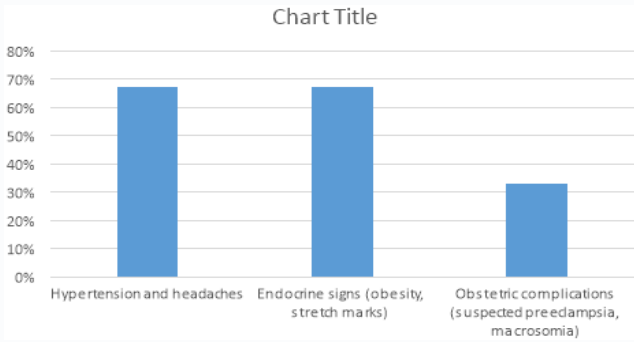

Figure 1: Distribution of clinical presentations among our patients.

Discussion

Cushing's syndrome during pregnancy remains a rare entity but with serious consequences. Fertility is generally impaired by hypercortisolism, explaining the rarity of reported cases [5]. Nonetheless, recognizing this condition is crucial as delayed diagnosis can lead to severe complications.

Classic clinical features of CS (faciotronicular obesity, moon face, purple striae, hypertension) are often masked or confused with normal pregnancy changes, making diagnosis challenging [6]. The presence of more specific signs or severe, resistant hypertension should raise suspicion.

Biochemically, usual tests are disrupted by physiological cortisol increases during pregnancy, especially due to elevated cortisol-binding globulin [7]. Twenty-four-hour urinary free cortisol and late-night salivary cortisol are more reliable, though cutoff values must be adjusted [8].

Etiology varies, with adrenal causes predominating in pregnancy as seen in our cases 1 and 3. Adrenal adenomas produce autonomous cortisol. Case 2 illustrates pituitary Cushing's disease recurrence, where pregnancy often necessitates delaying surgery.

Surgical treatment is the standard of care, ideally in the second trimester to reduce obstetric risks. Medical alternatives are limited due to scarce safety data in pregnant women [9]. Clinical and biochemical monitoring remains essential.

Multidisciplinary management (endocrinology, obstetrics, surgery) optimizes outcomes, as shown in our series. Maternal complications (severe hypertension, preeclampsia, gestational diabetes) and fetal complications (macrosomia, prematurity) are common without appropriate care [10].

Conclusion

Cushing's syndrome in pregnancy, though rare, is a significant cause of maternal-fetal morbidity. Diagnosis relies on high clinical suspicion and adapted investigations considering pregnancy-specific changes. Surgery remains the main treatment when feasible. Multidisciplinary management and careful monitoring improve prognosis.

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