Cortical adrenal adenoma as a cause of Cushing’s syndrome during pregnancy

Adenoma suprarrenal cortical como causa de síndrome de Cushing durante el embarazo

The prevalence rate of Cushing’s syndrome (CS) in the general population is 1 per 500,0001. Cortisol-secreting adrenal adenoma is the most common cause of CS in pregnant women. Unlike adrenal carcinoma or hyperplasia, which are associated with excess androgen production, most adrenal adenomas are pure cortisol producers. The predominance of adrenal adenoma as a cause of CS in pregnancy may be related to the lack of suppressant effects of androgens on ovulation1-5. A female patient in her 20th week of pregnancy with CS due to cortical adrenal adenoma is reported.

This 30-year-old patient in her first pregnancy attended the clinic for high blood pressure values at 20 weeks of pregnancy. She had no history of severe medical diseases. From the beginning of pregnancy the patient had noticed changes in her appearance, including several stretch marks in her lower limbs and abdomen, as well as rash and acne in her face and body. Four weeks before admission, the patient experienced difficulty in standing, persistent headache, visual disturbances, epigastric pain, and increased lower limb volume.

Physical examination revealed all the typical features of CS (round face, with trunk obesity and thin limbs, buffalo hump, and supraclavicular fat accumulation). Many areas with acne and hirsutism were also seen in the face, and the skin was atrophic with wide reddish stretch marks in the proximal part of the arms, abdomen, and thighs. Cardiovascular assessment was normal, and no abdominal masses were palpated. Proximal muscle weakness was found in all four limbs. Visual examination was normal, and eye fundus examination revealed a disk with well defined margins and no hypertensive changes.

CS was suspected and confirmed by a marked increase in cortisol levels in 24-hour urine (5,049 nmol/day; normal range: 55-300 nmol/day) with decreased adrenocorticotropic hormone (ACTH) levels (2.1 picomol/L; normal range: 2-15 picomol/L). Urinary cortisol was not suppressed (7,611 nmol/day) by dexamethasone (0.5 mg every 6 hours). The suppression of serum and urine cortisol levels by dexamethasone is impaired during pregnancy, and the rate of false positive results in this test may therefore be increased. Since the bioavailability of dexamethasone remains unchanged during normal pregnancy, the results may reflect changes in the hypothalamus-pituitary-adrenal function, leading to ovulation changes. Oligomenorrhea and amenorrhea, which are directly associated with the disease, have been reported in 75% of childbearing women with CS5.

Buescher et al2 reviewed the histories of 65 pregnancies associated with CS in 58 patients and found that 50% of cases were caused by adrenal adenoma, as compared to 15.7% in non-pregnant women.

Pregnancies complicated by a CS, while rare, should be considered as carrying a high risk. These patients are at risk of developing diabetes, severe hypertension, preeclampsia, healing difficulties, muscle weakness, congestive heart failure, pulmonary edema, or death5. The incidence rates of hypertension and diabetes are 58.8% and 25% respectively4,6. The risk of miscarriage and perinatal death is also increased7. Intrauterine growth restriction of the fetus is seen in 26% of cases due to the presence of diabetes and hypertension5.

Misdiagnosis of CS during pregnancy is common, and a high level of clinical suspicion is warranted. Normal endocrine changes occurring during pregnancy, including increased serum and urine cortisol and ACTH levels, further complicate the diagnostic process.

Cortisol and ACTH levels increase during pregnancy, while urinary cortisol levels increase in the second and third trimesters. The reasons for increased ACTH levels during pregnancy include placental synthesis and the release of corticotropin-releasing hormone and ACTH, pituitary desensitization to cortisol feedback, or an increased pituitary response to corticotropin-releasing factors. The circadian rhythm of these hormones is maintained during pregnancy, but evening cortisol nadir is higher than in non-pregnant women. The cut-off point for cortisol levels in 24-hour urine considered as pathological is two to three times above the normal value4.

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Figure 1 Abdominal MRI of a tumor in the right adrenal gland suggesting cortical adenoma.
axis or increases in total serum cortisol and cortisol-binding protein during pregnancy\textsuperscript{1,9}.

Ultrasound images of the adrenal gland, a suppression test with high-dose dexamethasone, and the measurement of ACTH levels are recommended for initial diagnosis. If the patient has borderline or low ACTH levels or no suppression after the dexamethasone test, the condition may be adrenal in origin. Ultrasonography identifies adrenal tumors in 73\% of cases\textsuperscript{9}. MRI is a second-line test for localization diagnosis\textsuperscript{1}.

Therapeutic alternatives for adrenal adenoma include unilateral adrenalectomy during pregnancy or medical treatment followed by surgery after delivery\textsuperscript{10}. No ideal time for performing adrenalectomy has been reported, but most obstetricians and surgeons think that the second trimester is the best time for surgery\textsuperscript{a}. A trend to less neonatal complications has been reported in women undergoing surgery during pregnancy, provided maternal conditions are not affected\textsuperscript{1}. Blood pressure, glucose and potassium levels, and water balance should be strictly monitored after surgery.

Successful results have been reported after treating hypercorticoïdism with metyrapone\textsuperscript{10}. Metyrapone, an 11-beta-hydroxylase inhibitor, decreases plasma cortisol levels. Although metyrapone may cross the placenta and affect adrenal corticosteroid synthesis, no adverse effects attributable to this treatment have been reported. Other drugs such as ketoconazole, aminoglutethimide, cyproheptadine, or mitotane are contraindicated in pregnancy because of their known teratogenic potential\textsuperscript{9}.

References


Helen De Nobrega-Correa, Jhoan Aragón-Charris, Duly Torres-Cepeda, Eduardo Reyna-Villasmil*  
Servicio de Obstetricia y Ginecología-Maternidad Dr. Nerio Beloso, Hospital Central Dr. Urquinaona, Maracaibo, Estado Zulia, Venezuela

*Corresponding author.  
E-mail address: sippenbauch@gmail.com  
(E. Reyna-Villasmil).