Revista Colombiana de Anestesiología
Colombian Journal of Anesthesiology
www.revcolanest.com.co

Case report

Functional adrenal adenoma in a pregnant woman with a 32 week gestation scheduled for cesarean section☆

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ARTICLE INFO

Article history:
Received 29 July 2011
Accepted 30 April 2012

Keywords:
Cushing syndrome
Pregnancy
Anesthesia
Cesarean section

ABSTRACT

The coexistence of Cushing syndrome and pregnancy is rare. Diagnosis is difficult because pregnancy can be accounted for signs and symptoms of hypercortisolism. Ideally, the treatment is surgical, though it implies a significant rise in morbidity and mortality for both the mother and the fetus. This is due to the increased number of complications such as hypertension, pre-eclampsia, gestational diabetes, abortion and preterm delivery. We present the case of a primiparous patient with a 32 week gestation and Cushing syndrome secondary to a functional adrenal adenoma who has been scheduled for a caesarean section.

Adenoma suprarrenal funcional en gestante de 32 semanas programada para cesárea

Palabras clave:
Síndrome de Cushing
Embarazo
Anestesia
Cesárea

RESUMEN

La coexistencia de síndrome de Cushing y embarazo es rara. El diagnóstico es difícil, ya que la gestación produce síntomas y signos de hipercortisolismo. Su tratamiento idealmente es quirúrgico, pero conlleva un importante incremento de la morbimortalidad materna y fetal debido a complicaciones como hipertensión, preeclampsia, diabetes gestacional, aborto y parto pretérmino. Presentamos el caso de una primigestante de 32 semanas con síndrome de Cushing secundario a un adenoma suprarrenal funcional programada para cesárea.

☆ Please cite this article as: Berrío Valencia MI, Vallejo Yepes C. Adenoma suprarrenal funcional en gestante de 32 semanas programada para cesárea. Rev Colomb Anestesiol. 2012; 40:231–4.
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2256-2087/$ – see front matter

Introduction

It is rare for Cushing syndrome to appear during pregnancy. Nearly 140 cases have been reported with an average gestational age of 18 at the time of diagnosis.[1,2] Most of them had adrenal adenomas that were successfully resected during pregnancy. Few cases reported persistence of the tumor and its associated complications after abortion or pregnancy termination. This report discusses the anesthetic management of a patient with Cushing syndrome caused by a functional adrenal adenoma who underwent an emergency caesarean section and its special considerations.

Case report

This is the case of a previously healthy primiparous patient, age 33 and 26 weeks into her gestation, who first consulted at 19 weeks because of peripheral edema, asthenia, adynamia, diaphoresis, hirsutism, hypertension and lower extremity ecchymosis. On physical examination, the findings were: blood pressure at 130/90 mmHg, heart rate at 104/min, respiratory rate at 20/min, body mass index (BMI) at 27 kg/m^2, bloated fascies, hirsutism, acne, Malampati III, thyromentonian length of 6 cm, fair cervical extension, abdominal striations, telangiectasias, grade III lower extremity edema and fetal tachycardia (160–170/min). No cervical masses or fever were found.

The O'Sullivan test results were positive and the glucose tolerance test was altered. Proteinuria in 24 h urine collection was found at 360 mg. The dexamethasone suppression test was carried out with 1 mg orally, yielding no cortisol suppression. Arterial gas measurements and rheumatologic testing were normal. The abdominal ultrasound showed a solid lesion in the upper pole of the left kidney. The gadolinium contrast resonance showed a left adrenal mass of 5 cm × 5 cm × 4 cm, with hypointensity in T1 sequences, an intensity drop in out-of-phase sequences and right adrenal gland atrophy. Table 1 shows the biochemical profile and Table 2 shows the hormonal profile. With these results, the patient was diagnosed with Cushing syndrome secondary to a functional adrenal adenoma associated to gestational diabetes and pre-eclampsia.

Cardiac ultrasound findings showed an ejection fraction of 66%, mild pulmonary hypertension (systolic pressure of the pulmonary artery at 27 mmHg) and pericardial effusion of 350–400 ml with no hemodynamic compromise.

The ultrasound revealed an anterior body placenta and a single fetus. Cervix evaluation was normal. The biophysical profile score was 8/8 and the fetus Doppler examination was normal. Uterine artery Doppler showed increased resistance of the uterine arteries. No paraclinical data for discarding pheochromocytoma were found, probably because clinical examination was not consistent.

The management of this patient initiated lung maturation, prophylactic enoxaparin, anti-embolic measures, alphamethyldopa and insulin therapy due to poor metabolic control. During hospital stay she reached week 32 of her pregnancy. An interconsultation with general surgery was carried out and the patient was considered for postpartum adrenalectomy, due to the fact that the risks of non-obstetric surgery in the third trimester may surpass the net benefit. She was assessed by the Anesthesiology group, which suggested a guided draining of the pericardial effusion. However, the patient then presented metabolic acidosis, uncontrolled hypertension and spontaneous membrane rupture with blood in fluid. She was taken for an emergency c-section. Enoxaparin was suspended 24 h before the surgery; the patient was previously treated with ranitidine at 50 mg IV, metoclopramide 10 mg IV and hydrocortisone 100 mg IV. Three red blood cells and 5 fresh frozen plasma packs are reserved, as well as neonatal intensive care unit and special care unit services for the mother. Peripheral venous access proved difficult.

At operating room admission, the patient's blood pressure was at 170/90. An arterial line is placed and IV labetalol boluses were administered until systolic blood pressures under 160 mmHg (total 140 mg) were achieved, plus magnesium sulfate (4 g IV bolus, 2 g/h infusion). A right subclavian central venous catheter was placed and an intrathecal puncture is carried out in the L3–L4 space with a 25G pencil point needle for a slow injection of bupivacaine 7.5 mg, fentanyl 25 mcg and morphine 100 mcg, achieving sensitivity at T4. During the procedure the patient remained hemodynamically stable. No vasoactive drugs or transfusions were required. Glucose measured during surgery was at 119 mg/dl. The product was a premature newborn that weighed 1570 g who had a proper neonatal adaptation. The mother was placed in the intensive care unit for 5 days because of a urinary sepsis due to *Escherichia coli*. She needed vasoactive and inotropic treatment.

Table 1 – Biochemical profile.

Marker	Patient score	Reference range	Marker	Patient score	Reference range
Creatinin (mg/dl)	0.62	0.6–1.2	Total bilirubin (mg/dl)	0.7	0–1
Hemoglobin (g/dl)	15.5	12–16	Indirect bilirubin (mg/dl)	0.7	≤1
Leukocytes (/mm^3)	8900	5000–11,000	Direct bilirubin (mg/dl)	0	0–0.4
Platelets (/mm^3)	150.000	150,000–400,000	Urine proteins (mg/24 h)	360	0–130
AST (U/l)	25	30–70	Na (mmol/l)	135	135–145
ALT (U/l)	29	9–52	K (mmol/l)	4	3.5–4.5
DHL (U/l)	710	110–210	Cl (mmol/l)	105	100–108
FA (U/l)	88	44–147	Total Ca (mg/dl)	9.6	8.5–10.5
Urine cytochemistry	Proteins+		Urine culture	Negative	Negative
Uric acid (mg/dl)	3.52	2.5–7–5	PCR (mg/dl)	0.8	0–1
Lactic acid (mmol/l)	3.4	0.7–2.1	Albumin (g/dl)	3	3–4

Table 2 – Hormonal profile.

Marker	Patient score	Reference range
TSH (mUI/l)	0.65	0.46–4.68
Total T3 (ng/dl)	50	83–200
Free T4 (mcg/dl)	5.3	4–11
ACTH (pg/ml)	<10	0–46
AM cortisol (mcg/dl)	55	5–23
PM cortisol (mcg/dl)	48	5–23
Free urine cortisol ELISA (mcg/24 h)	843.2/3400 ml	20–130

Peripartum cardiomyopathy was discarded and a pericardial window was carried out with a positive outcome. The pericardial fluid showed chronic inflammation without infection or malignancy. The patient was then discharged and returned two months later for laparoscopic surgery, which was successful and had no complications.

Discussion

Cushing syndrome is the set of signs and symptoms caused by an excess of glucocorticoids regardless of its etiology.[3–5] The main cause of Cushing syndrome is exogenous due to the taking of steroid drugs.[3,4] It is classified into:

1. Adrenocorticotropic Hormone (ACTH) dependent, which is the most common form, and 80% of cases are secondary to pituitary tumors and the remaining 20% to ectopic ACTH secreting foci.[3,4]
2. Independent of ACTH, of which 20% of cases are due to adrenal adenomas.[3,4]

Incidence is estimated to be 2.3 million cases per year, with a male/female ratio of 1:3.[3] The diagnosis of Cushing syndrome during pregnancy requires a high degree of clinical suspicion. Screening is also affected given that the changes caused by pregnancy can be very similar to those caused by hypercortisolism, such as weight gain, amenorrhea, fatigue, plethora, back pain and mood swings.[2,6]

Adrenal adenomas cause 40–50% of Cushing syndrome cases during pregnancy, compared to only 15% in patients who are not pregnant.[2,7] Complications for the mother include glucose intolerance, gestational diabetes, hypertension, pre-eclampsia, heart failure, surgical wound infection, pulmonary edema, myopathy, osteoporosis, fractures, tissue healing alterations, psychiatric alterations and death of the mother. There are two cases reported of Cushing syndrome and early, rapid development of severe HELLP syndrome.[2,8] Fetal complications are abortion, early delivery, intrauterine growth restriction, hypoadrenalism and perinatal death.[6,9]

The objectives for proper treatment are confirming cortisol excess, determining the cause and treating it in order to avoid further complications.[6]

The diagnosis is confirmed with biochemical testing. The level of free cortisol in urine is increased (scores during the second or third trimester three times as high as the upper limit scores) and cortisol circadian rhythm alteration (which prevails in pregnancy).[5,8–10] The rise in daytime cortisol is not diagnostic because it is also caused by pregnancy.[7] ACTH is not suppressed in adrenal causes. Finally, the secretion site must be confirmed with imaging methods, preferably Magnetic Resonance Imaging (MRI), whenever possible.[10]

The first line treatment during the second trimester is surgical, for both adrenal and pituitary adenomas. As an alternative, treatment could be based on metyrapone, a cortisol synthesis inhibitor that has been well tolerated but is currently unavailable. Ketoconazole has been proven to be teratogenic in trials in rats, it can pass the placental barrier and there is little experience with its use in humans.[6,10]

The patient was asymptomatic before her pregnancy and the adrenal tumor was present at the time the caesarean section was scheduled.

A mother with Cushing syndrome requires multidisciplinary management that includes an endocrinologist, an obstetrician, an anesthesiologist, a neonatologist, a surgeon and a nutritionist. In the preoperative assessment, mixed tumor and pre-eclampsia worsen the prognosis and must be discarded because they modify the management of the patient.[6] Airway management can be difficult due to obesity and accumulated fat tissue in the areas of the neck and the sternum (buffalo neck) which is a limitation for cervical extension.[11] Fragile skin and blood vessels makes venous access more difficult.[11] Electrolyte alterations must also be discarded, especially hypokalemic alkalosis, and metabolic control must be ensured and optimized with insulin. These patients often have episodes of persistent hyperglicemia due to gluconeogenetic stimulation and an overall reduction of peripheral glucose use.

During the intraoperative period there must be utmost care with the positioning of these patients due to the high risk of fractures secondary to osteoporosis.[12] Aseptic and antiseptic measures must be fulfilled strictly given that these patients are prone to infections.[12] The regional anesthetic procedure must be carried out if there are no contraindications to invade the neuraxis.

The postoperative period must include ventilation failure risk vigilance. This can occur due to associations with decreased muscle mass, hypokalemia and obesity.[11]

Conclusion

Cushing syndrome during pregnancy is a rare medical situation that can be easily mistaken with pre-eclampsia or gestational diabetes. A proper multidisciplinary approach is key for accurate diagnosis and anesthetic planning for patients scheduled for caesarean section or non-obstetric surgery in order to ensure the best possible clinical outcome for the mother and the child.

Funding

None.

Conflicts of interest

None.

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