Eplerenone Use in Primary Aldosteronism During Pregnancy

To the Editor:

Primary hyperaldosteronism has rarely been reported in pregnancy (≈30 cases have been described since 1962) and is most often caused by an adrenal adenoma.1–2 Aggressive management is strongly recommended, because the risk of complications in both the mother and the fetus is high.3 Difficulties arise because of limited therapeutic options attributed to fetal toxicity.

The following is a case report of primary aldosteronism during pregnancy, treated with eplerenone, an antagonist of mineralocorticoid receptors.

In April 2009, a 34-year-old African woman, gravida 1 para 1, at 21 weeks’ gestation with a male fetus, was referred to our obstetrics and gynecology department for palpitations, uncontrolled hypertension, and severe hypokalemia. Before pregnancy, normokalemia was reported, and blood pressure (BP) was controlled with nifedipine GITS-20 mg/d. At the time of admission, her BP was 155/110 mm Hg and pulse rate was 76 beats per minute. Her physical examination was normal. A fetal ultrasound showed normal growth for gestational age. A 12-lead ECG showed a sinus rhythm (82 beats per minute), supraventricular and ventricular premature beats, and a long QTc (524 ms; normal value <400 ms). A 24-hour ECG showed frequent ventricular premature beats (18 174 in 24 hours) with couplets and several runs of ventricular tachycardia. Laboratory tests revealed severe hypokalemia (K 1.9 mEq/L; normal range: 3.5–5.3 mEq/L) and hypomagnesemia (Mg 1.3 mg/dL; normal range: 1.5–2.5 mg/dL), metabolic alkalosis (pH 7.48; HCO3– 32 mEq/L), and normal liver and renal function. Urinalysis showed 1+ proteinuria. Supplementations with K and Mg were immediately started both IV (KCl = 160 mEq/d in half-normal saline 2000 mL and MgSO4 = 2 g/d) and PO (KCl = 8 mEq TID), and nifedipine GITS increased to 60 mg BID. Hypertension and severe hypokalemia strongly suggested primary hyperaldosteronism. MRI (Figure A) showed a mass on the left adrenal gland compatible with an adenoma. Plasma renin activity (supine position) was not suppressed (3.26 ng/mL per hour), and both plasma aldosterone concentration (288 ng/mL) and plasma aldosterone concentration:plasma renin activity ratio (88; normal value <20) were elevated. A saline infusion test showed no suppression of plasma aldosterone concentration, nor did an orthostatic test show an increase. Urinary free cortisol and metanephrine levels were normal. The option of a left adrenalectomy by laparoscopic surgery was excluded because of the risk related to the gestational age (24 weeks). After 2 weeks, serum K levels remained low (2.5 mEq/L) and urinary K excretion high (62–95 mEq/d). A central venous line was placed in the right jugular vein to increase KCl infusion to 461 mEq/d. On the new schedule, serum K levels reached 3.2 mEq/L, and the number of ventricular premature beats dramatically dropped (1124 per day) in a 24-hour ECG registration. –Methyldopa (500 mg TID) was added for better BP control. At week 27, 50 mg/d of eplerenone, a more selective aldosterone receptor antagonist than spironolactone, was started after being approved by the ethics committee and increased up to 50 mg BID. Serum K increased to 3.9 mEq/L.

Figure. A, Abdominal MRI/coronal/C–image of left adrenal mass (see white arrow; 24th week of gestation). B, Abdominal CT/axial/C–image of left adrenal mass (see white arrow; 10 days after delivery). C, Low- and (D) high-power magnification of clear cells of the adrenal cortical adenoma (hematoxylin/eosin; original magnification: ×10; ×400).

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within 1 week, so the KCl infusion was reduced to 80 mEq/d. The pregnancy continued regularly until 35 weeks of gestation, at which time, because of a resistant increase in BP, a cesarean section was performed and a 2280-g male infant was delivered (Apgar score 1 at first minute and 8 at 5 minutes), without any signs of feminization on macroscopic examination. After delivery, an abdominal CT scan with contrast media confirmed a left adrenal mass (39×22 mm; Figure B) and a laparoscopic left adrenalectomy was performed 3 weeks after the delivery. The histological analysis confirmed the diagnosis of cortical adrenal adenoma composed of zona glomerulosa-like cells (Figure C and D). At 2-year follow-up, the woman is still normotensive, and the infant male’s psychophysical development is normal.

If an adrenal adenoma is detected, unilateral adrenalectomy is the best therapeutic option in the late first and the early second trimesters, providing a rapid normalization of BP and serum potassium levels.4 On the other hand, in middle and late pregnancy, primary aldosteronism is best treated medically.1 Pharmacological options such as spironolactone, the aldosterone-receptor antagonist, which is primarily used in nonpregnant patients, is contraindicated in pregnancy, because it crosses the placenta and has potent antiandrogenic effects that can cause ambiguous genitalia in a male fetus.5 However, most case reports and letters in the literature report the use of spironolactone in pregnancy.1 Angiotensin-converting enzyme inhibitors and angiotensin II receptor 1 antagonists are also contraindicated. Although never reported in the literature, we chose to use eplerenone (not commercially available in Italy) based on the fact that the molecule is much more selective than spironolactone on the mineralocorticoid receptor, reducing the risk of antiandrogenic effects.5 Eplerenone gave a good control of K levels and BP, allowing the pregnancy to continue. This is the first report of eplerenone use instead of spironolactone to treat primary hyperaldosteronism in a male-bearing pregnant woman. There are no human data in the literature supporting or discouraging its use in pregnancy; therefore, particular caution should be taken and the potential benefit:risk ratio always very well weighed.

Disclosures

None.

References


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