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PRENATAL DEXAMETHASONE USE FOR THE PREVENTION OF VIRILIZATION IN PREGNANCY AT RISK FOR CLASSICAL CONGENITAL ADRENAL HYPERPLASIA

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Background:

✓The most common form of congenital adrenal hyperplasia (CAH) is 21- hydroxylase deficiency, which in its severe form can cause genital ambiguity in females.

✓This can be ameliorated by administering dexamethasone to the pregnant mother with affected fetus.

Case:

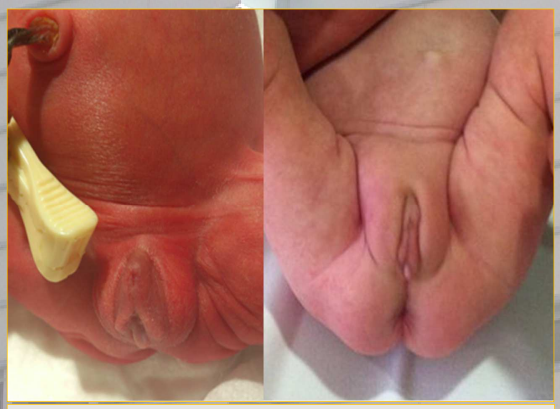
This is a family whose index case is a first son diagnosed at the Newborn Screening Program of CAH in Madrid, Spain.

He presented a salt-wasting form of 21-hydroxylase deficiency. Molecular diagnosis:

"Hybrid deletion" includes the 655G splicing mutation at intron 2 and 8 pairs deletion of exon 3 from paternal line and a "large conversion " of the gene in maternal line.

Both mutations are a severe type and involve significant virilization.

In the second pregnancy, dexamethasone treatment (20 µg/kg/day) was initiated at 4+5 weeks gestation → At 9 week gestation chorionic villous sampling confirmed female fetus affected (46XX) by CAH (same mutations as her brother) so mother was treated until term. → Pregnancy was unremarkable until 31 weeks' gestation when spontaneous rupture of membranes ocurred.



Genitalia at birth (A) and at 2 months of age (B)

✓Birth weight 950 g (-2.06DS) and height 35.5 cm (-2.47DS).

✓Genitalia were assessed as normal at birth, with hypertrophied clitoris according to her prematurity.

✓At 16 days of age her 17OHP concentration was elevated (163 µg/L) and mild symptoms of salt-losing form were detected.

✓Replacement therapy was started, hydrocortisone (150 mg/m²/day the first days with progressive decreasing to 20 mg/m²/day at 35 days of life), fludrocortisone (0.025 mg/day) and sodium chloride (4-5 mEq/kg/day).

✓Maternal side effects of dexamethasone administration were weight gain, facial acne and gestational diabetes that only required diet control. Secondary adrenal insufficiency to taking exogenous steroid was treated with progressive decrease in dose, with complete recovery of adrenal function at 3 months postpartum

✓Fetal exposure to dexamethasone may be related to intrauterine growth restriction and prematurity.

Conclusions:

✓Prenatal treatment of the affected female fetus with CAH is directed toward reducing the need of future genital reconstructive surgery. In this patient the treatment was effective and genitoplasty was avoided.

✓Treatment is offered to women who have previously given birth to a child with a severe form of CAH.

✓Dexamethasone prenatal treatment appears to be effective, however more studies are needed to demonstrate long-term effects.