Normal external genitalia in a female with classic salt-wasting 21-hydroxylase deficiency

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Introduction

- 21-hydroxylase deficiency is the most common cause of congenital adrenal hyperplasia, a family of autosomal recessive disorders involving impaired synthesis of cortisol by the adrenal cortex.
- Because of the impaired cortisol secretion, ACTH levels rise via a negative feedback system and stimulate adrenal hormone secretion, resulting in hyperplasia of the adrenal cortex.
- Females with classic 21-hydroxylase deficiency are exposed to excess androgens prenatally and are born with virilized external genitalia.
- This form is further divided into the simple virilizing form and the salt-wasting form, in which aldosterone production is inadequate which predispose to life-threatening salt-wasting crises.
- Multiple cases reported normal female genitalia in classic congenital adrenal hyperplasia after treating the mother with dexamethasone during pregnancy.

Clinical Case

- The patient is a baby female presented at the age of 6 weeks with fever, poor feeding, and decreased activity for 2 days. Also she had runny nose and cough but no history of vomiting or diarrhea.
- She was born full term, normal vaginal delivery without any complications with APGAR score of 9 at 5 minutes. Birth weight was 3.1 kg.
- Mother was a healthy primigravida with regular prenatal care. She didn’t have hirsutism or change in her voice and was not taking any medications.
- Mother had history of UTI (twice) during pregnancy which was treated with oral cefuroxime. No PROM or fever before delivery.
- Parents are first degree relatives with no history of miscarriage, sudden neonatal deaths, amnorrhea or infertility in the family.
- Patient presented to the emergency department febrile, lethargic and cachectic with signs of severe dehydration. No dysmorphic features were noticed.
- HR: 156 bpm, RR: 56 breaths/minute, Bp: 78/48 mmHg (normal). Her Wight: 3.2 kg (on 25th centile) and her height : 49 cm (on 50th centile).
- External genitalia showed 2 labial folds and three opening (urethral/vaginal/anus), normal clitoris, no labial fusion and no palpable gonads.
- Skin and nipples were hyper-pigmented but other systemic exam was unremarkable.

Investigations

- Sever hyponatremia with sodium of 114mEq/L (reference range 135-145, mEq/L) and sever hyperkalemia with potassium of 7.3mEq/L (reference range 3.5-5.0, mEq/L).
- No hypoglycemia (HGT was 4.1 m mol and glucose level in the serum was 5.4 mmol).
- Acute kidney injury with urea of 19.6 mmol/L and creatinine of 108 umol/L.
- Ammonia and lactic acid levels were normal.
- Urine analysis by catheter showed WBC of 116 with positive nitrite and culture grew E.Coli.
- CSF analysis and culture obtained from lumbar puncture were normal.
- US pelvis showed normal uterus and ovaries.
- Chromosomal analysis showed normal female 46XX.

Response to Treatment

- Hyponatremia was corrected gradually with IV 3% normal saline then 0.9% normal saline.
- She received 25 mg of hydrocortisone as stress dose then shifted to maintenance as 15mg/BSA/day
- Fludrocortisone was added with starting dose of 0.05 mg daily then shifted to 0.15 mg daily.
- Pt was covered with ampicillin and cefotaxime then shifted to cefotaxime.
- She was discharged on oral hydrocortisone and fludrocortisone.
- After discharge she started to gain weight and gradually her skin color improved.

Conclusion

- A cardinal feature for females with classic 21-hydroxylase deficiency is genital ambiguity and salt wasting.
- The cause of normal external genitalia in this case is unknown but we can consider classic 21 hydroxylase deficiency in females with normal external genitalia and hyper-pigmented skin presenting with salt loosing crisis.
- If the disorder isn’t recognized and treated patient may suffer from fatal hypovolemia and shock.

References: