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

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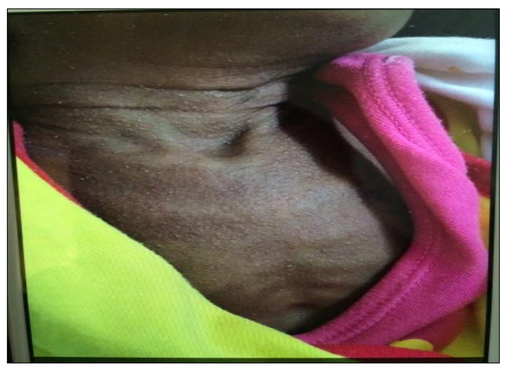
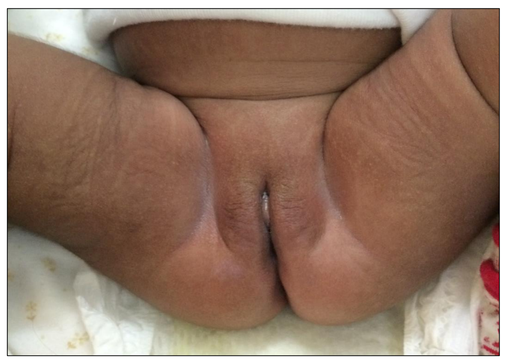
Introduction

- 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.



Hyper-pigmented skin



Patient's External genitalia

Investigations

- High anion gap metabolic acidosis (PH: 7.22, HCO3: 12, CO2: 28, BE: -14.9).
- 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 mmol 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.

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, amenorrhea 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.

17-hydroxyprogesterone (pre ACTH stimulation)	2541 ng/dL	(reference range 13-106 ng/dL)
17-hydroxyprogesterone (post ACTH stimulation)	2946 ng/dL	(reference range 13-106 ng/dL)
Androstenedione	544 ng/dL	(reference range 0-81 ng/dL)
11-deoxycortisol	0.34 ug/dL	(reference range <1 ug/dL)
Testosterone	11.4 nmol/L	(reference range 0.42-0.72, nmol/L)
Renin	>550 uIU/ml	(reference range 4.2 - 59.7 uIU/ml
ACTH	196 pmol/L	(reference range 1.6-13.9, pmol/L)
DHEAS	27 mcmol/L	(reference range 0.86-11.7 mcmol/L)
Estradiol	182 pmol/L	(reference range 22-139, pmol/L).

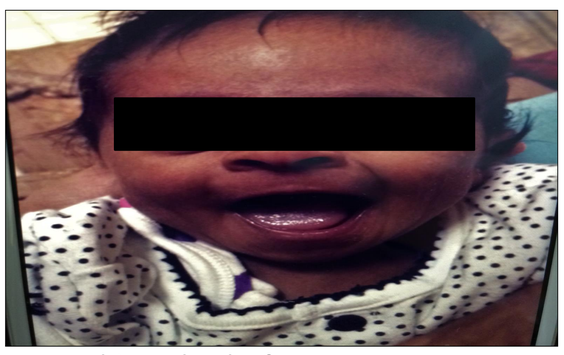
Intervention

- 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.

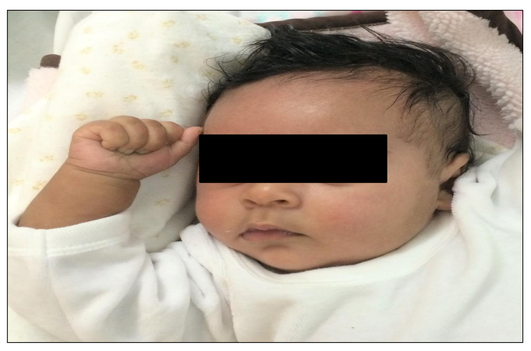
Conclusion

- 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.

Response to Treatment



skin color before treatment



skin color after 3 months of treatment

- References:
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- Quercia N, Chitayat D, Babul-Hirji R, Niw MI, Daneman D (1998) Normal external genitalia in a female with classical CAH who was not treated during embryogenesis. Prenat Diagn 18:83–85

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Sex differentiation, gonads and gynaecology or sex endocrinology

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