CAH Diagnostic Dilemmas: Two Case Reports

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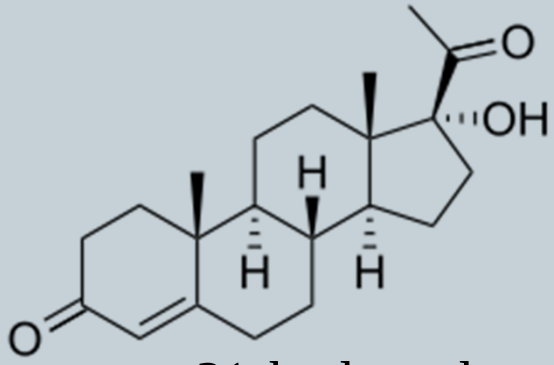
Overview

- Present two case reports of infants with abnormal 17-OHP dried blood spot screens
- Illustrate the challenges of confirming a diagnosis of non salt-wasting CAH



21-hydroxylase

Scheme of Newborn CAH Diagnosis

- Elevated 17-hydroxyprogesterone (17-OHP) on dried blood spot
- Referral to pediatric endocrinologist
- Newborn physical exam & electrolytes
- Serum 17-OHP & steroid panel
- ACTH Stimulation test
- DNA mutational analysis of *CYP21A2* gene (in some cases)

Birth History

Case 1

- 1470g Caucasian male delivered at 28 wks gestation to a diabetic mother
- Hypoglycemic & hypotensive - first 24 hrs
- Baby remained in NICU for 2 months - primarily feeding & growth issues

Newborn Screens/Dx Labs

- 1st NBS @2 hrs = 16.83 ng/mL (normal)
- 2nd NBS @14 d = **155.18 ng/mL (presumptive)**
  - *Serum electrolytes normal*
- 3rd NBS @34 d = **90.83 ng/mL (borderline)**
  - ***Serum 17-OHP @40 d = 58 ng/mL (ELEVATED)***

Further Diagnostic Work-up

- Urine electrolytes; androstenedione, testosterone & renin levels @43 d NORMAL
- Diagnosis: **CAH, 21-hydroxylase deficiency, non-classic form**
- Rx @48 d: ¼ of 5 mg hydrocortisone q 8hrs

At 15 Months of Age

- Healthy toddler at 3rd %ile for height & weight; 40th %ile head circumference
- Labs indicated mild adrenal over-suppression
- **DNA analysis negative** for common & rare *CYP21 (21-hydroxylase)* mutations

Final Disposition

- ACTH stimulation test performed: results indicated ***normal adrenal response***
- Revised diagnosis - child does **NOT** have CAH
- Hydrocortisone discontinued

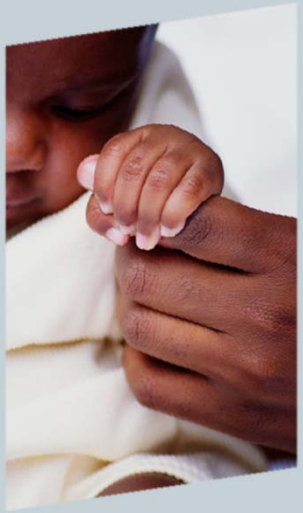
Challenges in this Case

- “Premie” with persistent elevations in 17-OHP
- Too sick to perform earlier ACTH stimulation test
- Delay in DNA mutation analysis

Birth & Neonatal History

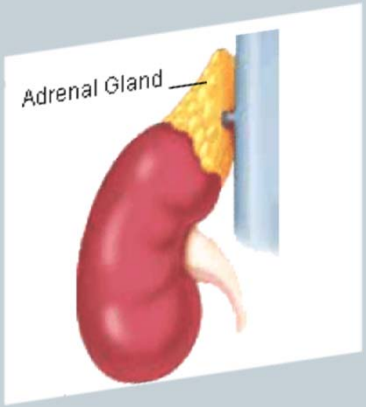
Case 2

- Full term 3470g Black/Asian female
- Ambiguous genitalia (fusion of labioscrotal fold, single vaginal urethral opening, clitoromegaly)
- Karyotype: 46, XX



Birth & Neonatal History continued

- Diagnostic adrenal work-up initiated
- Serum 17-OHP @2 d = 4.23 ng/mL (normal)
- Electrolytes & androstenedione normal
- CAH ruled out; possible adrenal tumor?



Newborn Screens & 2nd Opinion

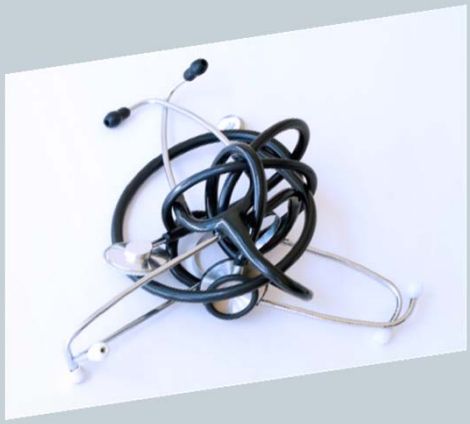
- 1st NBS @51 hrs = 31.82 ng/ml (normal)
- 2nd NBS @12 d = **116.17** ng/ml **(presumptive)**
- Possibility of CAH re-opened
- Consult with different pediatric endocrinologist

Final Disposition

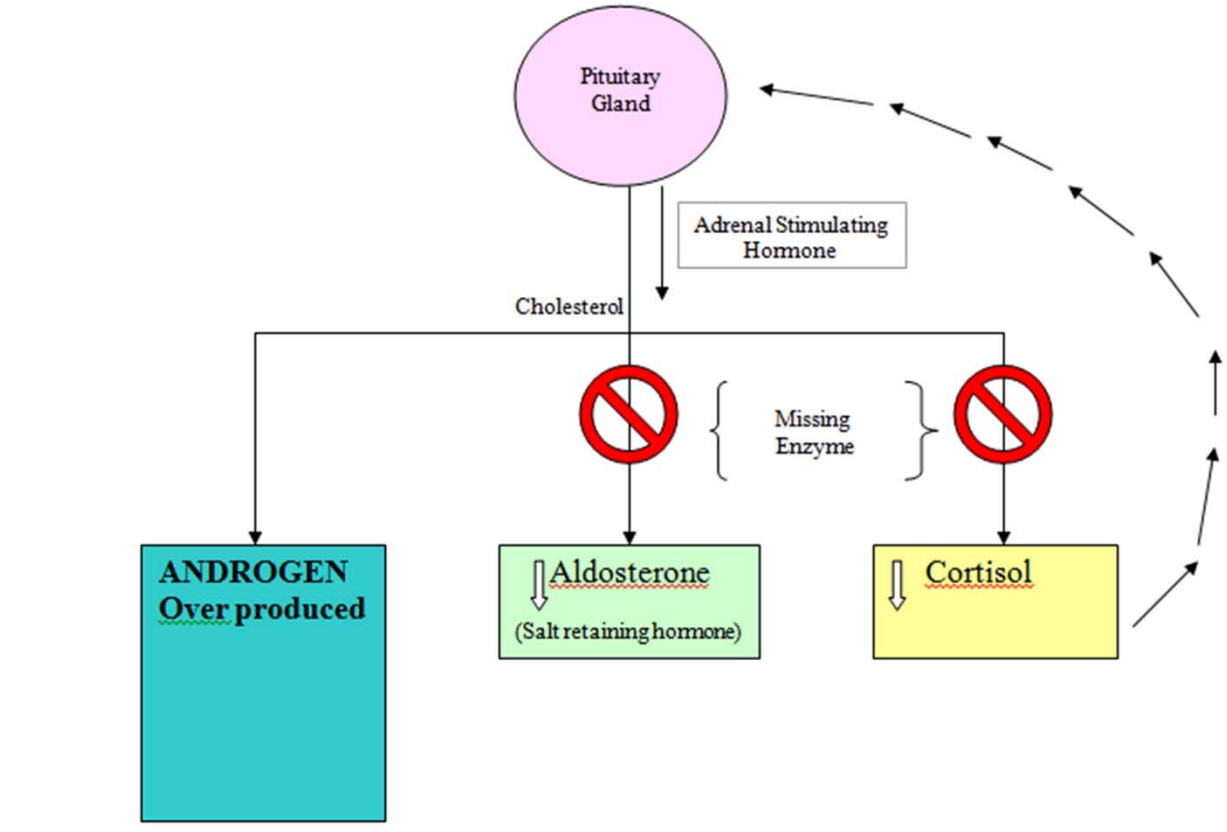
- ACTH stimulation test indicated ***abnormal adrenal response, but no salt-wasting***
- CYP21 DNA: I172N/I172N (or complete deletion)
- Diagnosis: **CAH, 21-hydroxylase deficiency, simple-virilizing form**
- Rx @85 d: ¼ of 5 mg hydrocortisone q 8hrs
- Referral to Disorders of Sex Development Clinic

Challenges in this Case

- Slow to rise 17-OHP level & other steroids
- Incomplete initial evaluation: no ACTH stimulation test or DNA analysis
- Differing professional judgment



21-Hydroxylase Deficiency



Adrenal Gland Hormone Production in CAH

Different Forms of CAH

	Salt-Wasting	Simple-Virilizing	Non-Classic
17-OHP	↑↑↑	↑↑	↑
Cortisol	↓↓	near normal	normal
Aldosterone	↓↓	↑*	normal
Androgens	↑↑↑	↑↑	↑

* to compensate for salt-losing tendency

In Summary …

- CAH is a complex group of disorders that can make a correct diagnosis difficult, especially a non salt-wasting form
- Long-term follow-up by NBS programs, & strong relationships with specialists, are helpful for accurate data collection & program evaluation

Questions?