Case of Non-classic Congenital Adrenal Hyperplasia Patient With Compound CYP21A2 mutations Combined with CYP11B1 Mutation

Rami Salameh, Janna Prater
Einstein Medical Center, Philadelphia, PA

BACKGROUND

Congenital adrenal hyperplasia(CAH) is an autosomal recessive disorder, requiring two copies of an abnormal gene for disease to occur.

Heterozygotes are thought to be generally asymptomatic. Although it has been reported that heterozygote status is associated with hyperandrogenic state, decreased fertility, and adrenal incidentalomas.

21-hydroxylase deficiency(21OHD) accounts for 90% of all CAH cases, while 11-beta-hydroxylase deficiency(11OHD) accounts for 4-8% of CAH cases.

CASE PRESENTATION

A 22-year old female, with no significant past medical history, was evaluated for increased facial hair and acne.

Menarche at the age of 11. Periods regular.
Not sexually active, no biological children.
Family history noncontributory. Patient's father was Jewish, and mother Slavic.

Physical Exam relevant for Normal Blood pressure and normal BMI, Acne on back and upper arms, Ferriman-Gallwey hirsutism score 5.

RESULTS

AM cortisol, CMP, CBC and TSH were normal.
Total testosterone **68** ng/dL (2-45), free testosterone **7** pg/mL (0.1 - 6.4),
FSH 5.7 mIU/mL (2.5-10.2), LH 10.6 mIU/mL (1.9-12.5) , Progesterone **2.1** ng/mL (<1) ,
Estradiol 51 pg/mL (19-144), 17-hydroxyprogesterone **6728** ng/dL (45-285),
Androstenedione **710** ng/dL (35-250), DHEA **1216** ng/dL (102 - 1185),
11-Deoxycortisol **204** ng/dL (<107), Pregnenolon **661** ng/dL(22-237), DHEAS **435** ng/dL (18-391).

Abdominal CT, and pelvic ultrasound were negative for any adrenal or ovarian masses.

3-day dexamethasone suppression test was done and it completely normalized all biochemical abnormalities that the patient had.

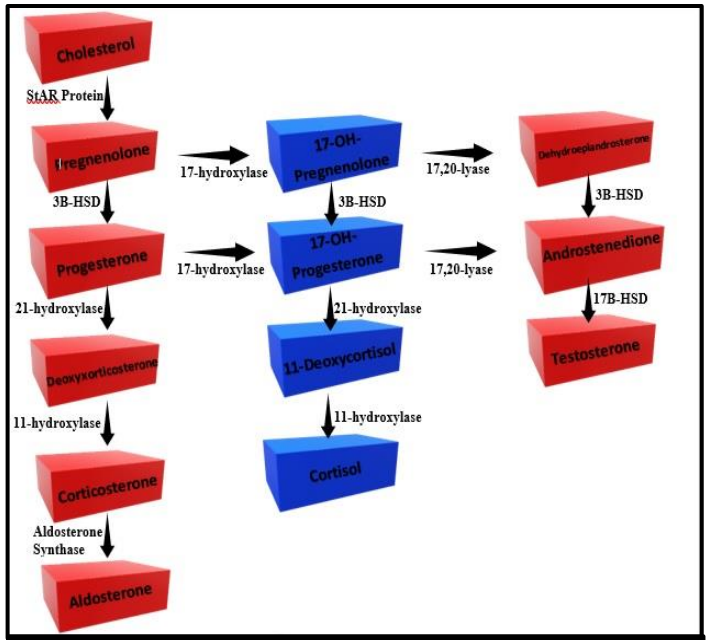
Genetic testing showed: CYP21A2 c.844G>T(which is a non-classic 21OHD CAH mutation), and CYP21A2 c.923dupT(which is a classic 21OHD CAH mutation). Also it showed CYP11B1 c.953C>G mutation.

DISCUSSION

Diagnosis of non-classic 21OHD CAH, and carrier status of 11OHD CAH was made. She was started on PO Dexamethasone 0.25 mg every other day.

Interestingly, in this patient 11-Deoxycortisol was elevated which can't be explained by 21OHD alone.
Her carrier state to the CYP11B1 mutation also doesn't clearly explain the elevated 11-Deoxycortisol level.

We hypothesize that it could be elevated either from extra adrenal conversion of 17-hydroprogesterone to 11-Deoxycortisol, or from 11-beta-hydroxylase inhibition by excess intra-adrenal androgens.



Adrenal Steroid Biosynthesis Pathway
3B-HSD: 3-beta-hydroxysteroid dehydrogenase
17B-HSD: 17-beta-hydroxysteroid dehydrogenase

CONCLUSION

Our case reports a rare finding of both CYP21A2 and CYP11B1 mutations in the same individual.

Which has implications in family planning, and genetic screening for partner and relatives.