



A novel mutation associated with non-classical congenital adrenal hyperplasia in an Emirati female

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Introduction

- ❑ Deficiency of steroid 21-hydroxylase, encoded by CYP21A2 gene, accounts for 95-99% of all congenital adrenal hyperplasia (CAH) cases.
- ❑ We report a case of non-classical CAH (NCAH) due to a novel CYP21A2 mutation c.337T>C p.(Tyr113His), with unusual biochemical features.

Case

- ❑ A 24-year old Emirati female (BMI 25.72 kg/m²) presented with a history of repeated pregnancy loss (RPL) of both spontaneous pregnancy and in-vitro fertilization (IVF), hair fall, and irregular menstrual cycles.
- ❑ She had acne, hirsutism; autoimmune thyroiditis and a thyroid nodule which were duly addressed.
- ❑ The level of 17-OH progesterone was very high (1071 ng/dL); however, testosterone, DHEAS and androstenedione levels were normal.
- ❑ Ovarian ultrasound showed no abnormalities.
- ❑ A short synacthen test done for screening of adrenal insufficiency (in view of her known thyroid immunity and history of fatigue) showed normal baseline, 30 and 60 minute values (239 nmol/L, 717 nmol/L and 850 nmol/L respectively); unfortunately, paired 17-OH progesterone was not checked at the time.
- ❑ A novel heterozygous mutation c.337T>C p.(Tyr113His) in the CYP21A2 gene was identified on genetic testing; this mutation is in a highly conserved region, bioinformatic analysis suggests that it is highly likely to be pathogenic and a deletion of 8 codons (c332-339) including codon 337 is pathogenic (1) .

Conclusion

- ❑ We report a patient with uncommon features of NCAH, including absence of classical hyperandrogenism, in an Emirati female with a novel heterozygous variant.
- ❑ Genetic tests amongst relatives and additional molecular as well as clinical studies are planned to understand the role of this variant in CAH pathology.

References

1. ClinVar: https://www.ncbi.nlm.nih.gov/clinvar/variation/12164/?new_evidence=false