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3β-HSD2 deficiency due to compound heterozygosity of a missense mutation (p.Thr259Met) and a frameshift deletion (p.Lys273ArgFs*7) in an under-virilized infant male with salt wasting

S. LEKA-EMIRI[1], L. TAIBI[2], A. FOTINOU[3], E. VLACHOPAPADOPOULOU[1], ST. MICHALACOS[1], N. de ROUX[2]

[1] Division of Endocrinology-Growth and Development, "P&A KYRIAKOU" Children's Hospital, Athens, Greece
[2] Biochemistry-Hormonology laboratory, Robert-Debré Hospital, Paris Diderot University, Paris, France
[3] Division of Biochemistry-Hormonology, "P&A KYRIAKOU" Children's Hospital, Athens, Greece

Objectives

Describe clinical, hormonal and genetic findings of an undervirilized infant male, 13 month old, Afghan origin, presented at the emergency department with salt-wasting adrenal crisis.

Presenting case

A 13 month old male infant presented at the emergency department with complaints of vomiting and fever.

❖ Physical examination / Personal history

➢ Physical examination was significant for severe deshydratation along with perineal hypospadias, bifid scrotum, penile chordee and undescended left testicle (fig. 1)

➢ He was he was under cortisone treatment that was stopped 15 days before referral to our hospital.

❖ Laboratory evaluation

➢ Revealed hyponatremia, Na: 130 mEq/L (135-145 mEq/L) with concurrent hyperkalemia, K: 5.5 mEq/L (3.5-4.5 mEq/L).

➢ Steroid hormone testing obtained before treatment revealed a complex pattern suggestive of congenital adrenal hyperplasia (CAH) due to 3β-HSD deficiency (table 1).

❖ Scrotal u/s revealed the right testicle in the scrotal area (1,82χ1,34,0,92) cm (Vol: 1,12cm3) and the left testicle in the upper inguinal area (1,38χ0,89χ0,93)cm (Vol:0,58 cm3), both harboring microcalcifications.

DHEA-S	**13,35 (<0,600)μgr/ml**
17-OH-Progesterone	**35,07 (0.200-0,800)ng/ml**
Testosterone	**0,946 (<0,025)ngr/ml**
Cortisol	**1,15 (6,2-23,00)μgr/dl**
Chromosomal karyotype	**46,XY**

Table 1

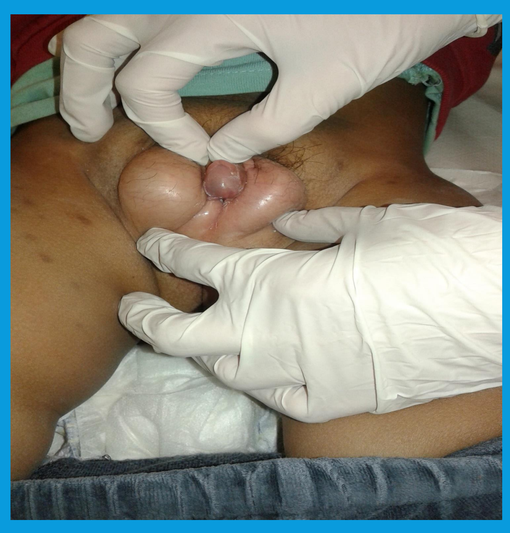

Figure 1

❖ Molecular analysis performed by next generation sequencing revealed

❖ a missense mutation : c.776C>T (p.Thr259Met), already described in a patient with the disease, transmitted by the mother and

❖ a frameshift deletion: c.818-819delAA (p.Lys273ArgFs*7 transmitted) , a very rare mutation never described so far, transmitted by the father.

❖ Both mutations are described in HGMD as pathogenic

❖ Treatment:

➢ Replacement therapy with hydrocortisone, fludrocortisone, and sodium chloride was started

➢ Clinical outcome:

➢ The patient recovered from his acute illness, was discharged home on steroids.

➢ In the near future he will have urologic surgery to correct his urogenital

Conclusions

Deficiency of 3-beta hydroxysteroid dehydrogenase type II (3β-HSD2) is a rare autosomal recessive form of congenital adrenal hyperplasia (CAH). More than 40 mutations have been found in theHSD3B2 gene causing 3βHSD2D. Our patient is the first undervirilized male with severe salt wasting presenting compound heterozygosity of missense c.776C>T, p.Thr259Met and frameshift deletion: c.818-819delAA, p.Lys273ArgFs*7 maybe due to a founder effect for people leaving in that area.

The authors declare that they have no conflict of interest.

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