Presented at: Classical salt wasting congenital adrenal hyperplasia (CAH) due to 21-hydroxylase deficiency (21OHD) is a rare disorder, as is isolated growth hormone (GH) deficiency Type II (IGHD II) due to mutation of the growth hormone gene GH1.

Here we present a highly unusual and instructive case in which both diseases occurred in parallel and a new mutation in the GH1 gene was discovered.

**Case**

- **Early Childhood:**
  - Diagnosis of classical salt wasting CAH due to 21OHD by hormonal and genetic analyses
  - Adolescence:
    - Failure of growth spurt at puberty to reach family target height range.
    - At the age of 15 years height of 148.3 cm (-2.8 SDS) (parental target height 155 cm (-2.03 SDS)

- **METHOD**
  - Testing for growth factors IGF-I and IGF-BP3
  - X-ray of the left hand (bone age)
  - GH stimulation test (arginine test)
  - SHOX diagnostics
  - Next generation sequencing gene panel (biosencia Humangenetik, Ingelheim)

- **RESULTS**
  - Growth hormones
    - IGF-I level low (84 µg/L, SDS -3.39)
    - IGFBP-3 normal (2.95 mg/L, -SDS 0.54)
  - X-ray:
    - Unusual for a patient with CAH, bone age was delayed by 3 years
  - GH stimulation test (arginine test)
    - GH increase to max. 12.6 ng/mL
  - SHOX Diagnostics
    - Negative
  - Next generation sequencing gene panel
    - Heterozygous variant c.235T>G p.(Cys79Gly) in exon 3 of the GH1 gene was detected

- **CONCLUSIONS**
  - GH exon 3 mutation of our patient is highly likely to cause the formation of partially bioinactive GH as has been described for the mutation Exon 3, c.236G>C by Besson et al. (1)
  - This mutation (loss of cystein) interrupts the disulfide bridge at position 53 of the mature GH peptide which is important for the correct tertiary structure
  - A "toxic" GH variant is formed, which interferes with the secretion of normal GH and further leads to the destruction of somatotropic cells.
  - Negative dominant effect in heterozygous: IGHD type II patients
  - Additional genetic analysis of both parents, detected the same heterozygous variant of the GH1 gene in the father
  - Paternally inherited, autosomal dominant form of IGHD type II was diagnosed
  - Important: a normal GH stimulation test does not rule out growth hormone deficiency in any case!

The authors have nothing to disclose.

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