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Case report:

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Normal minipuberty in a patient with DAX-1 mutation: additional evidence of a differential role for DAX-1 during development?

DAX-1 gene encodes for an orphan member of the nuclear receptor superfamily. Dax-1 is expressed in the adrenal cortex, gonads, hypothalamus and anterior pituitary. DAX1 is known to play a critical role in the development of the hypothalamic-pituitary-adrenal axis. Its role in regulation of the hypothalamic-pituitary-gonadal axis is still debated.

Here we report the case of a five week-old male patient, referred to the hospital because of failure to thrive. An adrenal insufficiency was diagnosed and the genetic testing showed a nonsense mutation in exon 1 of the DAX-1 gene.

Classically, mutations in the DAX-1 gene cause an adrenal hypoplasia congenita associated with adrenal insufficiency and hypogonadotropic hypogonadism.

In our patient, physical examination showed normal male sexual differentiation (normal penile length and descended testes) and the laboratory evaluation reveals a normal minipuberty onset (basal testosterone: 1.9 µg/L; LH: 1.3 UI/L and FSH: 6.3 UI/L at 10 weeks of age) suggesting normal function of the pituitary-gonadal axis during the perinatal period.

DAX-1 mutations are classically reported to cause hypogonadotropic hypogonadism. Our observation as well as gonadotropin-dependent precocious puberty in a patient with a similar nonsense mutation (Horm. Res. Paediatr., Darcan et al, 2011) suggest that hypothalamic-pituitary-gonadal function could not be impaired till adolescence or adulthood in patients with DAX1 mutations. Accordingly, DAX-1 might not be a major player in the early life activation of the hypothalamic-pituitary-gonadal axis while it could be involved in the central control of reproduction later in life. This further highlights the difficulty for clinicians to predict pubertal timing and reproductive functions in patients with DAX-1 mutation.