

INTRODUCTION

Thyroid hormones play an essential role in growth and metabolic homeostasis in humans as well as in animals. In the last decades, growing attention has been focused on the effects of TH during fetal life in terms of tissue differentiation and development. The retina, brain, and spinal cord are the first regions where deiodinases can be found, suggesting a potential role in early CNS development.

CASE REPORT

We report the case of a seven-year-old boy, unicogenised child, born at 33w. Birth auxological parameters were: weight 1.540 kg (11th percentile), length 39 cm (3th percentile) and head circumference 29.5 cm (18th percentile). APGAR score was 8-10. He was hospitalized in neonatology unit for 30 days, invasive respiratory assistance was not necessary. At birth evidence of hypospadias with penile incurvation, oval fossa defect,. Cranial sonography revealed an agenesis of the corpus callosum. Normal male karyotype. For positivity to screening for IC (in-situ normal thyroid), he started L-thyroxine therapy. When he was six he presented an adrenarache, normal testicular volume, associated with acceleration of growth rate and advanced bone age. An ACTH stimulation test was performed, showing elevated concentrations of 17-hydroxyprogesterone (17-OHP) with a basal value of 2.3 ng/ml and a post-stimulation value of 27.3 ng/ml. The molecular genetic testing for analysis of CYP21 gene confirmed non classical adrenogenital syndrome (double heterozygous V281L - R26W). Clinical examination revealed broad forehead, down-slant eyelid, bulbous nose tip with long filter, malarial hypoplasia, large auricles, normal IQ (Figure 1). Therefore, CMA test was performed with detection of microduplication in region 3p25.3 about 546 Kb which partially involves the OMIM Disease gene causing ATP2B2 and a paternal segregation microduplication of the chromosome long arm 4, of the 4p23 region, extended about 181 Kb not involving OMIM Disease Causing genes.



Figure 1 – Clinical features in our patient.

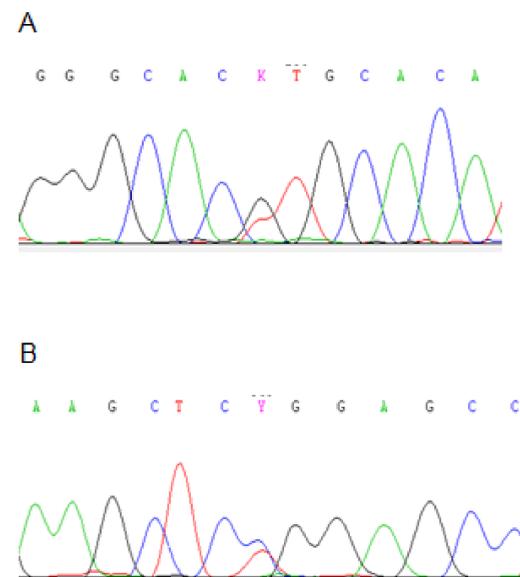


Figure 2 - Electropherograms showing *CYP21A2* sequence of the patient in the regions carrying the mutations V281L (A) and c.76C>T (R26W) (B) in heterozygosis.

DISCUSSION AND COCLUSION

In our patient, the V281L mutation, associated with non-classical adrenogenital syndrome, was detected in a heterozygous state. In addition, during the sequence of *CYP21A2* to find a possible association with P30L mutation, the novel and previously undescribed variation c.76C>T (p.Arg26Trp or R26W) in *CYP21A2* sequence was detected in heterozygosis (Figure 2).

In addition, in our patient CMA test revealed two microduplications that to date are not associated with syndromic frameworks or clinics highlighted in the patient.

Therefore, it is not possible to predict the phenotype of the child and a monitoring follow-up over time is required.

REFERENCES

Morvan Dubois G, Sebillot A, Kuiper GG, Verhoelst CH, Darras VM, Visser TJ et al. Deiodinase activity is present in *Xenopus laevis* during early embryogenesis. *Endocrinology*. 2006 Oct;147(10):4941–9