CONGENITAL CENTRAL HYPOTHYROIDISM (CCH) DUE TO A NEW VARIANT IN IGSF1 GENE: CLINICAL CASE OF 2 SIBLINGS

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INTRODUCTION

The immunoglobulin superfamily member 1 (IGSF1) is the gene responsible for the so-called X-linked IGSF1 deficiency syndrome, characterized by an estimated incidence of 1:100,000. The main features are central hypothyroidism (CeH), delayed/disharmonic pubertal development, macroorchidism, variable prolactin and occasionally transient/partial GH deficiencies.

AIM

• Diagnostic and clinical management of CeH is still nowadays a challenging condition due to the lack of accurate clinical and biochemical parameters.

• Our aim was to describe the case of two siblings affected by this peculiar form of CCH.

METHOD

• Two siblings affected by CeH

• Suggestive phenotypic features (relative macrocrania, non-harmonic growth, high BMI, macroorchidism)

• Diagnosis reached by genetic investigations

RESULTS

Index case (9 years old)

- Relative macrocrania
- Non-harmonic growth
  - High BMI
- Macroorchidism

Suggestive clinical features

- TSH in the reference range
- FT4 in the lower part of reference range

Normal Hypothalamic-pituitary region

Brother (10 years old)

Normal response during TRH test

Genetic analysis for CeH-related genes revealed the presence of a p.T614A (c.1804A>G) hemizygote genetic variant on exon 12 of IGSF1 gene. This is a newly described allelic variant of uncertain significance (VUS) inherited from the mother.

CONCLUSIONS

- Diagnosis of CeH is often difficult

- We advise genetic evaluation of IGSF1 gene in all patients with CeH of unknown cause especially in presence of a typical X-linked inheritance and/or peculiar clinical signs such as macrocrania and/or macroorchidism.

- Genetic analysis may allow early diagnosis and a prompt therapeutic approach in order to avoid possible sequelae of untreated CeH.

REFERENCES

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