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.

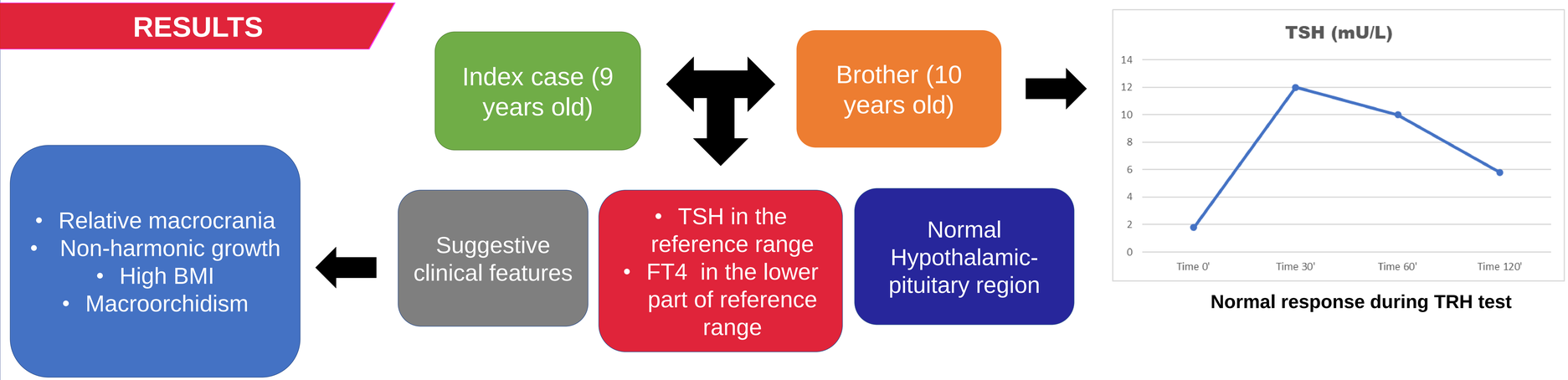
AIM

- **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



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.**

Suppression of TSH and FT4 in the upper part of reference range confirmed a good response to therapy with levothyroxine.

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 promt therapeutic approach in order to avoid possible sequelae of untreated CeH.**

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