Screening for SOX2 mutations in Bulgarian patients with congenital hyposomatotropism: first results

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Background: The most common cause of congenital combined pituitary hormone deficiency (CPHD) is mutations in the transcription factor (TF) PROP1 gene, followed by PIT1 mutation. Bulgarian pituitary TF study showed an allele frequency of PROP1 mutations in 12.2% and no confirmed PIT1 mutations (1).

The TF SOX2 (sex determining region Y box 2) is a member of high-mobility group transcription factor family. It is one of the earliest TFs during the development. SOX2 is expressed most notably in the development of the central and peripheral nerves system, pituitary (fig.1), corpus callosum, hypothalamus, eye and ear (2). The first SOX2 mutation is revealed by Fantes in 2003 (3). Since then more than 40 mutations have been found. Heterozygous mutations have been associated with ocular abnormalities like anophthalmia/microphthalmia, coloboma, nistagmus, impaired anterior pituitary development with reduced levels of anterior pituitary hormones, and male genital tract anomalies (4).

Objective: To implement a mutational screening for SOX2 as a diagnostic tool in congenital CPHD and to assess the overall allele frequency in Bulgarian hyposomatotropic patients.

Study population: 22 patients, aged (x±SD) 12.9±10.6, median 10.3 years, 13 females (12.7±10.9, median 9.3 years), 9 males (13.1±11.0, median 9.3 years).

Results: No mutations in SOX2 gene were verified in the selected patients.

Conclusions: Mutations in SOX2 are a rare cause of hypopituitarism. For a precise etiological diagnosis patients with complex phenotype including pituitary and extrapituitary manifestations should undergo whole genome sequencing.

References:

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