

Combined pituitary hormone deficiency with restricted neck mobility and progressive skeletal deformities mimicking an LHX3-related phenotype: A genetically unsolved case

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Abstract

Background: Combined pituitary hormone deficiency (CPHD) with restricted cervical spine rotation is a rare phenotype classically linked to LHX3 mutations. We report an adult male with panhypopituitarism, progressive skeletal deformities, and a significant family history of unexplained deaths, in whom a targeted genetic panel including LHX3 was negative- highlighting a gap between phenotype and current genetic testing.

Case summary: A 34-year-old male, 6th issue of non-consanguineous parents, presented with initial growth failure in childhood followed by attainment of normal height later and failure to attain secondary sexual characteristics & weakness. He was diagnosed with hypogonadotropic hypogonadism and hypothyroidism at 23 and had an adrenal crisis at 30. From age 17, he developed progressive restriction of neck movement, dorsal kyphosis, pectus excavatum, and elbow flexion deformity. Family history included two stillbirths and one sibling death at 1.5 years. Examination showed eunuchoid habitus and the above skeletal findings. Investigations confirmed deficiency across the gonadotropin, thyrotropin, growth hormone, and corticotropin axes, with diabetes mellitus; karyotype was normal. MRI showed a partially empty sella with disc desiccation at all vertebral levels. A 23-gene congenital hypopituitarism NGS panel (including LHX3, HESX1, PROP1, POU1F1) showed no pathogenic variant.

Conclusions: This case shows a phenotype strongly suggestive of LHX3-related CPHD without a molecular diagnosis on panel testing, emphasizing the limitations of current NGS panels (CNV/non-coding regions) and the value of broader genomic testing in phenotype-genotype-negative CPHD. [*J Assoc Clin Endocrinol Diabetol Bangladesh*, 2026;5(Suppl 1): S75]

Keywords: Combined pituitary hormone deficiency; LHX3, Restricted cervical spine mobility

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