Pituitary Hypoplasia

Mariam Gangat, MD[a,*], Sally Radovick, MD[b]

KEYWORDS

- Pituitary development • Transcription factor
- Combined pituitary hormone deficiency • Hypopituitarism

KEY POINTS

- Coordinated temporal and spatial expression of several transcription factors is essential for normal pituitary gland development and function.
- The pituitary gland is responsible for the production of hormones that play a crucial role in growth, metabolism, puberty and reproduction, lactation, and stress response.
- Several mutations in patients with hypopituitarism have been identified; however, the vast majority of patients remain labeled idiopathic.
- Next-generation sequencing technology is expanding our understanding of the underlying genetic mechanisms of hypopituitarism, and has the potential of revolutionizing clinical care.

INTRODUCTION AND CLINICAL PRESENTATION OF HORMONE DEFICIENCIES

The pituitary gland lies in the hypophyseal fossa, the deepest part of the sella turcica, located in the sphenoid bone of the neurocranium. It is composed of 2 distinct structures, the adenohypophysis (anterior and intermediate lobes) and neurohypophysis (posterior lobe), which differ in embryologic origin. The anterior originates from the Rathke pouch, an invagination of the oral ectoderm, and the posterior lobe arises from the neuroectoderm. Multiple transcription factors act in a coordinated temporal and spatial sequence during pituitary development, and ultimately result in the differentiation of specific pituitary cell lineages (**Table 1**). The anterior lobe has 5 distinct cell types that produce 6 hormones: somatroph (growth hormone [GH]), thyrotroph (thyrotropin [TSH]), gonadotroph (luteinizing hormone [LH] and follicle-stimulating hormone [FSH]), lactotroph (prolactin), and corticotroph (adrenocorticotropin [ACTH]). These

The authors have nothing to disclose.

[a] Department of Pediatrics, Child Health Institute of New Jersey, Rutgers-Robert Wood Johnson Medical School, Rutgers, The State University of New Jersey, 89 French Street, Room 1360, New Brunswick, NJ 08901, USA; [b] Department of Pediatrics, Child Health Institute of New Jersey, Rutgers-Robert Wood Johnson Medical School, Rutgers, The State University of New Jersey, 89 French Street, Room 4212, New Brunswick, NJ 08901, USA
* Corresponding author.
E-mail address: gangatma@rwjms.rutgers.edu

Endocrinol Metab Clin N Am ■ (2017) ■–■
http://dx.doi.org/10.1016/j.ecl.2017.01.003 **endo.theclinics.com**

Table 1
Mutations causing abnormal pituitary development and function

Gene	Chromosome	Pituitary Deficiencies	Associated Syndromes/ Malformations	Inheritance
HESX1	3p21	IGHD, CPHD (GH, TSH, LH, FSH, Prolactin, ACTH)	SOD	AR, AD
LHX3	9q34	CPHD (GH, TSH, LH, FSH, Prolactin)	Rigid cervical spine, limited neck rotation, sensorineural hearing loss	AR
LHX4	1q25	CPHD (GH, TSH, ACTH)	Cerebellar defects	AD
PROP1	5q35	CPHD (GH, TSH, LH, FSH, Prolactin, ACTH)		AR
POU1F1	3p11	CPHD (GH, TSH, Prolactin)		AR, AD
OTX2	14q22	CPHD (GH, TSH, LH, FSH, Prolactin, ACTH)	Microphthalmia, retinal dystrophy	AD

Abbreviations: ACTH, adrenocorticotropin; AD, autosomal dominant; AR, autosomal recessive; CPHD, combined pituitary hormone deficiency; FSH, follicle-stimulating hormone; GH, growth hormone; LH, luteinizing hormone; SOD, septo-optic dysplasia; TSH, thyrotropin.

hormones play a crucial role in growth, metabolism, puberty and reproduction, lactation, and stress response.

Combined pituitary hormone deficiency (CPHD), involvement of more than 1 anterior pituitary hormone, is associated with severe morbidity and can be life-threatening. The clinical presentation varies depending on age as well as the number and severity of hormone deficiencies. Many findings are nonspecific, especially in the newborn period, mandating a high index of suspicion, particularly in patients with midline defects.

Newborns with growth hormone deficiency (GHD) may not show overt growth failure; however, may present with hypoglycemia and prolonged jaundice. When combined with gonadotropin deficiency, genitourinary abnormalities such as microphallus and cryptorchidism are seen. Children present with growth failure evidenced by poor growth velocity, short stature, and increased weight-to-height ratio. Pulsatile secretion of GH limits the use of random serum GH levels. However, insulin-like growth factor 1 (IGF-1), the primary mediator of the actions of GH, and its most abundant carrier protein IGF-BP3, are stable throughout the day and therefore are useful screening laboratory tests. Growth hormone stimulation testing, although flawed,[1] can be performed using several protocols,[2] and can aid in establishing the diagnosis of GHD. Recombinant GH is the treatment of choice, and commonly administered once daily via subcutaneous injections.

Although congenital hypothyroidism (CH) due to TSH deficiency is rare, early diagnosis and treatment are critical to prevent adverse neurologic outcomes.[3] Infants can present with myxedema, hypotonia, hoarse cry, poor feeding, macroglossia, umbilical hernia, large fontanels, hypothermia, and prolonged jaundice. Some symptoms overlap with those seen in childhood, such as lethargy, constipation, and dry skin. Additional features seen in children include poor linear growth, cold intolerance, brittle hair, and a decline in academic performance. Newborn screening protocols for CH vary by state, and central hypothyroidism can be missed with primary TSH with