Combined Pituitary Hormone Deficiency

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Combined pituitary hormone deficiency is a condition that causes a shortage (deficiency) of several hormones produced by the pituitary gland, which is located at the base of the brain. A lack of these hormones may affect the development of many parts of the body. The first signs of this condition include a failure to grow at the expected rate and short stature that usually becomes apparent in early childhood.

Keywords: genetic conditions

1. Introduction

People with combined pituitary hormone deficiency may have hypothyroidism, which is underactivity of the butterfly-shaped thyroid gland in the lower neck. Hypothyroidism can cause many symptoms, including weight gain and fatigue. Other features of combined pituitary hormone deficiency include delayed or absent puberty and lack the ability to have biological children (infertility). The condition can also be associated with a deficiency of the hormone cortisol. Cortisol deficiency can impair the body's immune system, causing individuals to be more susceptible to infection.

Rarely, people with combined pituitary hormone deficiency have intellectual disability; a short, stiff neck; or underdeveloped optic nerves, which carry visual information from the eyes to the brain.

2. Frequency

The prevalence of combined pituitary hormone deficiency is estimated to be 1 in 8,000 individuals worldwide.

3. Causes

Mutations in at least eight genes have been found to cause combined pituitary hormone deficiency. Mutations in the *PROP1* gene are the most common known cause of this disorder, accounting for an estimated 12 to 55 percent of cases. Mutations in other genes have each been identified in a smaller number of affected individuals.

The genes associated with combined pituitary hormone deficiency provide instructions for making proteins called transcription factors, which help control the activity of many other genes. The proteins are involved in the development of the pituitary gland and the specialization (differentiation) of its cell types. The cells of the pituitary gland are responsible for triggering the release of several hormones that direct the development of many parts of the body. Some of the transcription factors are found only in the pituitary gland, and some are also active in other parts of the body.

Mutations in the genes associated with combined pituitary hormone deficiency can result in abnormal differentiation of pituitary gland cells and may prevent the production of several hormones. These hormones can include growth hormone (GH), which is needed for normal growth; follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which both play a role in sexual development and the ability to have children (fertility); thyroid-stimulating hormone (TSH), which helps with thyroid gland function; prolactin, which stimulates the production of breast milk; and adrenocorticotropic hormone (ACTH), which influences energy production in the body and maintains normal blood sugar and blood pressure levels. The degree to which these hormones are deficient is variable, with prolactin and ACTH showing the most variability. In many affected individuals, ACTH deficiency does not occur until late adulthood.

Most people with combined pituitary hormone deficiency do not have identified mutations in any of the genes known to be associated with this condition. The cause of the disorder in these individuals is unknown.

3.1. The Genes Associated with Combined Pituitary Hormone Deficiency

- HESX1

- OTX2
- PROKR2
- PROP1
- SOX2

4. Inheritance

Most cases of combined pituitary hormone deficiency are sporadic, which means they occur in people with no history of the disorder in their family. Less commonly, this condition has been found to run in families. When the disorder is familial, it can have an autosomal dominant or an autosomal recessive pattern of inheritance.

Autosomal dominant inheritance means one copy of an altered gene in each cell is sufficient to cause the disorder.

Autosomal recessive inheritance means both copies of a gene in each cell have mutations. The parents of an individual with an autosomal recessive condition each carry one copy of a mutated gene, but they typically do not show signs and symptoms of the condition. Most cases of familial combined pituitary hormone deficiency are inherited in an autosomal recessive pattern.

5. Other Names for This Condition

- CPHD
- panhypopituitarism

References

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