Hypopituitarism

Growth Hormone and Corticotropin Deficiency

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KEYWORDS

• Hypopituitarism • Growth hormone • Adults • Corticotropin • ACTH • Deficiency • Replacement treatment

KEY POINTS

- Adult growth hormone deficiency (AGHD) is associated with increased cardiovascular risk and alterations in substrate metabolism, in addition to impaired body composition, muscle strength, bone mass, and quality of life.
- Growth hormone (GH) replacement therapy with individualized dosing regimens improves most features of the clinical syndrome of AGHD.
- Corticotropin deficiency (central adrenal insufficiency; CAI) can present with chronic, nonspecific symptoms, or acutely, with life-threatening adrenal crisis.
- If acute CAI is suspected, immediate treatment should be initiated.
- Chronic management of CAI requires lifelong glucocorticoid administration with mandatory dose adjustment during stressful events.

INTRODUCTION

Hypopituitarism refers to the decreased secretion of 1 or more pituitary hormones caused by pituitary or hypothalamic disease. The clinical manifestations of hypopituitarism depend on its cause, in addition to the type and severity of the hormonal deficit. In most etiologic scenarios, the secretion of gonadotropins and growth hormone (GH) are more likely to be affected than corticotropin (adrenocorticotropic hormone; ACTH) and thyroid-stimulating hormone (TSH), but isolated deficiencies of any hormone can

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occur. The diagnosis is made by separately documenting the subnormal secretion of each pituitary hormone. The treatment of ACTH deficiency (central adrenal insufficiency; CAI) is life saving and consists of lifelong glucocorticoid administration. The treatment of adult growth hormone deficiency (AGHD) consists of recombinant human GH (rhGH) preparations according to criteria devised by national regulatory bodies.

ETIOLOGY

In most cases of acquired AGHD and CAI, the etiology is common with that of other types of noninherited hypopituitarism (**Box 1**).[1,2] Most frequently, a pituitary adenoma

Box 1
Etiology of growth hormone (GH) and corticotropin (ACTH) deficiency in adults

Acquired Causes of Adult Growth Hormone Deficiency and/or Adult Central Adrenal Insufficiency (CAI)

- Pituitary tumor
- Craniopharyngioma
- Pituitary/brain surgery
- Pituitary/brain irradiation
- Other central nervous system tumor, including metastatic tumor in the hypothalamic/pituitary area
- Traumatic brain injury
- Subarachnoid hemorrhage
- Empty sella syndrome
- Granulomatous diseases (hemochromatosis, sarcoidosis, Wegener granulomatosis, histiocytosis)
- Infectious diseases (tuberculosis, actinomycosis)
- Hypophysitis (can cause isolated CAI)
- Pituitary apoplexy
- Internal carotid artery aneurism

For CAI only: adult-onset isolated CAI (mostly autoimmune, frequently as part of polyglandular autoimmune syndrome); drug-induced (exogenous glucocorticoids, mifepristone, various antipsychotics); following total removal of an ACTH-secreting pituitary adenoma

Congenital Causes of Growth Hormone Deficiency (GHD) and CAI

GHD

- Isolated
- Combined pituitary deficiencies:
  - Mutations of *PROP1*, *HESX1*, *LHX3*, *LHX4*, *POU1F1* (encoding PIT1)
  - Associated with brain structural defects

CAI

- Isolated congenital CAI (*POMC* or *TPIT* gene mutations, POMC processing defect)
- Combined pituitary deficiencies:
  - Mutations of *PROP1*, *HESX1*, *LHX3*, *LHX4* (panhypopituitarism)
  - Midline forebrain defects