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Acromegaly and Hyperprolactinemia

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Acromegaly and Hyperprolactinemia

Bryan McIver, MB, PhD

INTRODUCTION

The pituitary-hypothalamic axis functions as a central regulator of hormone action, interconnecting the central nervous system with most of the major endocrine organs. Diseases of this system are due to overproduction or underproduction of one or more hormones or to the development of an expansile pituitary mass, which causes compression of surrounding structures, most commonly the optic chiasm and hypothalamus.

In most cases, excess pituitary hormone production is caused by the development of a pituitary adenoma, a benign neoplasm that retains almost complete differentiated cell function but that fails to respond normally to pituitary-hypothalamic feedback control mechanisms. An enlarging pituitary mass may compress the remaining normal pituitary tissue, resulting in gradual loss of function of the pituitary hormones secreted by these tissues, which may complicate the diagnosis and management of these diseases. Reduced pituitary function also may occur as a result of a nonfunctioning pituitary mass, most often an adenoma, or because of destruction arising from trauma, infection, inflammation, or infiltration of the pituitary fossa.¹

At least eight functional hormones are secreted from the pituitary gland, six from the anterior lobe (the adenohypophysis), and two from the posterior lobe (the neurohypophysis). Most of these hormones can cause specific syndromes of oversecretion or undersecretion (Table 1). All of these disorders are rare and the symptoms may be vague and nonspecific, complicating the diagnosis. Pituitary diseases may be among the most challenging of all endocrine diseases to diagnose and treat.

ACROMEGALY

OVERVIEW

Excess secretion of growth hormone (GH) causes two overlapping syndromes: *gigantism*, which occurs in childhood and adolescence, prior to fusion of the bony epiphyses; and *acromegaly*, which occurs in adults. In

both cases, the condition results from hypersecretion of GH from the adenohypophysis, almost always caused by a pituitary adenoma or, more rarely, by hypersecretion of growth hormone-releasing hormone (GH-RH) from the hypothalamus or elsewhere.² The cause of the condition is poorly understood, although there is some evidence that altered hypothalamic control might influence the development of some pituitary adenomas.³

Acromegaly is a rare disease, with an estimated annual incidence of approximately 3 cases per million persons and a prevalence of approximately 50 cases per million. Men and women are equally affected.² The average age at diagnosis is approximately 40 to 45 years, and there is evidence that an earlier onset is associated with more aggressive tumors. In most cases, however, the clinical features develop slowly and insidiously. Disease presentation often is overshadowed by secondary conditions including diabetes, hypertension, and vascular disease. Because the diagnosis is frequently made late in the disease process, the causative pituitary tumor has the opportunity to grow and by the time of diagnosis is usually a macroadenoma, often extending beyond the pituitary fossa.⁴

High circulating concentrations of GH stimulate hepatic production of insulin-like growth factor 1 (IGF-1; somatomedin C), which mediates virtually all of the end-organ effects of GH. IGF-1 acts on a broad array of organ systems, most prominently connective tissue, skeletal and cardiac muscle, and bone. Prior to closure of the epiphyses in late adolescence, GH stimulates longitudinal growth of the long bones, increasing stature and limb length. Children and adolescents with gigantism can therefore reach unusual height and will continue to grow unless puberty proceeds normally. Interruption of pubertal development is a common consequence of the pituitary compression that accompanies a GH-secreting pituitary macroadenoma.⁵ Such interrupted puberty permits longitudinal growth to continue unchecked without medical intervention. In contrast, onset of acromegaly in adulthood does not increase height. However, cortical bone thickness does increase in adult acromegalic patients and, along with thickening of subcutaneous connective tissue, results in the characteristic phenotypic features of acromegaly (Table 2, Figure 1).²