Pituitary gigantism: a case series from Hospital de San José (Bogotá, Colombia)

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ABSTRACT

Introduction: Gigantism is a rare pediatric disease characterized by increased production of growth hormone (GH) before epiphyseal closure, that manifests clinically as tall stature, musculoskeletal abnormalities, and multiple comorbidities. **Materials and methods:** Case series of 6 male patients with gigantism evaluated at the Endocrinology Service of *Hospital de San José* (Bogotá, Colombia) between 2010 and 2016. **Results:** All patients had macroadenomas and their mean final height was 2.01 m. The mean age at diagnosis was 16 years, and the most common symptoms were headache (66%) and hyperhidrosis (66%). All patients had acral changes, and one had visual impairment secondary to compression of the optic chiasm. All patients underwent surgery, and 5 (83%) required additional therapy for biochemical control, including radiotherapy (n = 4, 66%), somatostatin analogues (n = 5, 83%), cabergoline (n = 3, 50%), and pegvisomant (n = 2, 33%). Three patients (50%) achieved complete biochemical control, while 2 patients showed IGF-1 normalization with pegvisomant. Two patients were genetically related and presented a mutation in the aryl hydrocarbon receptor-interacting protein (*AIP*) gene (pathogenic variant, c.504G>A in exon 4, p.Trp168*), fulfilling the diagnostic criteria of familial isolated pituitary adenoma. **Conclusions:** This is the largest case series of patients with gigantism described to date in Colombia. Transsphenoidal surgery was the first-choice procedure, but additional pharmacological therapy was usually required. Mutations in the *AIP* gene should be considered in familial cases of GH-producing adenomas. Arch Endocrinol Metab. 2019;63(4):385-93

Keywords

Pituitary diseases; gigantism; growth hormone; pituitary neoplasms; acromegaly

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INTRODUCTION

Gigantism is a rare pediatric disease, with an incidence of 8 to 11 cases per million individuals per year. This disease is characterized by increased production of growth hormone (GH) when the epiphyses are still open, and in most cases is secondary to a pituitary adenoma (1). Gigantism can occur sporadically or have a hereditary component (2); in a case series by Rostomyan and cols. (3), a genetic cause was identified in 46% of the cases, of which the most common was a mutation in the hydrocarbon receptor-interacting protein (*AIP*) gene (28%), followed by X-linked acrogigantism (X-LAG; 10%). McCune-Albright syndrome (5%), Carney complex (1%), and multiple endocrine neoplasia type 1 (1%) are less common causes of gigantism (3). The main symptom of the disease is abnormal accelerated growth affecting the musculoskeletal system associated with some other comorbidities (1). The first-choice treatment for gigantism is transsphenoidal surgery (TSS) (4). However, complete remission of the disease is not usually achieved with surgical intervention alone and pharmacological therapy becomes necessary (2,5-7), of which somatostatin analogues (SSA) is the most common. If no response is obtained with SSAs, dopamine receptor agonists (cabergoline) or GH receptor antagonists (pegvisomant) can be added (8-10). In cases that fail to respond to surgery and pharmacological treatment, radiotherapy is used; however, the risk of hypopituitarism should be taken into account (8).

The purpose of this study is to present 6 cases of gigantism treated in Colombia, including a 6-year follow-up and treatment outcomes. We also present the clinical history of 2 patients with gigantism secondary to familial isolated pituitary adenoma (FIPA) and *AIP* mutation.