

Growth without Growth Hormone Syndrome in a Patient with Craniopharyngioma

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Introduction

Although growth hormone (GH) deficiency is the main cause of short stature in patients having neurosurgery for sellar/suprasellar tumors, some patients show normal height velocity despite severe deficiency of GH, a phenomenon described as “growth without growth hormone (GWGH)”. The phenomenon of GWGH was recognized for over 50 years and was first described by Matson in 1962 as “Normal postoperative height velocity following craniopharyngioma surgery” (1). Later, clinical situations associated with GWGH were described by M. Geffner as follows (2): Postcraniopharyngioma surgery, other sellar, suprasellar and hypothalamic disorders such as tumors, empty sella syndrome and septo-optic dysplasia. Other situations where GWGH is described include acromegaloidism (pseudoacromegaly), fetal life and obesity. Here, we present a case with craniopharyngioma and GWGH and discuss the etiopathogenesis of GWGH.

Case Report

A 9-year-old girl presented with headache and vomiting. She had the diagnosis of craniopharyngioma and after the operation, she developed panhypopituitarism. On follow-up, she needed a series of surgical interventions for the recurrences. After 3 years of poor growth, [height: -4.1 standard deviation score (SDS), weight: -2.42 SDS, body mass index (BMI): -0.56 SDS], she started to gain weight and then, grow well at the age of 12²/₁₂ years despite demonstrated GH deficiency [insulin-like growth factor-1 (IGF-1) of <25 ng/mL, IGF binding protein-3 (IGFBP-3) of 1.51 µg/mL and peak GH of <0.05 ng/mL in GH stimulation tests]. Without any GH replacement therapy, her height, weight and BMI SDSs were -1.35, 1.35 and 2.64 respectively at the age of 17⁹/₁₂ years. Her prolactin level was 1.24 ng/mL and fasting insulin level was 17 µU/mL when the blood glucose was 74 mg/dL.

Although its cause still remains elusive, four basic hypothesis have been proposed to account for GWGH (2). It is possible that 24 h GH secretion may be normal despite failed provocative testing. Alternatively, GH bioactivity may be normal despite deficient immunoreactivity. Hyperinsulinemia is another mechanism thought to be responsible for GWGH (3). It has been described in many patients and is presumably because of associated obesity-induced insulin resistance. Obesity in these patients may be caused by abnormal hypothalamic function leading also to increased insulin secretion. Insulin receptors have high homology with IGF-1 receptors. Although its affinity is less, insulin can bind to IGF-1 receptors and accelerate bone growth (2). Insulin also suppresses serum IGFBP-1 resulting in an increase in plasma levels of free (bioactive) IGF-1 (4). The fact that not all the patients are hyperinsulinemic as our patient made us assume that there might be other GF in the etiopathogenesis of GWGH. Since prolactin is known to stimulate mitogenesis and DNA synthesis in in vitro studies, it is a good candidate for the explanation of mechanisms of GWGH (2). However, human prolactin does not bind to somatogenic receptors to stimulate bone growth. Additionally, not all the patients are hyperprolactinemic and even serum prolactin levels are reduced along with GH levels in some patients with GWGH. There are many other GF in the human sera like IGF-2, pituitary-derived chondrocyte factor, other peptide GF including fibroblast GF, epidermal GF, colony-stimulating GF and interleukins, but their involvement in GWGH has not been elucidated (2).

As a conclusion, GWGH is still an unknown enigmatic phenomenon. Evaluating each single case would give insight into the mechanisms and help us to design research studies to enlighten these mechanisms.

References

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