NOTE

Growth Hormone Secretion in a Patient with Deprivation Dwarfism

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Synopsis

Plasma levels of human growth hormone (HGH) were measured in a 16-year-old boy with deprivation dwarfism. Plasma HGH response to insulin-induced hypoglycemia was absent, whereas its response to arginine infusion was slightly subnormal. An exaggerated response of plasma HGH was observed when insulin was injected during the infusion of a beta adrenergic blocking agent, propranolol. Intravenous infusion of an alpha adrenergic stimulating agent, methoxamine, caused a significant increase in plasma HGH. Plasma HGH response to insulin-induced hypoglycemia was within normal limit when re-tested during the period of accelerated growth. These results suggest a functional disorder of HGH secretion in this patient, which seemed to be caused by the inhibition through beta adrenergic receptors.

It has recently been recognized that deranged familial environment may cause growth retardation simulating idiopathic hypopituitary dwarfism. Powell et al. (1967) observed deficiency in growth hormone secretion in most of their patients with maternal deprivation syndrome, which returned to normal when they were removed from an emotionally disturbed environment. We have studied growth hormone secretion in a patient with maternal deprivation syndrome and obtained results suggesting a functional disorder in growth hormone secretion.

Case Report

A 16-year-old boy was admitted to the hospital with a chief complaint of short stature. His father left home when he was a baby and he grew up in a family consisting of his grand-parents, mother, 3 unmarried uncles and an aunt (2 of them were psychotic), living in a solitary house on a mountain. No family history of short stature was noted. His birth weight as well as physical and mental development in his early childhood were unknown. He was the shortest in his class when he attended a primary school at the age of 6 and had been shortest throughout the school life. His growth rate during the primary and middle school days is listed in Table 1. His school marks were nearly the lowest in his class. He has no bizzare drinking habit, but his appetite seems to fluctuate with frequent occurrence of nausea.

On physical examination, he was 136.5 cm (4 feet 6 inches) in height and weighed 32.5 kg (71.7 lb), with normal body proportion. Secondary sex characteristics were absent, except for a few acneiform eruptions on his face. Early testicular and penile enlargement was noted.

Laboratory data: Urinalysis gave trace albuminuria. Serum electrolytes and proteins were within normal limits. Serum cholesterol

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was 131 mg/dl, cholesterol ester, 90 mg/dl, and \( \beta \)-lipoprotein (an immunoprecipitation method, using Eiken's Beta-Lipo kit), 1.5 mm. Triosorb resin uptake was 27.2\%, PBI, 6.0 \( \gamma \)/dl, urinary 17-OHCS excretion, 1.1–1.9 mg/day and urinary 17-KS excretion, 1.4–2.7 mg/day. Oral metyrapone test performed on the 73rd hospital day gave normal response of urinary 17-OHCS. Bone age was 12.5 years. Psychological examination revealed his hostility to his mother.

Course: After admission, he showed a rapid gain in weight (10 kg) and accelerated growth (3.3 cm) within 3 months.

**Methods**

All experiments were performed after overnight fasting and in the resting state. For insulin tolerance test, glucagon-free insulin (0.1 U/kg body weight) was injected intravenously, and for arginine test, arginine monochloride (0.5 gm/kg body weight) solution was infused intravenously for 30 mins. Insulin stimulation test was performed also during the infusion of 10 mg of propranolol dissolved in 300 ml of saline solution, over a period of 2 hrs. The effect of intravenous infusion of 25 mg of methoxamine dissolved in 300 ml of saline was also studied.

Blood was withdrawn every 15–30 mins into a heparinized syringe by repeated venipuncture. Blood glucose was measured by orthoaminobiphenyl method (Shibata, 1961). Plasma human growth hormone (HGH) was determined by radioimmunoassay of Schalch and Parker (1964) and plasma cortisol by a competitive protein binding assay.

**Results**

As shown in Figure 1, plasma HGH response to insulin-induced hypoglycemia was absent when first tested on the 13th hospital day, whereas plasma cortisol significantly responded to hypoglycemia. Intravenous infusion of arginine elicited subnormal response of plasma HGH, when tested on the 24th hospital day.

A remarkable HGH response to insulin-induced hypoglycemia was observed when insulin was given 30 min after the start of intravenous infusion of a beta adrenergic blocking agent, propranolol, on the 35th hospital day (Fig. 2). Plasma cortisol response to hypoglycemia was also slightly higher during the infusion of propranolol than in the control experiment, although not conclusive from the present experiment. Intravenous infusion of an alpha adrenergic stimulating agent, methoxamine, caused a significant rise in plasma HGH and cortisol when tested on
the 50th hospital day. Insulin stimulation test performed on the 52nd day gave low normal response of plasma HGH and normal response of plasma cortisol, as shown in Figure 2.

**Discussion**

The present patient showed thin, short stature with very poorly developed secondary sex characteristics. Although there are very few reports of deprivation dwarfism at the age of puberty, the diagnosis of deprivation dwarfism was made for the following reasons: (1) significant environmental disruption from early childhood, (2) remarkable weight gain and acceleration of growth during hospitalization, (3) no evidence of systemic disease or abnormality to account for growth failure, (4) absence of plasma HGH response to insulin-induced hypoglycemia which returned to normal when re-tested during the period of accelerated growth. Idiopathic hypopituitary dwarfism was excluded first by slightly sub-normal but significant response of plasma HGH to arginine infusion and later by restoration of plasma HGH response to insulin-induced hypoglycemia.

A very remarkable plasma HGH response to insulin-induced hypoglycemia observed during the infusion of propranolol and a significant rise in plasma HGH during the infusion of methoxamine may suggest that the disorder of HGH secretion in this patient was not organic but functional, and that HGH reserve in the pituitary was normal. Recent studies performed by us (Imura et al., 1968 and 1971; Kato et al., 1970) and by others (Blackard and Heidingsfelder, 1968; Heidingsfelder and Blackard, 1968) demonstrate that an adrenergic mechanism may be involved in HGH secretion, and that alpha receptors stimulate HGH secretion, whereas beta receptors inhibit it. It is also assumed that the adrenergic mechanism involving HGH secretion may reside in the hypothalamus. The present study suggests, therefore, that the HGH secretory mechanism in this patient may be inhibited through beta adrenergic receptors in the hypothalamus.

**References**

276, 1279.
