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**NOTE**

# Suppressed levels of growth hormone and insulin-like growth factor-1 during successful pregnancy in persistent acromegaly

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**Abstract.** Pregnancy is a rather rare event in acromegaly because fertility is often reduced during active disease. Previous reports of pregnancy in acromegalic patients showed that the pituitary growth hormone (GH) level was unaffected and the insulin-like growth factor (IGF)-1 level was elevated during the second and third trimesters. We describe here a case of persistent acromegaly that showed suppressed levels of GH and IGF-1 during pregnancy. The suppression of GH secretion and IGF-1 may be due to increased estrogen or other factors circulating in mid- to late pregnancy.

*Key words*: Acromegaly, Pregnancy, IGF-1, Octreotide, Radiosurgery

**PREGNANCY** is a rather rare event in acromegalic women because fertility is often reduced during active disease [1, 2]. Previous reports of pregnancy in acromegalic patients [3, 4] showed that pituitary growth hormone (GH) levels were unaffected and the levels of serum insulin-like growth factor (IGF)-1 were elevated by increased placental GH variant during the second and third trimesters. We report here a case of persistent acromegaly that showed suppressed levels of GH and IGF-1 during pregnancy.

## Case Report

The patient had demonstrated amenorrhea, body weight gain and progressive enlargement of the hands and feet since the age of 31 after a normal pregnancy and delivery. At the age of 36, she was examined for suspected acromegaly. Mean basal GH levels were 44.7ng/mL, which decreased to 28.8ng/mL during an oral glucose tolerance test with elevated IGF-1 levels (1515ng/mL). Pituitary magnetic resonance imaging (MRI) showed an adenoma measuring 20 mm in diameter invading the right cavernous sinus. The patient underwent adenomectomy by the transsphenoidal approach, but basal GH levels remained elevated (17.1ng/mL) after surgery. She received 300 μg octreotide acetate subcutaneously (s.c.) daily, and stereotactic radiosurgery was performed with a marginal dose of 18Gy to the residual adenoma in the right cavernous sinus. Basal levels of GH and IGF-1 decreased to 8.5ng/mL and 753ng/mL, respectively, and ovulatory menstrual cycles resumed. Eleven months later, octreotide was discontinued because of pregnancy, and at 5 weeks of pregnancy, GH was 17.3ng/mL and IGF-1 1100ng/mL. At 10, 21 and 33 weeks of pregnancy, GH and IGF-1 levels were both suppressed to 9.9, 5.5 and 5.9ng/mL, and 878, 291 and 446ng/mL, respectively. Normal vaginal delivery took place at 43 weeks. Postpartum GH levels were 5.0 and 7.0ng/mL; IGF-1 levels increased to 640 and 782ng/mL 3 and 9 weeks after delivery. Repeated MRI after delivery showed moderate shrinkage of the residual adenoma.

Serum GH concentrations were determined by immunoradiometric assay (IRMA; GH Kit "Daiichi", TFB Inc., Tokyo) and did not cross-react with the placental GH variant. Plasma IGF-1 concentrations were also determined by IRMA (IGF-1 IRMA "Daiichi", TFB Inc., Tokyo).

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## Discussion

In normal pregnancy, the placental GH variant steadily replaces pituitary GH after the first trimester. From the second trimester until delivery, pituitary GH is suppressed and IGF-1 levels rise [1]. GH secretion from the pituitary adenoma is considered autonomous even during pregnancy. Beckers *et al*. [3] reported that, in active acromegaly, pituitary GH levels are not significantly altered from the pre-pregnant state; however, in our patient with persistent acromegaly, there was a reduction in both GH and IGF-1 levels during pregnancy. GH levels were stable but IGF-1 levels were significantly elevated after delivery. Similar cases of suppressed GH and/or IGF-1 during pregnancy have recently been reported by other investigators [5-9], and some patients showed clinical and biochemical improvement during pregnancy [8]. These data suggest that GH secretion in pregnant acromegalic patients may not be entirely autonomous and may be associated with a degree of negative feedback control that could be exerted by a circulating factor of placental origin, probably human placental lactogen or placental GH variant. Suppressed IGF-1 levels may be due to the increasing concentration of estrogen, which inhibits IGF-1 production in the liver [8]. Further cases with a detailed description of pituitary and placental GH and IGF-1 are required to clarify the mechanism of GH and IGF-1 dynamics during pregnancy.

Another point to be discussed is the management of acromegaly before and during pregnancy. Amenorrhea and infertility are associated with reduced gonadotropin secretion and/or hyperprolactinemia [2]. Bromocriptine, somatostatin analog and assisted reproductive therapy have been used to resume fertility [10-12]. In the present case, surgery and adjuvant octreotide treatment successfully induced the ovulatory menstrual cycle and resulted in spontaneous conception. The safety issue of using somatostatin analog during pregnancy was the subject of a recent paper [13].

The metabolic effects of acromegaly, such as diabetes and hypertension, may exacerbate during pregnancy and may be harmful to both mother and fetus; therefore, control of disease activity before conception is desirable. Pregnancy may induce the disease to worsen, with expansion of the pituitary adenoma [14, 15]. Pituitary apoplexy and subsequent emergent neurosurgery have been reported during pregnancy [16, 17]. In the present case, previous debulking surgery and prophylactic radiotherapy might have controlled tumor growth during pregnancy.

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