Successful Pregnancies and Deliveries in a Patient With Evolving Hypopituitarism due to Pituitary Stalk Transection Syndrome: Role of Growth Hormone Replacement

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Abstract

We herein report a 31-year-old Japanese woman with evolving hypopituitarism due to pituitary stalk transection syndrome. She had a history of short stature treated with growth hormone (GH) in childhood and had hypothyroidism and primary amenorrhea at 20 years old. Levothyroxine replacement and recombinant follicle stimulating hormone-human chorionic gonadotropin (FSH-hCG) therapy for ovulation induction were started. GH replacement therapy (GHRT) was resumed when she was 26 years old. She developed mild adrenocortical insufficiency at 31 years old. She succeeded in becoming pregnant and delivered twice. GHRT was partially continued during pregnancy and stopped at the end of the second trimester without any complications.

Key words: pregnancy, delivery, hypopituitarism, pituitary stalk transection syndrome, hormone replacement

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Introduction

Patients with growth hormone (GH) deficiency who have a history of abnormal birth injury such as breech delivery occasionally show an atrophic anterior lobe of the pituitary gland, the formation of an ectopic posterior lobe at the median eminence, and a thin or absent pituitary stalk on brain magnetic resonance imaging (MRI) (1). Those patients are diagnosed with “pituitary stalk transection syndrome”. In most cases, GH insufficiency develops first, followed by insufficiencies of gonadotropins and thyroid stimulating hormone (TSH) during childhood, and finally adrenocorticotropic hormone (ACTH) insufficiency in later adulthood (2, 3). They also have a potential risk of secondary adrenal insufficiency (2).

Successful pregnancy in hypopituitarism is rare, given its association with an increased risk of pregnancy complications, such as abortion, anemia, pregnancy-induced hypertension, placental abruption, premature birth, and postpartum hemorrhage, as reviewed by Du et al. (4). Therefore, hypopituitarism during pregnancy should be managed carefully during gestation (4, 5). GH replacement therapy (GHRT) is not officially licensed for use during pregnancy because of the lack of sufficient safety data. Pregnant patients receiving GHRT are often concerned about whether or not they should stop GHRT, and most physicians have reported making a decision on whether or not to continue GHRT in agreement with the patient’s wish (6). We herein describe the successful pregnancies and deliveries in a patient with evolving hypopituitarism due to pituitary stalk transection syndrome who partially continued GH, thyroid hormone, and glucocorticoid replacement therapy during pregnancy.

Case Report

A 31-year-old Japanese woman visited our hospital because of adrenal insufficiency after her first delivery. She was born by breech delivery at 31 weeks’ gestation, weighing 1,040 g. At the age of 7 years, she presented with...
Table 1. Clinical Course of Hormonal Data in a Patient with Evolving Hypopituitarism at and after the First Delivery.

| 1st delivery | somatropin 0.4 mg/day |
|--------------|-----------------------|
| 29y2m       | 30y0m                 |
| IGF-1 ng/mL | 207.8                 | 37.5 |
| GH ng/mL    | 12.0*                 | 0.09 |
| ACTH pg/mL  |                       | 32.3 |
| Cortisol μg/dL | 13.6        | 3.1  |
|              |                      | 1.5  |

*before delivery

growth retardation and was diagnosed with GH deficiency using an insulin-induced hypoglycemia and arginine test. She received GHRT from age 7 until age 14. She did not visit our hospital for 5 years from age 15 until age 20 but returned to the Department of Obstetrics and Gynecology because of primary amenorrhea. She succeeded in becoming pregnant after several inductions of ovulation and delivered a healthy male baby weighing 2,795 g, as described by Fukuta et al. (7). She received GHRT again 10 months after the first delivery from her primary care doctor (Table 1).

She was referred to the Department of Endocrinology and Metabolism at our hospital by her primary care doctor because her laboratory tests showed adrenocortical insufficiency at age 31 years of age. Her free T4 was low despite levothyroxine replacement, and her adrenocortical function was diagnosed as mildly insufficient for the first time on the basis of her endocrinological data (Table 2). A low dose of hydrocortisone (5 mg daily) was added to levothyroxine (50 μg daily) and somatropin (0.45 mg daily).

She became pregnant again at 31 years of age after several inductions of ovulations. Her GHRT was reduced to two-thirds of the pregestational dose (0.3 mg daily) at 8 weeks’ gestation and discontinued at 26 weeks’ gestation. Thyroxine was increased to 75 μg daily after 8 weeks’ gestation and 100 μg daily after 26 weeks’ gestation, so that the serum free T4 levels remained 0.7-1.1 ng/dL during pregnancy. Hydrocortisone replacement was continued at the same dose as in the pregestational period. We carefully followed her with monthly measurements of the serum levels of GH, insulin-like growth factor (IGF)-1, ACTH, cortisol, and thyroid hormone during her second pregnancy, as shown in Figure. Her GH levels rose gradually after the second trimester, but the IGF-1 levels were maintained until delivery. She had remained normotensive, and neither proteinuria nor glycosuria was observed during her second pregnancy. Under spontaneous labor, she delivered a male baby weighing 3,320 g at a gestation of 40 weeks and 1 day. Her serum GH and IGF-1 levels fell rapidly three days after delivery, and so the GHRT was restarted. The latest follow-up showed that her two children aged 5 and 2 were both mentally and physically healthy.

Discussion

An intact GH-IGF1 axis is not always essential for normal fertility, but it has been claimed that GH deficiency leads to difficulties in conception and subfertility (8). The role of GH supplementation in the prevention of fertilization problems or early gestational complications in GH-deficient women (8-10) should be clarified. The efficacy and safety of GHRT during pregnancy is also a matter of debate (9-12). During normal pregnancy, the pulsatile release of pituitary GH is progressively suppressed and replaced by a continuous secretion of placental GH. Placental GH is a major regulator of maternal serum IGF-1 levels during pregnancy. GH does not cross the placenta, and its effects on the fetus are probably indirect and mediated by maternal IGF-1 production and actions on the substrate supply to the fetus (13). Therefore, it is justifiable to continue GHRT in women with definite GH deficiency at least until sufficient production of placental GH is achieved (14). In the present case, GHRT was discontinued at 26 weeks’ gestation. The proteinuria was observed at the late stage of third trimester in the first pregnancy but not in the second pregnancy, suggesting that proteinuria may not be an adverse effect of GHRT.

Very recently, Vila et al. (6) reported the pregnancy outcomes in a large group of patients (173 women in 15 countries) with GH deficiency and hypopituitarism. Three different GHRT regimens were adapted: 1) GHRT stopped before or as soon as the pregnancy was confirmed, 2) GHRT partially continued and stopped at the end of the second trimester, and 3) GHRT continued throughout the pregnancy. The different regimens did not seem to influence the percentages of live births (80.5% in women who continued GHRT and 80.4% in women who stopped GHRT completely). They concluded that pregnancy outcomes and pregnancy complications, such as gestational diabetes, pre-eclampsia and pregnancy-associated hypertension, were not related to the GHRT patterns, method of conception, or number of additional pituitary hormone deficiencies (6).

We reported the successful pregnancies and deliveries in a patient with evolving hypopituitarism due to pituitary stalk transection syndrome who partially continued GH, thyroid hormone, and glucocorticoid replacement therapy during pregnancy. We hope this report encourages patients with hypopituitarism who wish to have a successful pregnancy and delivery, although the optimal management of hypopituitarism during pregnancy and delivery has not been determined yet.

The authors state that they have no Conflict of Interest (COI).
Table 2. Endocrinological Data at 31 Years of Age.

| Endocrinological data at 31 years old | Insulin tolerance test (0.05 U/kg body weight) at 20 years old |
|--------------------------------------|-------------------------------------------------------------|
| TSH 1.9 µU/mL                        | Time (min)                                                  |
| freeT3 2.4 pg/mL                     | 0 30 60 90 120                                             |
| freeT4 0.6 ng/dL                     | ACTH (pg/mL)                                                |
| TgAb 145.2 IU/mL                     | 42.9 62.4 87.3 91.1 42.6                                   |
| TPOAb 9.3 IU/mL                      | Cortisol (µg/dL)                                            |
| GH 0.56 ng/mL                        | 9.2 13.6 17.4 14.7 15.0                                    |
| IGF-1 159.3 ng/mL                    | Rapid ACTH Test (250 µg) at 31 years old                    |
| ACTH 24.6 pg/mL                      | Time (min)                                                  |
| Cortisol 2.3 µg/dL                   | 0 15 30 60                                                 |
| LH 3.8 mIU/mL                       | Cortisol (µg/dL)                                            |
| FSH 3.8 mIU/mL                      | 2.8 9.8 12.9 15.5                                          |
| PRL 17.5 ng/mL                      | 24h-urinary free cortisol at 31 years old                  |
| ADH 1.5 µg/mL                       | 30.4 µg/day                                                |

Figure. Changes in the serum levels of IGF-1, GH, and cortisol, and in the plasma levels of ACTH during the second pregnancy and after delivery.

Disclosure

The clinical course of the present case was presented at the 87th Annual Meeting of the Japan Endocrine Society in April, 2014.

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