CASE REPORT

Spontaneous Pregnancy and Partial Recovery of Pituitary Function in a Patient with Sheehan's Syndrome

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Sheehan's syndrome is caused by pregnancy-related hemorrhage leading to ischemic necrosis of the anterior pituitary gland and hypopituitarism. Spontaneous pregnancy in Sheehan's syndrome is very rare. We report the case of a patient with Sheehan's syndrome who suffered from anterior pituitary insufficiency, but with sparing of gonadotropic function. The patient became pregnant spontaneously and, after her second delivery, thyrotropic function recovered. However, the patient's growth hormone and cortisol levels remained unresponsive to an insulin-tolerance test. This case demonstrates that pituitary function may recover from less extensive pituitary ischemia. We emphasize the importance of early identification of pregnancy in such cases. It is crucial to institute adequate hormone-replacement therapy during pregnancy, since hypopituitarism is associated with high fetal and maternal morbidity and mortality. [*J Chin Med Assoc* 2005;68(4):187–190]

Key Words: hypopituitarism, pregnancy, Sheehan's syndrome

Introduction

Sheehan's syndrome is caused by postpartum hemorrhage, leading to ischemic necrosis of the physiologically enlarged pituitary gland of pregnancy. Most patients with this syndrome have panhypopituitarism, with destruction of 95–99% of the anterior pituitary.[1] Classically, the syndrome presents with lactation failure, breast atrophy, amenorrhea, sterility, and signs and symptoms of hypothyroidism and hypoadrenalism. Less extensive pituitary destruction is associated with mild or moderate hypopituitarism, with loss of 1 or more tropic hormones.[1] It is rare for a patient with Sheehan's syndrome to get pregnant spontaneously,[2] but it is possible in patients with preserved secretion of gonadotropins. We report the case of a patient with Sheehan's syndrome and preserved gonadal function who became pregnant spontaneously. The patient's thyroid function recovered after her second delivery, although her growth hormone and cortisol response remained inadequate to an insulin-tolerance test.

Case Report

A 36-year-old woman suffered from anorexia, nausea, vomiting, amenorrhea, and depressed mood for about 6 months after delivery in June 2000. This was her second pregnancy. She failed to lactate and noted an abrupt bodyweight loss of 33 kg. She consulted a psychiatrist and was diagnosed with postpartum depression. She was given antidepressant therapy. She also visited her obstetrician, who checked her thyroid function and sex-hormone levels, which revealed subnormal results. The patient was then referred to an endocrine clinic for further work-up. A review of the patient's history revealed gravida 2, para 1. In 1994,

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she was operated on for ectopic pregnancy. A year later, hysterosalpingographic examination was performed due to infertility, and bilateral fallopian-tube occlusion was found. The patient then underwent fallopian tubal plasty and pelvic adhesiolysis. However, she remained infertile and 12 attempts at *in vitro* fertilization were performed. She eventually became pregnant in September 1999. At 3 months of pregnancy, she experienced intermittent vaginal bleeding for about a week. On arrival at the emergency room, she was diagnosed with threatened abortion. Her blood pressure was 80/50 mmHg, pulse rate 102 beats/min, hemoglobin 8.2 g/dL, and hematocrit 26.1%. Four units of packed red blood cells were given, and the patient was advised to adopt complete bed rest, which she did for the next 5 months, and then delivered twin boys by cesarean section.

Hormone studies showed a low level of insulin-like growth factor-1, secondary hypothyroidism, hypoadrenalism, hypogonadism, and hypoprolactinemia (Table 1). A pituitary function test was performed, and growth hormone (GH) and cortisol levels failed to respond to an insulin-tolerance test (Table 2). The responses of thyroid-stimulating hormone (TSH) and prolactin (PRL) to thyrotropin-releasing hormone (TRH) 200 μg were impaired, but luteinizing hormone (LH) and follicle-stimulating hormone showed normal responses to LH-releasing hormone (LHRH)

Table 1. Hormone levels in the patient after her first and second deliveries*

	First delivery	Second delivery
ACTH (pg/mL)	< 10	< 10
Cortisol (μg/dL)	< 1	< 1
E_2 (pg/mL)	16.9	60.90
FSH (mIU/mL)	6.61	4.25
GH (ng/mL)	0.99	0.05
IGF-1 (ng/mL)	65.60	56.80
LH (mIU/mL)	2.90	4.51
PRL (ng/mL)	3.10	1.31
T_4 (ng/mL)	0.47	0.96
TSH (mIU/mL)	0.32	1.69

**All hormonal assays were performed using an Immulite® 2000 Analyzer (Diagnostic Products Corp, Los Angeles, CA, USA). ACTH = adrenocorticotropic hormone; E_2 = estradiol; FSH = follicle-stimulating hormone; GH = growth hormone; IGF-1 = insulin-like growth factor-1; LH = luteinizing hormone; PRL = prolactin; T_4 = free thyroxine; TSH = thyroid-stimulating hormone.*

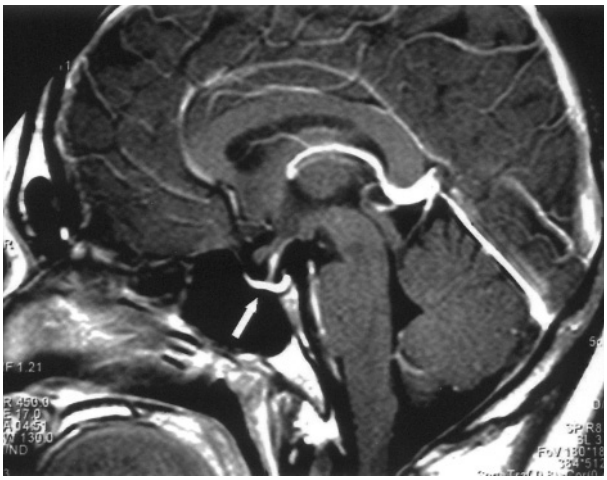

Figure 1. T1-weighted, sagittal, magnetic resonance imaging scan showing an extremely thinned anterior lobe of the hypophyseal gland.

Table 2. Serum levels of cortisol, glucose and growth hormone during insulin-induced hypoglycemia (after first delivery)

	Minutes				
	0	30	60	90	120
Cortisol (μg/dL)	< 1	< 1	2.07	4.52	0.36
Glucose (mg/dL)	79	18	123	97	86
Growth hormone (ng/mL)	0.99	1.00	0.83	0.48	0.34

Table 3. Serum levels of FSH, LH, PRL and TSH after administration of TRH 200 μg and LHRH 100 μg (after first delivery)

	Minutes				
	0	15	30	60	120
FSH (mIU/mL)	6.61	10.50	16.30	23.10	15.70
LH (mIU/mL)	2.90	8.16	22.30	34.10	29.40
PRL (ng/mL)	3.10	4.55	11.30	8.91	7.23
TSH (mIU/mL)	0.32	0.90	2.80	4.90	3.70

FSH = follicle-stimulating hormone; LH = luteinizing hormone; LHRH = LH-releasing hormone; PRL = prolactin; TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone.

100 μg (Table 3). A magnetic resonance imaging study of the pituitary showed thinning of the anterior lobe of the hypophysis on T1-weighted images (Figure 1).

The patient was diagnosed with Sheehan's syndrome with preserved gonadotropic function. She was given prednisolone 7.5 mg/day, L-thyroxine 100 μg/day, and GH 0.15 mg/day. About 2 months after treatment, the patient menstruated, but menstruation continued irregularly thereafter. About 2 years later, the patient became pregnant spontaneously in December 2002. She continued prednisolone and L-thyroxine therapy during pregnancy, and gave birth to a baby boy uneventfully in August 2003. After delivery, she failed to lactate, but she felt much better than after her previous pregnancy. She assumed that her pituitary function had recovered, and discontinued her hormone replacement therapy, without her doctor's permission, in December 2003. About 2 weeks later, she experienced fever, cough, vomiting, and dizziness. She consulted the emergency room. A pneumonic patch was found over the right lower lung lobe, and hypotension and leukocytosis were noted. The patient was admitted because of pneumonia and adrenal crises. A complete pituitary function test was performed after admission. The patient's cortisol, GH and PRL levels failed to respond to stimulation, but TRH and LHRH stimulation tests were normal (Tables 4 and 5). The patient is now maintained on prednisolone and GH-replacement therapy.

Discussion

Spontaneous pregnancy rarely occurs in patients with Sheehan's syndrome: about 20 pregnancies in 13 patients have been reported in the past 20 years.[2–5] Our patient's pituitary function was incompletely lost after her first delivery. In her LHRH test, gonadotropin reserve was intact, but the patient's menstruation remained irregular. As the patient had been infertile for 8 years after her wedding, she did not use contraception, but it was a surprise to her that she became pregnant spontaneously. Our patient adhered to hormone-replacement therapy throughout the pregnancy, and such treatment was indispensable for an uneventful delivery. Indeed, it has been reported that inadequate hormone replacement therapy in pregnant women with Sheehan's syndrome has resulted in about 50% fetal loss and 27% maternal death.[4]

The patient's TSH response returned to normal after her second delivery. Importantly, it has been reported that the secretion of pituitary tropic hormones is sensitive to pituitary ischemia in the following order: gonadotropin, TSH, GH, and adrenocorticotropic hormone; recovery of these hormones also occurs in the same order.[6] Our patient had a low PRL level throughout pregnancy and failed to lactate. Her PRL response remained inadequate to TRH. Further, measurement of PRL after TRH stimulation has been reported to be the

Table 4. Serum levels of FSH, LH, PRL and TSH after administration of TRH 200 μg and LHRH 100 μg (after second delivery)

	Minutes				
	0	15	30	60	120
FSH (mIU/mL)	4.25	5.71	8.20	7.34	7.20
LH (mIU/mL)	4.51	18.80	22.10	22.20	20.30
PRL (ng/mL)	< 0.50	1.26	1.31	1.08	0.67
TSH (mIU/mL)	1.69	6.15	7.03	5.54	5.71

FSH = follicle-stimulating hormone; LH = luteinizing hormone; LHRH = LH-releasing hormone; PRL = prolactin; TRH = thyrotropin-releasing hormone; TSH = thyroid-stimulating hormone.

Table 5. Serum levels of cortisol, glucose and growth hormone during insulin-induced hypoglycemia (after second delivery)

	Minutes				
	0	30	60	90	120
Cortisol (μg/dL)	< 1	1.20	2.00	2.50	3.00
Glucose (mg/dL)	102	70	42	82	106
Growth hormone (ng/mL)	0.05	0.61	0.45	0.13	0.05

best screening test for Sheehan's syndrome.[7] In addition, Sheehan[8] suggested that pregnancy might stimulate pituitary remnants to undergo hyperplasia; such a phenomenon might be due to the secretion of hypophysiotropic hormones by the hypothalamus or placenta.[9] Our patient recovered from pituitary hypothyroidism after delivery, perhaps because of the stimulatory effect of pregnancy on remnant thyrotrophs.

Sheehan's syndrome is less common nowadays because of advanced obstetric care. Less extensive pituitary destruction may result in an asymptomatic or atypical form of the syndrome with loss of 1 or more tropic hormones. The purpose of our report is to describe such a rare case, with spontaneous pregnancy and subsequent recovery of thyroid function after delivery. Since the signs and symptoms of hypopituitarism are non-specific, the diagnosis of Sheehan's syndrome should be considered in all patients with a history of hemorrhage during pregnancy or delivery. Since basal hormonal levels cannot confirm the diagnosis, pituitary stimulatory tests should be performed. Patients with preserved gonadal function should be advised of the possibility of becoming pregnant, and contraceptive measures should be taken if further pregnancy is not desired. It is also crucial to have an early diagnosis and initiation of appropriate therapy whenever pregnancy occurs in hypopituitarism; this prevents unnecessary fetal and maternal morbidity and mortality.

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