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# Gonadotropin secretory capacity in a patient with Sheehan's syndrome with successful pregnancies*

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Pregnancy is rare in a patient with antecedent Sheehan's syndrome.[1, 2] There are no studies concerned with the gonadotropin secretory capacity of the pituitary in such patients.[1]

This report concerns one patient with Sheehan's syndrome who had three subsequent successful pregnancies and whose pituitary function, including a detailed study of the gonadotropin secretory capacity, was investigated.

## CASE REPORT

The patient was a Caucasian woman, 26 years of age, who was first admitted to University Hospital in 1977. She had been in good health, with regular spontaneous menstrual cycles, following menarche at 13 years. Her first pregnancy, at 19 years of age, ended with a forceps delivery followed by a massive postpartum hemorrhage and hypotension. The infant died 12 hours later. The patient failed to lactate following delivery. Menses returned in 3 months, and 2 months later she became pregnant for the second time. During this pregnancy she had cold intolerance, fatigue, somnolence, and low blood pressure. A 3950-gm healthy male infant was delivered at full term without complications. The patient again did not lactate following delivery. Menstrual periods resumed 3 months later but occurred only three or four times per year, with normal volume and duration of flow. The symptoms of cold intolerance, fatigue, weakness, and somnolence gradually increased. There was a loss of axillary and pubic hair. One year after the second delivery, she was admitted to a rural clinic with vomiting and severe hypotension. A few months later, in spite of irregular menses, she had a third pregnancy followed by a 12-week spontaneous abortion without complications.

In the subsequent years these clinical manifestations gradually increased. There was a 6-kg weight loss, the libido was slightly decreased, and the menstrual periods occurred every 3 to 4 months. After another hypotensive episode, she was referred to University Hospital in May 1977.

On admission she weighed 46.3 kg and was 142 cm in height. Her skin was pale, dry, and flaky; and the extremities were cold. Axillary and pubic hair were scant. Blood pressure was 80/60 mm Hg, and the pulse was 76/minute. Breast tissue was present without atrophy or galactorrhea. Pelvic examination was normal, with slight vaginal atrophy. Visual fields and neurologic evaluation were normal.

Routine laboratory studies demonstrated a hemoglobin of 12.6 gm/dl, a fasting plasma glucose

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**Table 1.** *Integrated Functional Test of Adenohypophysis (August 1980)*

| Plasma levels | Test | | | | | | |
|---|---|---|---|---|---|---|---|
| | LH-RH | | Thyrotropin-releasing hormone | | Hypoglycemia | | |
| | LH | FSH | PRL | TSH | Glycemia | hGH | 11-OHCS |
| | *ng/ml* | *mIU/ml* | *ng/ml* | *mIU/ml* | *mg/dl* | *ng/ml* | *μg/dl* |
| Baseline | 69.9 | 6.8 | 14.5 | 1.3 | 95.0 | 0.7 | 5.7 |
| After | 166.5[a] | 17.6[a] | 25.0[a] | 2.4[a] | 25.0[b] | 0.4[a] | 14.4[a] |
| Normal responses | Rise > 50.0% | | Rise to 100.0 or more | Rise to 10.0 | Decrease 50.0% below 40.0 | Rise to 10.0 or more | Increase 16 |

[a]Highest value.
[b]Lowest value.

value of 75 mg/dl, with a serum sodium value of 128 and potassium value of 4.8 mEq/l.

Endocrinologic studies revealed a serum thyroxine iodine value of 0.6 μg/dl (normal, 3.1 to 7.0 μg/dl) and a triiodothyronine radioimmunoassay (RIA) value of 30 ng/dl (normal, 75 to 220 ng/dl). The 24-hour radioiodine uptake was 5.6% (normal range, 14% to 45%) and rose to 54.3% after stimulation with bovine thyrotropin (TSH) (10 U/day for 3 days). The 24-hour urinary neutral 17-ketosteroids and 17-ketogenic steroids were, respectively, 0.8 to 1.7 mg/day (normal, 4 to 10 mg/day) and 0.8 to 0.9 mg/day (normal, 7 to 13 mg/day). Plasma fluorimetric 11-hydroxycorticoids (11-OHCS) were 0 to 2.8 μg/dl at 9:00 A.M. (normal, 6 to 22 μg/dl) and 20.0 μg/dl 90 minutes after adrenocorticotropin (ACTH) stimulation, 25 U given intramuscularly.

Bioassay of 24-hour urine for gonadotropins was 80 to 160 mouse uterine U/24 hours (normal, 20 to 160 mouse uterine U/24 hours). Plasma luteinizing hormone (LH) was determined by RIA,[3] and the results are expressed in nanograms per milliliter (LER-907). The sensitivity, intraassay, and between-assay variations were, respectively, 2.0 ng/ml, 6.3%, and 14.0%. In June 1977, the mean baseline LH level was 30.9 ng/ml (normal early follicular phase, 16 to 55 ng/ml) and rose to 42.4, 47.0, 66.4, and 62.2 ng/ml, respectively, 15, 30, 60, and 120 minutes after intravenous administration of 100 μg synthetic LH-releasing hormone (LH-RH). Plasma LH increased to 46.2 ng/ml after the oral administration of clomiphene citrate, 3 mg/kg/day, for 9 days.

The skull x-ray and sella turcica tomogram were normal.

After endocrine evaluation, the diagnosis of Sheehan's syndrome with partial pituitary insufficiency was made, and the patient was treated with prednisone (10 mg/day) and combined thyroxine-triiodothyronine (60 to 15 μg) with dramatic improvement. Menses tended to be regular and monthly. One year later she became pregnant for the fourth time but had an 11-week spontaneous abortion. After 2 years on increased thyroid hormone replacement therapy, she had a normal vaginal delivery of a 3800-gm healthy infant after a 39-week gestation. There was no lactation. Menses returned 3 months later. After thyroid hormones and prednisone had been discontinued for 24 hours, further endocrine evaluation was carried out through an intravenous combined anterior pituitary test: 0.1 U/kg insulin hypoglycemia, 100 μg LH-RH, and 200 μg thyrotropin-releasing hormone. The LH, follicle-stimulating hormone (FSH), prolactin (PRL), TSH, and human growth hormone (hGH) plasma levels were determined by RIA and plasma 11-OHCS as described previously. The results are shown in Table 1.

On the basis of these results, the diagnosis of partial pituitary deficiency was reaffirmed, and thyroxine and prednisone therapy was resumed. In August 1981, after a 40-week gestation, she had a vaginal delivery of a healthy female infant. There was no lactation. Menses returned after 5 months of amenorrhea postpartum. In April 1982, the pituitary gonadotropin response to a constant intravenous infusion of LH-RH, 0.2 μg/minute for 4 hours, was studied. The results are shown in Figure 1. On this day the baseline plasma estradiol level was 87.5 pg/ml (normal early follicular phase, 30.0 to 100.0 pg/ml).

The patient presently is receiving prednisone and thyroxine and remains asymptomatic with menses every 2 months.

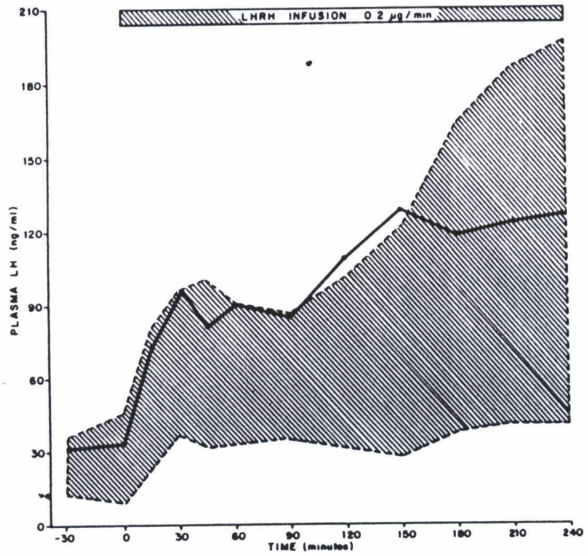


**Figure 1**
The response of plasma LH in a patient with Sheehan's syndrome (●——●) to a constant infusion of synthetic LH-RH (0.2 μg/minute for 4 hours). The *hatched area* indicates the range of responses seen in five normal early follicular phase women.

## DISCUSSION

The obstetric accident following her first pregnancy with subsequent lactation failure and the medical history and physical examination were clinically consistent with a diagnosis of Sheehan's syndrome with partial hypopituitarism due to postpartum pituitary necrosis. The laboratory studies indicated hypothyroidism and hypoadrenocorticism. The evident responses to exogenous TSH and ACTH demonstrated that these glandular deficiencies are secondary to anterior pituitary failure and not due to primary disease of the thyroid and adrenal, respectively. The direct functional stimulation of the adenohypophysis confirmed the diagnosis of pituitary deficiency of TSH, ACTH, hGH, and PRL.

The clinical evidence of preserved gonadotropin secretion in this patient following the episode of postpartum pituitary necrosis included the return of menstruation, subsequent pregnancies, together with maintained breast tissue, libido, and absence of complete involution of the genital tract. This diagnosis was supported by normal urinary gonadotropin levels, by bioassay, and by normal plasma levels of LH, FSH, and estradiol by RIA.

The acute response of LH and FSH to the administration of synthetic LH-RH was normal and was maintained during subsequent years. The pattern of LH release during a constant infusion of LH-RH was biphasic, which indicates normal sensitivity and a reserve of the gonadotrophs.[4] The clomiphene citrate test was normal. The data thus demonstrated preservation of gonadotropin secretion in this patient for 12 years following the obstetric accident.

In the early studies of Sheehan,[2] he originally reported pregnancies in some patients with this disease, although this situation is rare. In a 1980 review, only 19 patients with Sheehan's syndrome were found in the English literature who had a subsequent pregnancy and in whom hypopituitarism was substantiated by endocrinologic studies or by postmortem examination. In none were there studies of responsiveness of LH and FSH to LH-RH.[1] Other authors have described gonadotropin response to LH-RH in Sheehan's syndrome with blunted[5] or normal responses in some patients.[6, 7] However, all patients were amenorrheic; and our study is the first report of serial normal LH-RH tests in a patient with Sheehan's syndrome and successful pregnancies.

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