Primary Hypothyroidism, Pituitary Insufficiency and Pregnancy
A Case Report

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A 23-year-old woman presented with primary hypothyroidism and inability to lactate following uneventful childbirth. Endocrine evaluation revealed that she had autoimmune hypothyroidism and deficiencies of ACTH and prolactin. Despite partial hypopituitarism, she again conceived spontaneously, had an uneventful pregnancy and delivery but failed to lactate. Radiologic evaluation of the hypophysis, including CAT scan, was normal, and antibodies to anterior pituitary cells were not detected. The etiology of the pituitary insufficiency might have been autoimmune hypophysitis, a recently described entity in which anterior pituitary, along with the other endocrine glands, is destroyed by an autoimmune process. The clinical course suggested that women with pituitary insufficiency, although rare, are able to conceive and carry the pregnancy to term. Our patient illustrates that prolactin insufficiency does not preclude a successful outcome of pregnancy but can result in no lactation.

Introduction
Autoimmune disorders are a common cause of endocrine deficiency syndromes. Thus, primary hypothyroidism and Addison’s disease are generally considered to be autoimmune disorders. Insufficiency of these two glands may occur individually or may coexist (Schmidt syndrome). In addition, they frequently occur in association with other disorders also considered to be autoimmune, such as atrophic gastritis, ovarian failure and hypoparathyroidism. Although reported previously, isolated deficiency of a single pituitary hormone without a definite cause is a rare event. Involvement of pituitary by an autoimmune disorder may produce similar defects, but only about 15 such cases have been described. Below we report on a patient with primary hypothyroidism and deficiencies of ACTH and prolactin who became pregnant, had an uneventful pregnancy and delivery but failed to lactate due to prolactin deficiency.

Case Report
A 23-year-old white woman, gravida 1, para 1, was seen in January 1979 five months after the birth of her first child. Her pregnancy had been uneventful, and she had had an uncomplicated vaginal delivery. Labor lasted for 16 hours, and there was no abnormal postpartum bleeding. She was unable to breastfeed her baby since there was “insufficient” milk. She lost 35 pounds after the delivery without dieting. She stated that since the birth of her baby she had noticed increased weakness and fatigue and that her skin had become dry and scaly. Her scalp hair had begun to break off, and her voice had become hoarse. She had noted a decrease in axillary hair, and her pubic hair was more sparse than prior to delivery. She complained of dryness in her vagina and dyspareunia. About four weeks prior to admission she had a “flu-like” illness characterized by extreme tiredness, nausea and vomiting. At the same time she noticed dizziness on arising, which persisted until admission. Her husband stated that she had also become very forgetful in the previous few weeks.

The patient had a cousin with Addison’s disease and a younger sister who has developed amenorrhea recently. The sister had had no menstrual periods between January 1981 and August 1982, but a gynecologic examination, serum prolactin, cortisol and thyroid function tests were said to be
normal. Family, past and personal histories were otherwise unremarkable. On physical examination the patient appeared to be a moderately built and well-nourished white woman whose speech was slow and voice hoarse. The pulse was regular at 50/min; the supine blood pressure was 102/80. Pubic and axillary hair were scant. The scalp hair was coarse, and there was no loss of eyebrow hair. The thyroid was moderately enlarged, firm and without nodules. Deep tendon reflexes were difficult to elicit, but the relaxation phase appeared to be delayed. The remainder of the physical examination was with normal limits.

**Laboratory Findings**

A complete blood count and urinalysis were within normal limits. A multichannel chemistry profile revealed an elevated LDH of 320 U/liter (normal, 113–246) and an SGOT of 468 U/liter (normal, 2–45) but was otherwise normal. Serum Na⁺, k⁺ and Cl⁻ were 140, 4.0 and 103 mEq/liter, respectively. Radiographs of chest and skull for sella turcica were within normal limits. Computerized axial tomography revealed no abnormalities of the anterior pituitary region. On admission the serum T₄ was 1.0μg/dl (normal, 4.5–11.5μg/dl), T₃RU was 22% (normal, 25–35%), and serum TSH was 41μIU (normal, 0–10μIU). Thyroid antimicrosomal antibodies were present in a titer of 1:400. Prior to beginning therapy the serum TSH was repeated and was 51μIU. Serum prolactin was 27 μg/ml (normal, 0–22). Serum PSH was 22.1 mIU (normal, 6–30 in follicular phase), LH was 41.2 mIU (normal, 4–30 in follicular phase), and serum estradiol was 51 pg/ml (normal, 24–68 in follicular phase). Serum cortisol was <1μg/dl, and ACTH was 32 μg/ml (normal, <80). Plasma cortisol increased to 51μg/dl following ACTH stimulation (40 units given intravenously as an infusion over eight hours for three days).

A diagnosis of primary hypothyroidism due to autoimmune thyroiditis and ACTH deficiency was made on admission. The patient was begun on hydrocortisone, 25 mg/day, and L-thyroxine, 0.05 mg/day, which was gradually increased to 0.2 mg/day. Two months after beginning this therapy the patient felt much better and had her first normal menstrual period (seven months postpartum). When she became euthyroid, adrenal function tests were repeated. Baseline plasma cortisol level was <1μg/dl, and 24-hour urinary 17-hydroxysteroids were 0.6 mg (normal, 2–10). After three days of 25 units of ACTH administered intramuscularly the plasma cortisol level increased to 11.5μg/dl and 24-hour urinary 17-hydroxysteroids to 12.6 mg. The patient continued to have normal menstrual periods and conceived in January 1980. Her second pregnancy was also uneventful, but she complained of being more tired as compared to her first pregnancy. Serum prolactin at five months of gestation was 14 pg/ml (normal, 50–80). During labor the serum ACTH was 28 pg/ml and the serum prolactin was 7 ng/ml (normal, 150–250). The patient delivered a normal, full-term girl but had no milk in her breasts. Postpartum an insulin-induced-hypoglycemia test to evaluate the growth hormone function and a TRH test to evaluate prolactin function were performed while the patient was still receiving 0.2 mg L-thyroxine. The results are shown in Figures 1 and 2. In one specimen collected in July 1982 (nearly two years after the second delivery), antibodies to anterior pituitary cells were not detected.

**Discussion**

Our patient had signs and symptoms typical of

![Figure 1](image-url)  
*Growth hormone and cortisol response to insulin-induced hypoglycemia.*
In patients with primary hypothyroidism, TSH levels are increased and the TSH response to TRH is also exaggerated. When a TRH test was performed on our patient, the TSH level was normally suppressed (due to exogenous L-thyroxine administration), and the TSH level failed to increase. However, it is well known that small increases in the concentration of thyroxine and triiodothyronine in euthyroid individuals, while leaving them in the euthyroid range, inhibit the TSH response to TRH. It is thus possible that the 0.2 mg of L-thyroxine that our patient was receiving was slightly in excess of the minimum physiologic amount required. Primary hypothyroidism is also associated with increased prolactin secretion and exaggerated prolactin response to TRH secretion. This may explain the “normal” prolactin level obtained when the patient was seen by us initially and was clearly hypothyroid. Thus, the “normal” prolactin level may have been inappropriately low. Also, we wanted to ensure that our patient was euthyroid before the TRH test was performed. Whether the same dose of thyroxine, which inhibited the TSH response to TRH, was also sufficient to inhibit the prolactin release is not known.

In recent years a number of case reports have suggested that an autoimmune lesion of the anterior pituitary may cause pituitary insufficiency. With the exception of two patients, all of the patients were women. In 10 of 15, including our own, the onset was associated with pregnancy or began within 14 months of it. A number of the women had additional autoimmune disorders, including Hashimoto’s thyroiditis, chronic atrophic gastritis, pancreatitis and gestational diabetes. Our patient also had autoimmune thyroiditis. Some patients experienced an enlargement of the pituitary, were initially thought to harbor a neoplasm but subsequently were found to have hypophysitis on biopsy or autopsy; in others the pituitary was small. Radiologic investigations, including computerized axial tomographic scan, did not reveal any abnormalities of anterior pituitary in our patient.

Some of the patients with hypophysitis have presented with galactorrhea. In contrast, in some patients, as in ours, one of the presenting complaints was inability to lactate in the postpartum period. The patient of Mayfield et al had a blunted prolactin response to the administration of TRH. The prolactin response to TRH in our patient was also impaired. Although other explana-
tions are possible, destruction of lactotrophs, presumably by an autoimmune process, appears to be the mechanism of prolactin deficiency.

The pathogenesis of lymphocytic hypophysitis is unclear. The autoimmune etiology was first suggested by Goudie and Pinkerton and has been supported by other authors.6-14 The histopathologic features of the lesion (and two biopsy specimens studied with electron microscopy) resemble those of other autoimmune lesions.15 Association with other autoimmune lesions also supports the autoimmune nature of this disorder.6,8,10

The development of hypophysitis during pregnancy and postpartum in several patients, including our own, suggests that pregnancy and hypophysitis may be related.5,7,10,12,14-16 A similar association of chronic lymphocytic thyroiditis with pregnancy accompanied by hypothyroidism20 and hyperthyroidism21 has been described. We have also observed a patient with autoimmune thyroiditis who, during two pregnancies, had transient episodes of hyperthyroidism followed by hypothyroidism and eventual complete recovery.22 It is known that immune reactivity is suppressed to some degree during pregnancy.23 It has also been suggested that immunologic changes occurring after delivery may influence the course of autoimmune thyroiditis22; however, the exact pathogenetic effect of these immunologic alterations on the course of the other endocrine glands remains to be determined.

Antipituitary antibodies have been tested in only a few cases and were found to be present in a patient of Mayfield et al11 and in those of Burke et al13 but were negative in our patient and one of the patients of Asa et al.12 However, the pituitaries show nonspecific immunofluorescence with normal sera.24 Therefore, even when these antibodies are present, firm conclusions about their pathogenetic significance cannot be drawn. Although it has been shown that 25% of patients with elevated antipituitary antibodies and only 4% with no demonstrable antibodies develop signs of hypophysial insufficiency 6-12 months postpartum,25 Boltazzo and Doniach found little evidence of pituitary failure associated with pituitary antibodies.26 A negative test for pituitary antibodies, therefore, does not exclude the diagnosis of autoimmune hypophysitis.

It appears that thyroid failure in our patient was the result of autoimmune thyroiditis and deficiencies in ACTH and prolactin due to autoimmune hypophysitis. Amenorrhea in the presence of mildly elevated LH levels and FSH levels in the upper-normal range raises the possibility of coexistent oophoritis, but this association has not been confirmed. Serial repeated measurements of gonadotropins might have established their unequivocal elevation (if present) but unfortunately were not performed. It is possible that the administration of corticosteroids resulted in resolution of oophoritis and contributed to the restoration of normal periods. This occurrence of spontaneous menstruation in a patient with autoimmune ovarian failure after she was given high doses of prednisolone has been described previously.9

Another interesting aspect of the clinical history of our patient was the occurrence of a second pregnancy after development of pituitary insufficiency since conception is quite rare in patients with hypopituitarism.9,26 However, since her gonadotropin-ovarian axis was normal, it is not entirely surprising that when her adrenal and thyroid function was restored to normal, she was able to ovulate, conceive and carry the pregnancy to term. Although prolactin levels increase during normal gestation, the course of our patient’s pregnancy suggested that prolactin does not play a significant role in the maintenance of pregnancy. The absence of lactation postpartum, of course, was compatible with prolactin insufficiency.

The anterior pituitary, along with other endocrine glands, is a target organ for destruction by an autoimmune process. The predilection for this involvement may be increased during pregnancy and the immediate postpartum period; isolated deficiencies in pituitary hormones generally result. The possibility of lymphocytic hypophysitis, therefore, should be considered in women with symptoms of isolated deficiencies in pituitary hormones, such as insufficient or absent lactation.

Acknowledgments

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References


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