The Course of Lymphocytic Hypophysitis

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A 27-year-old woman presented to our institution in her seventh month of pregnancy with complaints of headache and visual field disturbance. Workup revealed bitemporal hemianopia, a markedly enlarged pituitary gland on computed tomography scan, and biochemical evidence of partial hypopituitarism. At surgery, a biopsy specimen of the pituitary gland was taken revealing lymphocytic hypophysitis. The patient was treated with steroids and replacement doses of thyroid hormone. Visual fields improved postoperatively. A repeat computed tomography scan obtained 2 months after an uneventful pregnancy showed that her pituitary had regained normal size and contour. Over the next 9 months she had gradual recovery of all pituitary function. This case allowed us to follow and document the course of lymphocytic hypophysitis from its presentation as a macroadenoma with partial hypopituitarism to full recovery of both size and hormonal function of the pituitary. Lymphocytic hypophysitis should be considered in the differential diagnosis of a pituitary mass or pituitary dysfunction presenting in pregnancy. In patients with suspected lymphocytic hypophysitis and a pituitary mass, a trial of steroids may be therapeutic.

KEY WORDS: Lymphocytic hypophysitis; Pituitary adenoma; Pregnancy; Hypopituitarism; Surgery

Lymphocytic hypophysitis (LHy), an unusual disorder of the pituitary in which the gland is infiltrated with mononuclear cells, was first described in 1962 by Goudie and Pinkerton [4]. Since then, a total of 24 patients have been reported in the medical literature. These patients were diagnosed at autopsy (with death presumably secondary to adrenal failure) or presented with a pituitary tumor that caused either mass effect, pituitary dysfunc-

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Case Report

History

A 27-year-old black primigravida woman developed severe bitemporal headaches in the 24th week of an otherwise normal pregnancy. The patient then noted a progressive decrease in her central and peripheral vision. There was no history of galactorrhea, and menses had been normal prior to conception. She was taking no medication other than vitamins.

Physical examination revealed a healthy-appearing pregnant woman with normal vital signs (blood pressure 110/60 mm Hg, heart rate 92, afebrile). Complete ophthalmologic examination was normal, except for bilateral loss of peripheral vision on gross confrontational testing. Goldman perimetry revealed a marked bitemporal hemianopia, greater on the left than the right. The remainder...
of the neurological examinations were entirely within normal limits for a woman in the third trimester of pregnancy.

A noncontrast-enhanced coronal computed tomography (CT) scan revealed a large intrasellar mass with marked suprasellar extension approaching the area of the optic chiasm (Figure 1A). At the time of this examination, magnetic resonance imaging was not performed at our institution on pregnant patients.

Laboratory evaluation, including CBC and SMA-18, was normal. CBC and SMA-18 were determined in the hospital’s clinical laboratory via standard automated methodology. All peripheral hormone determinations were performed in our laboratories by specific radioimmunoassay (RIA) techniques. The thyroid-stimulating hormone (TSH) was determined with the supersensitive immunoradiometric Serono assay. Adrenocorticotropic hormone (ACTH) was measured by RIA in unextracted plasma according to previously described methodology. Antithyroid, antimicrosomal, and antinuclear antibody tests were all negative. Serum T4, 9.3 µg/dL (normal 5.5–11 µg/dL); FT4, 0.5 ng/dL (normal 0.7–1.8 ng/dL); T3, 197 ng/dL (normal 100–190 ng/dL); TSH, 0.30 mIU/mL (normal 0.6–10 mIU/mL). A morning plasma cortisol was 27 µg/dL (normal nonpregnant range 5–20 µg/dL). Serum prolactin was 37 ng/mL (normal 0–18.5 ng/mL, 80–200 ng/mL during the third trimester of pregnancy).

These findings were consistent with relative hypoprolactinemia and secondary hypothyroidism (low FT4, low TSH); the normal T4 and T3 were secondary to the increase in thyroxine-binding globulin during pregnancy. Since basal gonadotropins and growth hormone levels are low during pregnancy, the status of these pituitary hormones could not be evaluated.

No provocative pituitary testing was performed because of the patient’s pregnant status.

Because of her secondary hypothyroidism, the patient was given replacement doses of L-thyroxine (0.1 mg). Fear of permanent visual impairment and the inability to differentiate a pituitary adenoma from hypophysitis led to the decision to perform immediate transphenoidal surgery. The pituitary was yellow, swollen, and soft, but without the appearance of an adenoma. A specimen of the pituitary tissue, of sufficient size to relieve pressure on the optic chiasm, was obtained. Histologic examination revealed diffuse infiltration of the anterior pituitary by mature lymphocytes and occasional plasma cells (Figure 2). No granulomas were present, and the pathologic diagnosis of LHs was made.

Following surgery, the patient was maintained on levothyroxine (0.1 mg). A slightly supraphysiologic dose of hydrocortisone was begun (40 mg AM and 20 mg PM) in an attempt to suppress the inflammatory infiltration of
the pituitary without harming the fetus. Visual acuity and peripheral fields improved steadily, and 1 month postoperatively she had a normal neuroophthalmologic evaluation. Following an uneventful pregnancy, she delivered a normal boy, whom she nursed with moderate success for 8 weeks. The dose of hydrocortisone was lowered to 20 mg AM and 10 mg PM.

Table 1 shows the results of provocative testing at 6 weeks postpartum with 500 μg of TRH and 100 μg of luteinizing hormone-releasing hormone.

The pituitary functions were entirely normal except for a suppressed TSH level. Since the patient was on exogenous LT4 at the time of testing, the dose was gradually tapered to determine if TSH recovery was being prevented by the exogenous thyroid hormone. The low cortisol was felt to be secondary to pituitary suppression from exogenous steroids.

Two months postpartum, a coronal CT scan demonstrated complete normalization of the size and contour of the pituitary (Figure 1 B). Five months postpartum, L-thyroxine was discontinued. Two months later, the patient demonstrated full recovery of her pituitary axis: T4, 10.1 μg/dL; TSH, 1.1 mIU/mL. A 24-hour urine-free cortisol, obtained after hydrocortisone had been withheld for 1 week, was 75 μg (normal 35–135 μg). The patient refused repeat provocative pituitary testing or an insulin tolerance test. All hormone replacement was discontinued, and she was clinically and biochemically euthyroid and euadrenal for the next 18 months. She subsequently moved out of state and was lost to follow-up.

Discussion

Review of the literature reveals that this is the sixth reported case of LHy diagnosed during pregnancy, and the first biopsy-proven case in which the course of both the pituitary size and function are well described. While LHy is a distinct pathologic entity, at the present time the diagnosis can be made only by surgical biopsy. Thus, it is presently impossible to determine the true incidence or clinical spectrum of this disease. However, the documentation of full recovery in our patient suggests that the incidence of LHy may be higher than previously suspected, since asymptomatic individuals cannot be
Table 1. Provocative Testing at 6 Weeks Postpartum with 500 μg TRH and 100 μg LHRH

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<td>61</td>
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<td>ACTH (pg/dL)</td>
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Abbreviations: ACTH, adrenocorticotropic hormone; FSH, follicle-stimulating hormone; LH, luteinizing hormone; PRL, prolactin; TSH, thyroid-stimulating hormone.

AM cortisol, 4.6 μg/dL (normal 5–25 μg/dL) (hydrocortisone had been withheld for the prior 24-hour period).

identified. Because the clinical manifestations of LHy are protean, including pituitary mass, hypersecretion or hyposecretion of pituitary hormones, the diagnosis of LHy is usually entertained only when the above occurs in a patient in the peripartum period. Another pituitary disorder with a marked temporal relation to pregnancy is Sheehan’s syndrome. Not every patient carrying this diagnosis has an impressive history of postpartum hemorrhage. A subset of these patients may also be missed cases of LHy which, unlike our patient, progressed to permanent pituitary insufficiency with an empty sella [6].

Lymphocytic hypophysitis should be considered as part of the differential diagnosis of a pituitary mass or pituitary dysfunction presenting during pregnancy or the postpartum period. In such a patient, if there is no surgical emergency (ie, impending loss of vision), conservative management, including observation, hormonal re-

placement if needed, and perhaps a trial of increased steroids, should, if possible, be attempted before surgical intervention is considered.

References