Pregnancy in lymphocytic hypophysitis: case report and review

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Lymphocytic hypophysitis has been reported in 22 cases, all but one in women. More than 80% of the cases in women occurred during pregnancy or in the postpartum period. We describe a girl with partial hypopituitarism secondary to lymphocytic hypophysitis who, five years after the diagnosis, successfully delivered a healthy infant at term. Of the previously reported cases, most patients remain amenorrheic after the diagnosis. From the present case report and review of the literature, it would appear that a diagnosis of lymphocytic hypophysitis does not necessarily preclude the patient's ability to conceive and successfully carry the pregnancy. Pituitary hormone deficiency in this disease, therefore, does not always include the gonadotropins. Wis Med J 1989;88(11):29-32.

LYMPHOCYTIC HYPOPHYSITIS is believed to represent an autoimmune disease usually associated with pregnancy. Biopsy of the pituitary gland in these patients have demonstrated extensive infiltration with lymphocytes, some plasma cells and occasional lymphoid follicles with germinal centers. The first case of lymphocytic hypophysitis was described in a woman two months postpartum by Goudie and Pinkerton, in 1962. Subsequently, 21 other patients have been described in the literature. All but one of these cases have been reported in women. Seventeen of the 21 cases reported in women (81%) noticed symptoms of hypopituitarism during pregnancy or postpartum. Most patients develop panhypopituitarism; however, a few regain menses, and one patient was able to become pregnant after the diagnosis was made. We report herein a patient who successfully delivered a male infant five years after the diagnosis of a lymphocytic hypophysitis was made.

Case report
In 1983, a 17-year-old girl was admitted to the hospital with weakness, anorexia, orthostatic dizziness, and severe headaches. These symptoms had developed within ten weeks following the birth of her second child. On physical examination, she appeared acutely ill, weak, and unable to stand without assistance. Her blood
pressure was 88/50. Admission laboratory was significant for a calcium level of 11.7 mg/dl.

Endocrine studies at that time included baseline serum cortisol and aldosterone levels which were less than 2 ug/dl (normal, 4–28 ug/dl) and 11 ng/dl (normal, 1–21 ng/dl), respectively. The adrenocorticotropic hormone level was 15 pg/ml (normal, 15–100 pg/ml), prolactin level was less than 15 pg/ml (normal, 0–23 pg/ml), luteinizing hormone level 12 mIU/ml (normal, follicular phase 5–20 mIU/ml), and follicle-stimulating hormone level was 11 mIU/ml (normal, 2–30 mIU/ml). The patient was hyperthyroid with hyperthyroxinemia and a low thyroid stimulating hormone level of 1.7 fU/ml (normal, 1–10 fU/ml) and a low thyroidal uptake of sodium iodine I131 consistent with silent thyroiditis.

Cosynotropin was infused intravenously on three consecutive days with appropriate rise in her plasma adrenocorticosteroid levels indicating secondary adrenocortical insufficiency. An insulin tolerance test was performed without a resultant increase in cortisol, prolactin or growth hormone. The antinuclear antibody was positive at a titer of 1:640 although the patient had no clinical evidence of lupus. A coronal computed tomography scan (CT scan) with contrast of the sella turcica demonstrated a homogeneously enhancing mass filling much of the pituitary fossa with some suprasellar extension.

It was decided to observe the patient closely and defer surgery on the pituitary mass until the patient was stable on hormonal replacement therapy. Four months later, a repeat CT scan of the sella turcica showed resolution of the mass with a normal appearing pituitary gland.

The patient became hypothyroid and a thyrotropin releasing hormone stimulation test failed to elicit an appropriate rise in thyroid-stimulating hormone or prolactin consistent with hypopituitarism. The patient responded well to thyroid replacement and cortisone acetate with resolution of her symptoms and hypercalcemia. She remained amenorrheic for nine months after the diagnosis but then regained normal menses. Repeat CT scan through the sella turcica, two years after the diagnosis, remained normal in appearance without evidence of tumor, hypodense areas or necrosis; a second repeat CT scan five years later showed a scant amount of homogeneous pituitary tissue lying in the floor of the sella characteristic of an empty sella. A diagnosis of lymphocytic hypophysitis was made.

Five years later, the patient successfully delivered a healthy infant at term. Prenatal care had been uncomplicated. The patient had been maintained on thyroid replacement and cortisone acetate since the diagnosis of lymphocytic hypophysitis was made.

The patient's physical examination on admission was appropriate for this stage of pregnancy. Her blood pressure was 122/82 with a pulse of 92. The visual fields were normal by confrontation. Examination of the thyroid gland, heart, lungs, and extremities also were normal. The abdomen was soft and was gravid with estimated fetal weight of 3500 grams. Fetal heart tones ranged between 120 and 140. On pelvic exam, the cervix was four centimeters dilated and soft. Admission laboratory data included the following values: creatinine, 0.7 mg/dl; blood urea nitrogen, 1 mg/dl; sodium, 140 mEq/L; potassium, 3.6 mEq/L; chloride, 107 mEq/L; bicarbonate, 25 mEq/L; glucose 96 mg/dl. The hemoglobin level was 13.5 g/dl with the hematocrit at 40%. The white blood cell count was 17,300 cmm with a normal differential. Hemoglobin electrophoresis was normal.

The labor was initiated with a spontaneous rupture of membranes followed by a vaginal delivery with shoulder dystocia. During labor, the patient was supplemented with an increased dose of hydrocortisone to compensate for the stress of labor. Postpartum care was uneventful and the patient and infant were discharged home two days after delivery.

**Discussion**

Lymphocytic hypophysitis should be considered in the differential diagnosis of hypopituitarism, partial or complete, developing in pregnancy or postpartum. The etiology of the disease is unclear; however, Goudie and Pinkerton were the first to suggest an autoimmune basis. The histologic features of this lesion are similar to those of other autoimmune disease with lymphoid follicle infiltration and electron microscopy demonstrating interdigitation of activated lymphocytes with pituitary cells. Anti-pituitary antibodies were detected in a patient with lymphocytic hypophysitis described by Mayfield et al and anti-nuclear antibodies are frequently detected. The patient in the present case had a high anti-nuclear antibody titer. Of the patients previously reported, 22% had associated autoimmune disease of other endocrine organs, most commonly lymphocytic thyroiditis as in our patient.

Signs and symptoms of lymphocytic hypophysitis mimick those of a pituitary mass with pituitary insufficiency. Of the 22 cases reported, headache, visual disturbances, amenorrhea, nausea, vomiting, and fatigue were the most common presenting complaints. Of the seventeen previous cases associated with pregnancy or the postpartum period, the majority of patients developed symptoms in the last trimester or within one month after delivery as shown in Table 1.

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Table 1—Onset of symptoms in 17 patients with lymphocytic hypophysitis related to pregnancy

<table>
<thead>
<tr>
<th>Onset of symptoms</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Third Trimester</td>
<td>6 (34)</td>
</tr>
<tr>
<td>1 month postpartum</td>
<td>4 (24)</td>
</tr>
<tr>
<td>2-6 months postpartum</td>
<td>3 (18)</td>
</tr>
<tr>
<td>7-12 months postpartum</td>
<td>1 (6)</td>
</tr>
<tr>
<td>12 months postpartum</td>
<td>3 (18)</td>
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The diagnosis of lymphocytic hypophysitis was made at autopsy in nine of the 22 reported cases, all other cases were diagnosed by biopsy either by a transphenoidal approach or craniotomy. A CT scan was performed on twelve cases before biopsy. All 12 patients had an intrasellar mass with many having suprasellar extension as in our patient. A repeat CT scan in our patient four months after the mass was detected showed complete resolution without any surgical intervention, consistent with the diagnosis of lymphocytic hypophysitis rather than a pituitary adenoma. These observations in our patient suggest that some pituitary masses related to pregnancy do not require surgical intervention, but rather should be observed closely with sequential CT scanning.

The majority of patients with lymphocytic hypophysitis had complete hypopituitarism, but many had only partial deficiencies as shown in Table 2. With pituitary disease, it is classically taught that anterior pituitary hormones fail in a predictable fashion; growth hormone and the gonadotropins disappear first followed by thyrotropin, prolactin, and ACTH, respectively. There are, however, many exceptions to this rule as illustrated in lymphocytic hypophysitis. For example, two previously reported cases had isolated corticotropin deficiency. Additionally, our patient had developed panhypopituitarism at first, but nine months later, regained the ability to secrete gonadotropins reflected by the return of menses and subsequent conception.

Table 2—Endocrinologic features in patients with lymphocytic hypophysitis who were appropriately tested

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. (%)</th>
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<tr>
<td>Complete hypopituitarism</td>
<td>9 (50)</td>
</tr>
<tr>
<td>Partial hypopituitarism</td>
<td>7 (44)</td>
</tr>
<tr>
<td>normal cortisol</td>
<td>1</td>
</tr>
<tr>
<td>normal menses</td>
<td>4</td>
</tr>
<tr>
<td>normal TSH*</td>
<td>4</td>
</tr>
<tr>
<td>Prolactin level</td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>5 (46)</td>
</tr>
<tr>
<td>elevated</td>
<td>6 (54)</td>
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</table>

*TSH = Thyroid-Stimulating Hormone

Of the ten previously reported cases of lymphocytic hypophysitis in premenopausal patients who survived after the diagnosis was established and a menstrual history was obtained, eight were amenorrheic and two had normal menses.

References

Two of the eight patients who were originally amenorrheic regained menses and one was able to conceive again. Hence, pituitary deficiency in this disease does not always include the gonadotropins not unlike that observed in Sheehan's syndrome. Grimes et al reviewed 19 cases of Sheehan's syndrome in which a total of 39 pregnancies occurred after the onset of hypopituitarism.

This summary is only the second reported case of a patient with lymphocytic hypophysitis who was able to conceive and carry the pregnancy to term after the diagnosis was established. The original diagnosis in our patient was based on clinical presentation of hypopituitarism postpartum, laboratory findings of pituitary insufficiency and a high ANA titer, associated thyroiditis, and most importantly, a disappearing mass on sequential CT scanning avoiding an invasive procedure to obtain a biopsy. This case, along with a review of the literature, indicates that a diagnosis of lymphocytic hypophysitis in a patient does not preclude the ability to conceive and successfully carry the pregnancy while on hormonal replacement therapy.


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This is a partial list. The complete list from 1841 to 1972 appeared in the January 1973 issue.

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