A 44-year-old woman was admitted to the hospital because of headache, blurred vision, and an intrasellar mass.

She had been well until nine months earlier, when a vaginal hysterectomy was performed because of uterine prolapse; no oophorectomy was performed. Three months before admission occipital headaches developed and persisted for five weeks. Seven weeks before admission a computed tomographic (CT) scan of the cranium (Fig. 1) disclosed a slightly enlarged, homogeneously enhanced pituitary gland (height, 12 mm). The patient began to have nocturnal hot flashes and insomnia. Hormonal studies were performed (Table 1).

Five and a half weeks before admission the patient

Table 1. Results of Hormonal Studies.*

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>7 WEEKS BEFORE ADMISSION</th>
<th>5½ WEEKS BEFORE ADMISSION</th>
<th>ON ADMISSION</th>
<th>NORMAL RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follicle-stimulating hormone</td>
<td>7.6</td>
<td>10.3</td>
<td>0.6–13.3</td>
<td></td>
</tr>
<tr>
<td>hormone (U/liter)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Luteinizing hormone</td>
<td>5.2</td>
<td>9.5</td>
<td>0.1–28</td>
<td></td>
</tr>
<tr>
<td>(U/liter)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroid-stimulating hormone</td>
<td>0.17</td>
<td>0.19</td>
<td>0.5–5</td>
<td></td>
</tr>
<tr>
<td>hormone (μU/ml)</td>
<td></td>
<td></td>
<td>0.86 (20 min)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.26 (30 min)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1.60 (60 min)</td>
<td></td>
</tr>
<tr>
<td>Thyroxine (μg/dl)</td>
<td>2</td>
<td></td>
<td>4.7–11.1</td>
<td></td>
</tr>
<tr>
<td>Free thyroxine index</td>
<td>1.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total triiodothyronine (ng/dl)</td>
<td>157</td>
<td></td>
<td>75–195</td>
<td></td>
</tr>
<tr>
<td>Thyroid hormone–binding index</td>
<td>0.76</td>
<td></td>
<td>0.77–1.23</td>
<td></td>
</tr>
<tr>
<td>Human growth hormone</td>
<td>3</td>
<td></td>
<td>2–5</td>
<td></td>
</tr>
<tr>
<td>(ng/ml)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somatomedin C (ng/ml)</td>
<td>192.3</td>
<td></td>
<td>141–389</td>
<td></td>
</tr>
<tr>
<td>Prolactin (ng/ml)</td>
<td></td>
<td></td>
<td></td>
<td>0.0–15</td>
</tr>
<tr>
<td></td>
<td>16.5</td>
<td>6.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>14.6 (10 min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>22.6 (20 min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>25.8 (60 min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha subunit</td>
<td></td>
<td>0.5</td>
<td>0.5–2.5</td>
<td></td>
</tr>
<tr>
<td>Cortisol (random level)</td>
<td></td>
<td>0.5</td>
<td>0.5–2.5</td>
<td></td>
</tr>
<tr>
<td>(μg/dl)</td>
<td>0.5</td>
<td>1.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5.3</td>
<td>(30 min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.1</td>
<td>(60 min)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Minutes in parentheses denote the interval after the intravenous injection of thyrotropin-releasing hormone and cosyntropin. To convert values for thyroxine to nanomoles per liter, multiply by 12.87. To convert values for total triiodothyronine to nanomoles per liter, multiply by 0.01536. To convert values for cortisol to nanomoles per liter, multiply by 27.59.

Figure 1. Axial CT Image through the Sella Turcica, Obtained without Contrast Material. The pituitary gland is slightly enlarged. There is no evidence of acute hemorrhage or calcification.

Figure 2. Coronal T1-Weighted MRI Scan through the Sella Turcica Obtained before the Administration of Gadolinium. A homogeneous mass with a smooth contour fills the sella and extends upward from it, causing a slight mass effect on the optic chiasm. There is no evidence of hemorrhage.
told her gynecologist that she continued to have hot flashes and insomnia, along with fatigue, diffuse "bone aches," and anorexia. Gynecologic examination was normal. Hormonal studies were performed (Table 1). Two weeks before admission magnetic resonance imaging (MRI) of the cranium, performed before and after the administration of gadolinium (Fig. 2 and 3), showed a smooth mass, 13 mm by 20 mm by 14 mm, that filled the sella turcica and extended superiorly, with a mass effect on the central portion of the optic chiasm. The infundibulum was buckled and displaced slightly toward the right and upward, without thickening or abnormal enhancement. The carotid arteries, cavernous sinus, and sphenoid sinus appeared normal. The mass was isotense with gray matter on T1-weighted and T2-weighted images before the administration of gadolinium and had homogeneous enhancement after the administration of gadolinium. Prominent Virchow–Robin spaces were noted. The ventricular system appeared normal.

Nine days before admission an endocrinologist examined the patient and reported that she constantly felt exhausted and cold, had occasional blurred vision in the right eye, and was anorectic, with a loss of 9.1 kg in weight. She had had three successful pregnancies and had lactated but had not breast-fed. She rarely drank alcohol and did not smoke. She had mild asthma that was treated with an albuterol inhaler. There was no history of galactorrhea, polydipsia, polyuria, loss of axillary or pubic hair, easy bruising, changed facial appearance, or increased shoe or glove size. Her mother had diabetes mellitus; her children, siblings, and father were well.

Physical examination showed that the pulse was 90 and the respirations were 16. The blood pressure was 140/90 mm Hg. There was a questionable defect of the right superior temporal visual field.

Hormonal studies were performed (Table 1).

The results of routine laboratory studies, which comprised a urinalysis, a complete blood count with a differential count, prothrombin and partial-thromboplastin times, and measurement of urea nitrogen, creatinine, glucose, and electrolyte levels, were normal. An electrocardiogram and radiographs of the chest were normal. An ophthalmologic consultant found no abnormality except for a very subtle bilateral defect of the superior temporal visual field, which was more prominent in the right eye. A transsphenoidal surgical exploration showed that the pituitary gland was enlarged, tough, fibrous, and yellowish; no separate mass was seen.

A diagnostic procedure was performed.

**DIFFERENTIAL DIAGNOSIS**

**DR. JEFFREY R. GARBER**: May we review the radiologic studies?

**DR. SHARON SELTZER**: The initial CT scan of the head (Fig. 1), obtained without contrast material, shows homogeneous intrasellar tissue at least 10 mm in height, without calcification or acute hemorrhage. After enhancement with contrast material, slightly thinner sections reveal that this tissue is 12 mm in height and homogeneously enhanced. An MRI scan, obtained seven weeks later, shows a homogeneous soft-tissue mass touching the optic nerves at the region of the chiasm.
on the coronal T₁-weighted image before the administration of gadolinium (Fig. 2). There is no abnormally high or low signal within this tissue and no evidence of hemorrhage. The maximal height is 13 mm, the width is 20 mm, and the anteroposterior diameter is 14 mm. On the T₁-weighted image there is no low signal suggestive of hemosiderin. The intrasellar tissue appears minimally hypointense, as compared with normal sellar tissue. On the T₁-weighted coronal scan obtained before the administration of gadolinium, the sellar mass is smoothly contoured, homogeneous, and isodense with gray matter and causes a very slight tenting of the chiasm. On images obtained after the administration of gadolinium (Fig. 3), there is homogeneous enhancement of the intrasellar tissue. There is no tissue with different enhancement suggestive of pituitary tissue separate from the mass. The infundibulum is buckled and slightly deviated to the right and upward, without abnormal thickening or enhancement. There is a mass effect on the central optic chiasm. On the sagittal section there is no abnormal enhancement of the hypothalamus, dura, or infundibulum after the administration of gadolinium.

**DR. GARBER:** This 44-year-old woman had partial hypopituitarism. I shall first review the evidence for that conclusion and the extent of the deficiency in her pituitary function. Her headaches commenced three months before admission, persisted for five weeks, and became temporally associated with nocturnal hot flashes, which presumably caused the insomnia and suggest estrogen withdrawal. Since this patient had undergone a hysterectomy, a menstrual disturbance is not available as a clue. Menopause or primary ovarian failure is documented by elevated gonadotropin levels and low estrogen levels. Since early menopause is associated with normal as well as elevated gonadotropin levels, random low levels may not be sufficient to document menopause. In this case, without measurement of the patient’s estrogen level, the gonadotropin levels are not helpful.

Headaches suggest a structural basis for the gonadotropin deficiency and secondary estrogen deficiency, and the CT scan obtained seven weeks before admission suggests a pituitary lesion as the cause. The previously held belief that hot flashes do not occur with a gonadotropin deficiency has been abandoned. Estrogen withdrawal itself has been shown to be the basis of the vasomotor lability that accounts for hot flashes. It is possible that the measurable gonadotropin levels reflected residual immunoreactive gonadotropin secretion that was biologically inactive, as seen with glycoprotein-secreting tumors, but the normal value for the alpha subunit of prolactin is evidence against that possibility. The absence of evidence of an estrogen deficiency on gynecologic examination leaves open the possibility that gonadotropin secretion and ovarian function were wholly or partially intact, suggesting an alternative basis for the hot flashes.

The free thyroxine index, an estimate of circulating free thyroxine, was quite low, which is consistent with hypothyroidism, and the thyroid-stimulating hormone level was subnormal, suggesting a pituitary–hypothalamic basis for the hypothyroidism. The value for total triiodothyronine was at the high end of the normal range. Normal levels may be seen with either primary or secondary hypothyroidism. Preservation of normal levels in secondary hypothyroidism is associated with alterations in the peripheral metabolism of thyroxine designed to preserve the more potent form of thyroid hormone. This patient’s fatigue, aches, and subsequent sensation of being cold could have reflected hypothyroidism. An alternative hypothesis for the relatively high total triiodothyronine level, the low thyroxine level, and the low free thyroxine index in conjunction with a low value for thyroid-stimulating hormone is ingestion of thyroid hormone, leading to the suppression of thyroid-stimulating hormone dependent on the secretion of thyroid hormone, but nothing in the case record suggests the surreptitious use of thyroid hormone.

The low random value for cortisol suggests hypoadrenalism, which might have caused the patient’s fatigue, aches, and anorexia. Although secondary hypoadrenalism that develops gradually is not usually associated with weight loss, profound acute or subacute hypoadrenalism with anorexia can result in weight loss. The history, physical examination, and laboratory testing showed no evidence of hypersecretion of growth hormone or diabetes insipidus. There is no history of postpartum hemorrhage or shock or of failure to lactate. The preservation of axillary and pubic hair suggests that the patient’s adrenal insufficiency was not long-standing, because adrenal androgens are necessary for the maintenance of axillary and pubic hair in females. Physical examination revealed minimal bilateral defects of the superior temporal field. The consistently normal prolactin levels, with normal prolactin release after a thyrotropin-releasing hormone stimulation test, rule out excessive or deficient secretion of prolactin. The subnormal response of thyroid-stimulating hormone to thyrotropin-releasing hormone and the subnormal response of cortisol to synthetic corticotropin are consistent with secondary hypothyroidism and primary or secondary hypoadrenalism. The growth hormone and somatomedin C levels suggest normal secretion of growth hormone.

In summary, this woman had hypopituitarism, with hypothyroidism, hypoadrenalism, and possibly hypogonadism, without evidence of hypersecretion of prolactin, growth hormone, corticotropin, thyroid-stimulating hormone, or gonadotropins. The absence of diabetes insipidus suggests that the hypothalamus and posterior pituitary gland were at least partially intact. Moreover, the headaches associated with temporal visual-field defects point to a structural lesion in the hypothalamic–pituitary region.

Pituitary enlargement was documented by the CT scan obtained seven weeks before admission. Although the MRI scan obtained two weeks before admission confirmed the enlargement of the pituitary gland, we cannot conclude that there had been much growth during the five weeks between the two imaging studies. In addition, the enlargement was mild to moderate,
diffuse, and symmetric, with minimal suprasellar extension, and was not associated with any evidence of hemorrhage, cysts, calcification, the formation of an aneurysm, meningeal involvement, or other brain lesions. Furthermore, the posterior pituitary gland appeared intact, without definite evidence of infundibular thickening, although the pituitary stalk may have been slightly compressed. There was no evidence of a bony abnormality or involvement of the sphenoid or cavernous sinus. Finally, the neurosurgeon’s description of the pituitary gland strongly suggests fibrosis.

I shall now review intrasellar processes that typically cause symmetric, solid enlargement of the pituitary gland and hypopituitarism. Pituitary adenomas account for approximately 10 percent of all diagnosed intracranial tumors. Prospective studies of normal persons and postmortem examinations reveal pituitary adenomas in approximately 10 percent of adults. These tumors are almost always small. The case report suggests initially the diagnosis of a pituitary adenoma. The CT and MRI findings of pituitary enlargement with enhancement with contrast material and the hormonal deficiencies are consistent with this diagnosis. When hypopituitarism is present, however, pituitary tumors are usually substantially enlarged, with a considerable extrasellar component. A discrete adenoma separate from other pituitary tissue is often noted. With an acute or subacute presentation that includes headache, visual compromise, and hypopituitarism, one must consider hemorrhage into a preexistent pituitary adenoma (referred to as apoplexy). Furthermore, when pituitary tumors reach the size that is usually associated with hypopituitarism and apoplexy, they typically do not appear uniform or symmetric, and a preserved diaphragma sellae accounts for the dumbbell or figure-eight shape of many of these masses. Evidence of subacute bleeding is usually seen on serial MRI scans. Remote bleeding and adenoma degeneration are often reflected by the presence of intratumoral cysts and fluid levels. The typical sequence of hormonal deficiencies associated with a large pituitary adenoma is early loss of growth hormone and gonadotropin secretion, with later loss of thyrotropin and corticotropin secretion. Moreover, many pituitary adenomas are hypersecretory. Prolactinomas account for most of these tumors. Tumors secreting growth hormone, corticotropin, glycoproteins, and least commonly, thyroid-stimulating hormone account for the remaining tumors.

Primary or secondary pituitary hyperplasia can cause symmetric, diffuse, solid pituitary enlargement but is not, at least in its early stages, associated with hypopituitarism. Lactotroph hyperplasia has been proposed as a cause of hyperprolactinemia with pituitary enlargement. Thyrotroph hyperplasia can result from profound primary hypothyroidism, with the sellar volume correlated with the increase in the level of thyroid-stimulating hormone. Gonadotroph hyperplasia is seen with all forms of primary gonadal failure, but the extent to which it is associated with substantial pituitary enlargement is unclear. Corticotroph hyperplasia, caused by primary adrenal insufficiency, rarely progresses to the formation of an adenoma. Corticotroph hyperplasia, when seen with ectopic production of corticotropin-releasing hormone, causes concomitant hypersecretion of cortisol. Similarly, somatotroph hyperplasia with ectopic production of growth hormone—releasing hormone causes excessive secretion of growth hormone. In the absence of elevations in the prolactin, thyroid-stimulating hormone, follicle-stimulating hormone, luteinizing hormone, and growth hormone levels, only corticotroph hyperplasia should be considered, but it seems unlikely without evidence of primary adrenal disease beyond a glucocorticoid deficiency — namely, hypotension, hyperpigmentation, loss of axillary and pubic hair, or suggestive electrolyte abnormalities.

The most common neoplasm in the hypothalamic–pituitary region in children is a craniopharyngioma, but it can develop at any age. It arises in a remnant of Rathke’s pouch, which can also be the site of nontumorous lesions, especially cysts. The intrasellar center of the lesion, without cyst formation or calcification, seen on CT scanning in this patient, in combination with her age, makes a craniopharyngioma very unlikely.

Metastasis to the pituitary gland, a potential cause of pituitary enlargement, is seen most commonly with breast and gastrointestinal cancers and is associated with substantial enhancement with contrast material and adjacent brain edema. Metastatic disease is typically accompanied by multiple lesions within the brain and evidence of tumor elsewhere. Pituitary carcinoma is very rare and is characterized by rapid growth, invasiveness, and extrapituitary involvement. Meningiomas can be intrasellar, but normal pituitary tissue is usually evident radiologically. Also, bony involvement is demonstrable on CT scans, and a dural tail is seen on MRI scans; neither was observed in this case. Other tumors that involve the sella include germ-cell tumors, which usually involve the pineal region, and melanomas, for which we have no evidence. There is nothing to suggest hemochromatosis, which in its late stages should appear as a small, dark pituitary gland. Amyloidosis presenting as an isolated pituitary mass without systemic abnormalities or structural pituitary abnormalities in a young woman seems a remote possibility.

Rare destructive inflammatory diseases of the pituitary gland can cause hypopituitarism that is disproportionate to the degree of pituitary enlargement, as...
Lymphocytic hypophysitis, which is rare, with approximately 60 reported cases, predominantly affects females and usually presents during late pregnancy or the first 14 months thereafter. Early reports emphasized a high frequency of associated autoimmune disease, particularly Hashimoto’s thyroiditis. Because of the occasional presence of antipituitary antibodies, a lymphoid infiltration similar to that seen in autoimmune thyroiditis, and the presence of activated lymphoid infiltration similar to that seen in autoimmune thyroiditis, the concept of lymphocytic hypophysitis as an autoimmune disease became firmly established relatively early. Subsequent experimental models of lymphocytic hypophysitis produced by the injection of pituicytes with Freund’s adjuvant into rabbits and mice supported this concept. More recently, rubella virus membrane-associated E1 and E2 glycoproteins were shown to induce hypophysitis in hamsters, with neonatal thymectomy prevented the development of hypophysitis. Although autoantibodies against the pituitary gland developed, passive transfer of the antibodies failed to induce hypophysitis in other hamsters. The authors concluded that the hypophysitis was both antigen-specific and mediated by T cells.

Authors of subsequent reviews reported that the loss of pituitary function was often out of proportion to the degree of pituitary enlargement; depending on the phase of the disease, the pituitary gland could be enlarged, normal in size, or small. An isolated deficiency of a hormone, especially corticotropin, could occur. Somatotroph function and gonadotroph function were more likely to be preserved than corticotroph or thyrotroph function, unlike the findings in hypopituitarism due to a sizable pituitary adenoma. The posterior pituitary gland and pituitary stalk were typically spared, so diabetes insipidus was not part of the characteristic picture. The presentation often included weight loss, weakness, anemia, a change in vision, and a low glucose level. The presence of a change in vision was associated with a better outcome, probably because of an earlier diagnosis. Prolactin levels were elevated in up to 40 percent of the cases, probably as a result of stalk compression. An unusually firm and tough pituitary gland was evident in approximately 30 percent of the cases. Radiologic studies, the majority of which were CT scans, could not distinguish the lesion from a macroadenoma that had not bled.

Although the diagnosis can be suspected preoperatively, the definitive diagnosis relies on a biopsy. The response to steroid therapy has not been consistent, and pituitary function, as well as pituitary size, may ultimately return to normal in any case. Because of the potential for the recovery of pituitary function, surgical intervention should be avoided whenever possible.

Lymphocytic hypophysitis is probably greatly underdiagnosed because of the number of cases with spontaneous resolution, the potential confusion with Sheehan’s syndrome (which is decreasing in frequency because of improved obstetrical techniques but is often diagnosed in parous women with hypopituitarism of unknown cause if they have small pituitary glands, even without a clear-cut history of postpartum shock or hemorrhage), and confusion with other cases of idiopathic hypopituitarism (particularly isolated corticotropin deficiency). In addition, in some cases of the empty-sella syndrome, there is evidence of the resolution of pituitary enlargement caused by previously unrecognized hypophysitis.

The second form of hypophysitis that I shall discuss is granulomatous hypophysitis. In 1951 Rickards and Harvey reported 113 cases of the disorder, mostly in young women; 23 cases were idiopathic. Pamir et al. pointed out that the diagnosis of idiopathic giant-cell granulomatous hypophysitis was made by biopsy in only 10 of 30 cases reported by 1993, with the diagnosis made at autopsy in the remainder. The pathological findings in granulomatous hypophysitis were first described in 1911 by Gougerot and Gy, and in 1917 by Simmonds, whose name has become the eponym for hypopituitarism on the basis of his description of hypopituitarism related to sepsis (an uncommon cause of the disorder today), as well as other causes. In both reports the authors pointed out that the pathological findings probably reflected the stage of the process, with the early stages characterized by purulence and the late stages by fibrosis.

Granulomatous hypophysitis should be suspected when evidence of pituitary enlargement is associated with hypopituitarism and diabetes insipidus. Some granulomatous diseases, such as sarcoidosis and Langerhans’ cell histiocytosis, have a predilection for the posterior pituitary gland and hypothalamus. The key to the diagnosis of granulomatous hypophysitis resulting from generalized granulomatous diseases is documentation of the systemic manifestations of these disorders, including evidence of sarcoidosis in the lungs, liver, or skin; positive serologic tests and gumma formation in patients with syphilis; and positive tests for acid-fast bacilli in patients with tuberculosis. Langerhans’ cell histiocytosis is typically associated with distinctive skull lesions, proptosis, and diabetes insipidus. Wegener’s granulomatosis would be characterized by ophthalmic, sinus, pulmonary, and renal findings. Tests for fungi, mycobacteria, and spirochetes should be part of the evaluation of granulomatous inflammation of the pituitary gland. Preoperatively, however, without evidence of granulomatous disease elsewhere, there are no well-established methods (CT or MRI scanning or other methods) to distinguish granulomatous hypophysitis from lymphocytic hypophysitis or either disorder from pituitary adenoma. However, there are some
clues to the diagnosis. The presence of diabetes insipidus and infundibular thickening is evidence in favor of granulomatous rather than lymphocytic hypophysitis. Sarcoïdosis involving the sella is more common than lymphocytic hypophysitis. Idiopathic granulomatous hypophysitis has no known relation to pregnancy and tends to be seen in patients over 40 years of age, whereas patients with lymphocytic hypophysitis are generally younger.

Idiopathic granulomatous hypophysitis and lymphocytic hypophysitis may be different stages of the same disorder. Viral meningitis has been reported in association with both diseases, as has Rathke’s cleft cyst. A craniopharyngioma and a prolactinoma have been reported in association with lymphocytic hypophysitis. Sarcoïdosis after an episode of lymphocytic hypophysitis has also been reported. Furthermore, ultrastructural studies by McKeel18 raise the possibility that the two disorders are related.

In conclusion, I believe that this patient had hypophysitis of either the lymphocytic or the granulomatous type.

Dr. E. Tessa Hedley-Whyte: Dr. Ross will comment on the preoperative considerations.

Dr. Douglas S. Ross: We thought that a pituitary macroadenoma was the most likely diagnosis.

**Clinical Diagnosis**

Pituitary macroadenoma, nonfunctioning.

**Dr. Jeffrey R. Garber’s Diagnosis**

Hypophysitis, either lymphocytic or granulomatous type.

**Pathological Discussion**

Dr. Hedley-Whyte: Dr. Swearingen performed the pituitary exploration.

Dr. Brooke Swearingen: After examination of a frozen-section biopsy specimen yielded a diagnosis of lymphocytic hypophysitis, we removed the lower portion of the gland to decompress the chiasm but left residual tissue in the hope of maximizing the recovery of pituitary function. The visual symptoms resolved postoperatively, but the pituitary function has not returned to normal, despite high-dose corticosteroid therapy.

Dr. Hedley-Whyte: Microscopical examination of the specimen revealed a diffuse infiltration of lymphocytes (Fig. 4 and 5), with a few plasma cells and eosinophils, as well as residual pituitary cells. Immunohistochemical staining for prolactin confirmed the presence of pituitary glandular tissue (Fig. 6). We found no microorganisms on special staining. We therefore made the diagnosis of lymphocytic hypophysitis.

Figure 4. Frozen Section Showing Sheet of Lymphoid Cells without Recognizable Pituitary Architecture (Hematoxylin and Eosin, ×60).

Figure 5. Lymphocytes Infiltrating Pituitary Tissue (Hematoxylin and Eosin, ×220).

Larger, paler pituicytes are visible in the background.

At least 50 cases of this disease have been reported in the English and French literature.19 Cases have also been reported in the Japanese and Italian literature, and presumably elsewhere as well.

Although early reports emphasized an association with pregnancy, six cases of this disorder have been reported in men and at least four in nulliparous and four in postmenopausal women.20 In 1994 alone, six patients with the disease were described in the literature; one was a nulliparous woman, and three were men.19,20 In rare cases the disorder is accompanied by sarcoïdosis in another organ.21

In the differential diagnosis of a lymphocytic infiltrate in the pituitary gland, the choice is between lymphocytic and granulomatous hypophysitis. In this case no granulomas or multinucleated giant cells were found. These entities probably overlap, however, and the ab-
sence of granulomas does not prove that this disorder is not part of a granulomatous process. The immediate risk for this woman was permanent loss of vision, which was averted by the decompression.

Dr. Ross, will you describe the patient’s subsequent course?

Dr. ROSS: She was given a two-week empirical course of high-dose corticosteroids. Her visual fields and vision returned to normal, and her headaches resolved, but the function of her pituitary–adrenal axis has not returned to normal. Cosyntropin stimulation tests performed three weeks ago showed that the basal cortisol level was 0.2 μg per deciliter (5.5 nmol per liter) and it rose to 2.2 μg per deciliter (61 nmol per liter) 60 minutes after the injection. She has continued to take levothyroxine (0.1 mg a day) and prednisone (5 mg a day), and we have not yet reevaluated her pituitary–gonadal axis.

Dr. ROBERT B. COLVIN: In view of the assumed autoimmune nature of this disease, is it worthwhile to look for autoantibodies in the circulation?

Dr. GARBER: The usefulness of looking for pituitary autoantibodies is unclear. In a study by Yoon et al., antipituitary antibodies developed in hamsters with hypophysitis, but passive transfer of these antibodies failed to induce hypophysitis in other hamsters. The review by Cosman et al. points out that antipituitary antibodies were detected in only two of five patients with documented hypophysitis in whom antibody testing was performed. Moreover, antipituitary antibodies have been detected in normal women in the postpartum period in whom hypophysitis did not subsequently develop. These observations suggest that autoantibodies may be associated with the development of lymphocytic hypophysitis but do not cause it. Therefore, the presence of antibodies supports but does not confirm the diagnosis of lymphocytic hypophysitis, whereas their absence does not rule out the diagnosis.

ANATOMICAL DIAGNOSIS

Lymphocytic hypophysitis.

REFERENCES


The Massachusetts General Hospital wishes to acknowledge the generous support of Glaxo, Inc., whose sponsorship makes possible the continued preparation of the Case Records.