Lymphocytic Hypophysitis

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ABSTRACT—Lymphocytic hypophysitis (LH) is a rare but increasingly recognized inflammatory disorder of the pituitary, usually associated with pregnancy. Knowledge of this condition is largely anecdotal; the cause, incidence, and natural history are unknown. Cases are usually discovered at biopsy and surgical intervention for a presumptive pituitary neoplasm. Here we describe two cases of lymphocytic hypophysitis. In the first case the patient underwent surgery for presumptive adenoma, and pathology at resection established the diagnosis of lymphocytic hypophysitis. The second case was strongly suspicious for LH by history, endocrine profile, and imaging, and was managed nonoperatively. Though magnetic resonance imaging (MRI) features are not diagnostic, knowledge of imaging features together with clinical history may permit avoidance of surgery.

Case Report

A 38-year-old female presented with a three to four month history of galactorrhea, amenorrhea and fatigue. The patient had a history of low thyroid-stimulating hormone (TSH), headaches, and periodic blurry vision. Because she had central hypothyroidism and hypocortisolism she was started on levothyroxin and hydrocortisone several months prior to presentation. An endocrine profile showed elevated prolactin (100 ng/ml, normal < 25 ng/ml), but no growth hormone excess or other pituitary abnormalities. The patient had no significant prior medical history. She had an 11 month-old son and had never breast fed.

An MRI of the pituitary was performed. (1.5 T, Signa, GE. Acquisitions included T1 and T2 axial and sagital images of the entire brain. 3mm cuts were obtained with .3 mm gap, as T1 sagital, axial, and coronal, with and without gadolinium contrast.) The study demonstrated enlargement of the pituitary which extended suprasellar, indenting but not compressing the optic chiasma. The pituitary demonstrated peripheral hyperintensity, mildly and heterogeneously enhancing, postcontrast. A tentative diagnosis of 1 cm pituitary adenoma was made. The patient underwent a transphenoidal resection. Frozen sections showed primarily lymphocytic cells (staining positively for markers LCA, UCHL1 and L26) together with intermixed larger cells that were ACTH, prolactin and GH positive and LH, FSH, and TSH negative. At frozen section a diagnosis of lymphoma or PNET tumor was entertained; closer study of fixed sections returned a diagnosis of lymphocytic hypophysitis.

After resection of the pituitary mass, this patient was placed on prednisone, 10 mg BID, for one week, and then 10 mg QD. At three months follow-up the patient...
is asymptomatic, though still requiring levothyroxin and hydrocortisone. Reimaging of the pituitary at that time shows reduced pituitary size with postoperative changes.

The second patient is a nulliparous 20-year-old female with irregular menses and increased thirst as her initial presentation of Graves’ disease. She had been treated with \textsuperscript{131}I and was currently on methimazole. Initial workup revealed hypogonadotropic hypogonadism but no other evidence of pituitary hormone hypersecretion or deficiency, and no visual field defects. Prolactin and growth hormone were normal; IGF was 165 (nml 182 – 780 ng/ml).

MRI demonstrated an enlargement of the pituitary and thickening of the pituitary stalk. The pituitary enhanced strongly and uniformly with contrast. With strong suspicion for lymphocytic hypophysitis she was managed nonoperatively, treated only for Graves’ disease without
steroids, and has remained stable for greater than 18 months.

**Discussion**

Lymphocytic hypophysitis is a rare but increasingly recognized inflammatory disorder of the anterior pituitary and infundibulum. The disease affects primarily young women in late pregnancy or postpartum, although cases have been described in postmenopausal woman, and rare cases in men. Few biopsy proven cases are described in the literature. First described in 1962, the disease is thought to be autoimmune, although details regarding the trigger or mechanism of the disorder are unknown. An association between LH and autoimmune thyroiditis has been noted.

MRI study of the first case demonstrates an ill-defined enlargement of the pituitary. The pituitary demonstrates peripheral hyperdensity and heterogeneous signal centrally, enhancing mildly postgadolinium. The posterior pituitary demonstrates decreased signal. The mass extends suprasellar, indenting but not compressing the optic chiasm.
The pituitary stalk is noted to be thickened and enhancing, post-contrast. The sellar floor is noted to be depressed on coronal view. The enhancement pattern of the posterior pituitary is decreased.

The second case also demonstrates diffuse enlargement of the pituitary and diffuse enhancement post-contrast. Pituitary enlargement extends to the pituitary stalk and hypothalamus. The pituitary fossa remains normal in size, with no expansion or bony erosion, and no involvement of the sphenoid sinus mucosa.

As a diffusely infiltrative process, lymphocytic hypophysitis does not have specific or diagnostic imaging features. Typically noted is a diffuse increase in size of the anterior pituitary which homogeneously enhances with contrast, and a decrease in enhancement of the posterior pituitary as the blood supply to the posterior pituitary is compromised by the inflammatory process. These findings are not generally typical for adenoma. In their study of five cases of LH, Honegger et al.9 offer perhaps the most detailed study of MRI characteristics of LH. We follow the format of description used in their report in description of the imaging features in these few cases (see Table).

In addition to diffuse pituitary enlargement and homogeneous enhancement post contrast, Honegger et al note, as seen in the first case, a plane sellar floor typically seen in LH is in contrast to the unilateral depression generally found in pituitary adenoma. These authors also emphasize that LH is characterized by increased size of the pituitary stalk and superior enlargement of the pituitary as a “tongue-like extension along the basal hypothalamus,” a finding exemplified in the second case. Finally, they discuss that “triangular enhancement of the lesion and enhancement of the diaphragm sellar are pathognomonic findings of LH but are found only in some cases,” a finding not evidenced in the cases described here.

### Table 1

<table>
<thead>
<tr>
<th>Case #1 (Op)</th>
<th>Case #2 (Nonop)</th>
<th>Honegger et al</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRI signal after contrast</td>
<td>hyperintense</td>
<td>hyperintense</td>
</tr>
<tr>
<td>Extension to the basal hypothalamus</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Pituitary stalk thickened</td>
<td>yes</td>
<td>yes</td>
</tr>
<tr>
<td>Sellar floor (coronal view)</td>
<td>depressed</td>
<td>no</td>
</tr>
<tr>
<td>Sellar floor (thickness)</td>
<td>thinned</td>
<td>no</td>
</tr>
<tr>
<td>Pituitary fossa (size)</td>
<td>enlarged</td>
<td>nml</td>
</tr>
<tr>
<td>Sphenoid sinus mucosa swelling</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

### Conclusion

Management of LH is controversial as the natural history of LH is not known. As in the first case, most cases are approached surgically, as a neoplastic process, with true diagnosis found only at biopsy. MR imaging features include diffuse enlargement of the pituitary which enhances with gadolinium. Suprasellar extension with increased size of the pituitary stalk is characteristic. Symmetric depression of the sellar floor is atypical of adenoma. Though nonspecific, these findings in a pregnant or postpartum female, or young female with a history of autoimmune thyroiditis, should raise consideration for lymphocytic hypophysitis. As in the second case, if the diagnosis is strongly suspected, i.e., imaging characteristics as discussed in a patient with appropriate clinically history and without focal neurological signs, medical treatment alone has been advocated.

### REFERENCES