Lymphocytic Adenohypophysitis: Contrast-enhanced MR Imaging in Five Cases

PURPOSE: To describe observations of adenohypophysitis on magnetic resonance (MR) images.

MATERIALS AND METHODS: Clinical, enhanced MR imaging, surgical, and histologic findings were retrospectively studied in four female patients and one male patient with adenohypophysitis who presented with headaches, pituitary insufficiency, or hyperprolactinemia. Results were compared with MR imaging, surgical, and pathologic findings in 128 consecutive cases of newly diagnosed pituitary adenomas.

RESULTS: In two of the four female patients, disease onset was not associated with a recent history of pregnancy. Imaging findings included a slightly lobulated, intensely enhancing pituitary mass (n = 5); enhancement along the infundibulum (n = 4); and absent neural enhancement (n = 4). Four patients had extrapituitary involvement. Some of these findings were noted in patients with pituitary adenomas complicated by infarction, hemorrhage, or necrosis.

CONCLUSION: The observed clinical and MR imaging findings are suggestive of adenohypophysitis; the latter, however, are not specific and may be seen in some complicated cases of pituitary adenoma and other rare forms of pituitary inflammation. Biopsy may be needed to establish the correct diagnosis if a trial of steroid therapy fails.

Index terms: Pituitary, diseases, 145.259 • Pituitary, MR, 145.12143 • Pituitary, neoplasms, 145.372

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Table 1
Clinical and MR Imaging Findings in Five Patients with Lymphocytic Adenohypophysitis

<table>
<thead>
<tr>
<th>Sex/Age (y)</th>
<th>Clinical and Laboratory Findings</th>
<th>MR Imaging Findings</th>
<th>Biopsy</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>F/29</td>
<td>Headache; amenorrhea; galactorrhea; elevated levels of prolactin, FSH, and LH</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>M/40</td>
<td>Headache; decreased libido; visual field defect; elevated levels of prolactin, FSH, and LH; decreased levels of ACTH and TSH</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>F/15</td>
<td>Headache, diplopia, palsy of sixth cranial nerve</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>F/33</td>
<td>Headache, joint pain, decreased levels of cortisol and ACTH</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>F/38</td>
<td>Headache; visual field defect; oligomenorrhea; elevated levels of prolactin; decreased levels of FSH, LH, TSH, and thyroxine</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

Note.—ACTH = adrenocorticotropic hormone, FSH = follicle stimulating hormone, LH = luteinizing hormone, TSH = thyroid-stimulating hormone.

Figure 1. Lymphocytic adenohypophysitis in a 29-year-old woman with headaches, amenorrhea, and galactorrhea. (a) Sagittal (400/18) and (b) coronal (400/18) precontrast T1-weighted images demonstrate a pituitary mass abutting the optic chiasm with an immediately contiguous sphenoid sinus submucosal component (curved arrow). The mass is slightly hyperintense relative to gray matter. (c) Sagittal (500/16) and (d) coronal (500/16) postcontrast T1-weighted images demonstrate intense but heterogeneous enhancement of the anterior pituitary gland extending along the infundibulum. There are enhancing strips of adjacent dura mater (open arrow in c). Focal area of nonenhancing tissue corresponds to the posterior pituitary lobe on both pre-and postcontrast sagittal images (straight arrow in a and c). Note enhancement of the extrapituitary component of the lesion extending into the adjacent sphenoid sinus (curved arrow) without evidence of disruption of the sellar floor.

In the three patients who underwent follow-up MR imaging, improvement of the adenohypophysitis, both clinically and radiologically, was noted over 18–36 months (Fig 3c).

In the four patients with histologically proved adenohypophysitis, the surgical reports described dural changes consisting of conspicuous adhesions to the adjacent abnormally firm pituitary mass. Histopathologic analysis of the biopsy material revealed varying degrees of infiltration by lymphocytes and other “inflammatory cells” and associated fibrotic changes. There was no evidence of neoplasia. Multinucleated giant cells were absent in all specimens. Cultures of surgical material were negative for bacteria, mycobacteria, or fungi. Immunohistochemical studies were negative for growth hormone, prolactin, adrenocorticotropic hormone, thyroid-stimulating hormone, luteinizing hormone, and α-subunits.

The comparison of MR imaging,
surgical, and histologic findings for the five patients with adenohypophysitis and the 128 cases of pituitary adenoma is shown in Table 2. Most cases of pituitary adenoma showed a typical alteration in signal intensity on both pre- and postcontrast MR images but without enhancement of the adjacent dura mater. However, a few pituitary adenomas complicated by hemorrhage, necrosis, or infarction had MR imaging, surgical, or pathologic findings similar to those of adenohypophysitis (Fig 4).

**DISCUSSION**

A variety of inflammatory processes such as sarcoidosis, fungal infections, tuberculosis, and idiopathic giant cell granulomas may involve the pituitary gland (17–19). Lymphocytic adenohypophysitis is an inflammatory disorder of the pituitary gland that has been recognized with increasing frequency (19). Adenohypophysitis is one of the causes of pituitary dysfunction and has been diagnosed primarily in women who were or had recently been pregnant (1,2,14,20,21). Lymphocytic adenohypophysitis may also occur in premenopausal women with no recent history of pregnancy (22), postmenopausal women (23–26), and men (15,27). Postpartum pituitary necrosis (Sheehan syndrome) may also result in pituitary dysfunction related to pregnancy. At clinical presentation, lymphocytic adenohypophysitis may be differentiated both clinically and pathologically from postpartum pituitary necrosis. Although Sheehan syndrome may be manifested months or years after delivery, the sine qua non for this diagnosis is a complicated (hemorrhagic or septic) delivery (1,28). Lymphocytic adenohypophysitis can be readily differentiated from pituitary hyperplasia both clinically and radiologically on the basis of enhancement of the adjacent dura mater and extrapituitary components, since such enhancement is absent in pituitary hyperplasia.

Review of the literature indicates that for many of the patients with lymphocytic adenohypophysitis, a misdiagnosis of pituitary adenoma has been made preoperatively (1,2,9–11). Preoperative differentiation between these two enti-
Lymphocytic

## Table 2
Comparison of MR Imaging, Surgical, and Histologic Findings in Lymphocytic Adenohypophysitis and Pituitary Macroadenoma

<table>
<thead>
<tr>
<th>Findings</th>
<th>Lymphocytic Adenohypophysitis (n = 5)</th>
<th>Pituitary Macroadenoma (n = 128)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postcontrast MR imaging</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Enhancement of adjacent dura</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Surgical</td>
<td>4*</td>
<td>6</td>
</tr>
<tr>
<td>Preservation of neurohypophysis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Histologic</td>
<td>4*</td>
<td>8</td>
</tr>
<tr>
<td>Inflammatory cells</td>
<td></td>
<td></td>
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</tbody>
</table>

* One patient did not undergo surgery.

Figure 4. Pituitary adenoma with extensive infarction and hemorrhage within the tumor in a 23-year-old woman. (a) Sagittal precontrast T1-weighted image (439/20) shows a large, slightly heterogeneous pituitary tumor compressing the optic chiasm. (b) Sagittal postcontrast T1-weighted image (439/20) shows heterogeneous enhancement in the mass with rim enhancement of a pseudocapsule and enhancement of the adjacent dura mater (arrow).

Differences have great clinical significance. For a pituitary adenoma, total resection is the desirable treatment, whereas for adenohypophysitis, extensive resection may exacerbate the often preexisting hypothalamic (1,2). As described in this article, the MR imaging features of lymphocytic adenohypophysitis (Figs 1–3) are quite different from those of a typical pituitary adenoma. An intensely enhancing pituitary mass associated with strips of enhancing dura mater adjacent to the mass are valuable clues in the preoperative differentiation of adenohypophysitis from typical pituitary adenomas. Extratumoral involvement within the subarachnoid space, sphenoid sinus, or cavernous sinus may have some significance in determining the diagnosis, but these findings can be seen in invasive pituitary adenomas as well (29).

Recognition of the cavernous sinus in one of our proved cases of lymphocytic adenohypophysitis resulted in narrowing of the cavernous portion of the internal carotid artery, mimicking an MR imaging feature of Tolosa-Hunt syndrome. However, lymphocytic adenohypophysitis involving the cavernous sinus has previously been reported (13,30). In one of these cases, it was associated with bilateral occlusion of the internal carotid arteries (13).

If the diagnosis of lymphocytic adenohypophysitis can be made with MR imaging, is a biopsy still necessary? Our experience (Fig 1) and that of others (4,12) suggest that if the clinical findings and MR imaging features are consistent with a diagnosis of lymphocytic adenohypophysitis (and if there is no visual field defect), then a therapeutic trial with steroids is justified. A positive response to steroid therapy would indicate that the correct diagnosis had been made. Such conservative management, however, should not be extended too long if the pituitary lesion does not respond to this regimen. In this situation, surgery offers the opportunity for both histologic diagnosis and surgical management of many pituitary pathologic conditions, especially adenomas (31). In the case of incomplete surgical removal or recurrence of pathologically proved lymphocytic adenohypophysitis, steroid therapy can be an optional treatment.

Inflammatory changes may occur within pituitary adenomas secondary to necrosis, infarction, or hemorrhage within the tumor. Such reactive changes may be so extensive that even an experienced neuropathologist may not be able to histopathologically differentiate lymphocytic adenohypophysitis from a complicated pituitary adenoma. One of our cases not included in the series of five patients underscores the occasional difficulties in substantiating pathologic diagnosis (Fig 5). In this case, histologic examination of the tissue obtained during pituitary surgery showed that the anterior pituitary gland was heavily infiltrated by chronic inflammatory cells, including lymphocytes and plasma cells, and contained prominent fibrosis within the residual anterior pituitary cells. The degree of chronic inflammation was consistent with a diagnosis of lymphocytic adenohypophysitis. However, specimens stained with Prussian blue demonstrated abundant hemosiderin pigment, indicating previous hemorrhage. Immunoperoxidase stains for pituitary hormones demonstrated a normal mixed population of anterior pituitary cells. Although no adenoma was found, the possibility of previous hemorrhage in an occult adenoma with a secondary inflammatory response must also be considered in the differential diagnosis. McConnon et al (32) have also reported a case of sparsely granulated growth hormone cell adenoma associated with lymphocytic adenohypophysitis.

Because lymphocytic adenohypophysitis is thought to have an autoimmune origin, assay of antipituitary antibodies has been suggested as a means of confirming the diagnosis of lymphocytic adenohypophysitis (5–8,22,32). These markers, however, are neither sensitive nor specific (11,12,33). Mayfield et al (11) found antipituitary antibodies in one of four patients with lymphocytic adenoma. In addition, antipituitary antibodies were present in 18% of women in the postpartum period (33). These antibodies were not measured in our patients.

Serum prolactin levels in three of our patients with adenohypophysitis were mildly elevated. Such an increase in prolactin levels had been reported in some cases of lymphocytic adenohypophysitis and had been explained by local compression of the pituitary stalk, which prevents the inhibitory regulation of prolactin release by hypothalamic dopamine (12).

Clinical and radiologic features described in this article (even if not en-
tirely specific) are suggestive of lymphocytic adenohypophysitis. However, complicated pituitary adenoma, sarcoidosis, and other rare pituitary inflammations should be included in the differential diagnosis. Biopsy is necessary if a trial course of steroid therapy fails. As others have noted (2, 34), if firm adhesions are encountered during surgery and examination of frozen sections reveals lymphocytes without evidence of tumor (assuming there is no extensive hemorrhage or necrosis), the surgery should be limited to biopsy only or, if needed, decompression of the optic chiasm.

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References
16. Reusch JE, Kleinschmidt DeMasters BK, Lillehei KO, Rappe D. Preoperative diagnosis of lymphocytic hypophysitis (adenohypophysitis) unresponsive to short course dexametha-