Treatment of Lymphocytic Hypophysitis by High-Dose Methylprednisolone Pulse Therapy

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Abstract

A 26-year-old woman 3 months post-partum was admitted to our hospital suffering from gross visual disturbance. Magnetic resonance imaging (MRI) revealed a pituitary mass, extending into the suprasellar cistern, with intense gadolinium enhancement. Lymphocytic hypophysitis (LHy) was suspected, and the patient received high dose methylprednisolone pulse therapy (HDMPT). Her visual disturbance was dramatically ameliorated on the first day following initiation of HDMPT, and MRI revealed marked mass reduction. Her pituitary function recovered 6 months after therapy. This case report suggests that HDMPT proved effective for mass reduction of severe LHy and could obviate the need for a useless surgery.

Introduction

Lymphocytic hypophysitis (LHy) is a rare autoimmune disease, usually diagnosed following pituitary biopsy, or diagnosed unexpectedly during assessment for a presumed pituitary adenoma. Recently, corticosteroid therapy has been recommended when LHy is suspected clinically, even without pathological confirmation (1, 2). Although high dose (1 mg/body weight) prednisolone is usually preferred in order to allow quick evaluation of the therapeutic response, when gross visual disturbance is present, the response time may be delayed. In fact, gross visual disturbance may be potentially irreversible, resulting in surgical intervention. The role of high-dose methylprednisolone pulse therapy (HDMPT) in such cases has rarely been reported.

In this report, we outline a case of LHy with gross visual disturbance, showing remarkable improvement of symptoms one day post-initiation of HDMPT therapy, with MRI confirmation of mass reduction.

Case Report

A 26-year-old woman was admitted to our hospital on January 12, 2001 with a headache and visual field defect. She had delivered without complication of a female infant on October 26, 2000. Two months postpartum, she consulted an ophthalmologist due to headache and poor vision. Ophthalmologic examination revealed bitemporal hemianopia and the patient was referred to our hospital for further examination.

At the time of admission, the patient was 159.2 cm tall and weighed 51.2 kg. Her blood pressure was 110/60 mmHg, with a pulse rate of 84/min. No goiter or enlargement of lymph nodes was noted. The remainder of the examination was unremarkable. Laboratory findings on admission revealed mild normochromic anemia as shown in Table 1. Her corrected visual acuity was 0.1 in the right eye and 0.01 in the left eye, and critical fusion frequency (CFF) was low, particularly in the left eye (right 41 Hz, left 10 Hz).

In the MRI study performed on January 15, the sagittal T1-weighted image of contrast material revealed a mass enlarging the sella turcica extending into the suprasellar cistern, and abutting the optic chiasm (Fig. 1A). The mass showed intense enhancement after administration of contrast material. The clinical course and MRI findings were suspicious for LHy.

The patient’s visual impairment was severe enough to...
Table 1. Laboratory Data on Admission

<table>
<thead>
<tr>
<th>Blood cell count</th>
<th>Urea nitrogen</th>
<th>Creatinine</th>
<th>Uremic acid</th>
<th>Sodium</th>
<th>139 mEq/l</th>
</tr>
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<tbody>
<tr>
<td>White blood cell</td>
<td>4,030/mm³</td>
<td>14.3 mg/dl</td>
<td>0.9 mg/dl</td>
<td>5.3 mg/dl</td>
<td></td>
</tr>
<tr>
<td>Band cell</td>
<td>8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segmented cell</td>
<td>32%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoid cell</td>
<td>41%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monocyte</td>
<td>11%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eosinophil</td>
<td>8%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basophil</td>
<td>0%</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red blood cell</td>
<td>406x10⁸/mm³</td>
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<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>11.1 g/dl</td>
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</tr>
<tr>
<td>Platelet</td>
<td>29.9x10⁴/µl</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood chemistry</th>
<th>Immunity tests</th>
<th>Endocrinological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein</td>
<td>Antinuclear antibody</td>
<td>Free T3: 2.1 pg/ml</td>
</tr>
<tr>
<td>Albumin</td>
<td>Anti TPO antibody</td>
<td>Free T4: 0.6 ng/dl</td>
</tr>
<tr>
<td>Amylase</td>
<td>Anti thyroglobulin antibody</td>
<td>TSH: 0.25 µU/ml</td>
</tr>
<tr>
<td>AST</td>
<td>Anti rat pituitary antibody</td>
<td>ACTH: 15 pg/ml</td>
</tr>
<tr>
<td>ALT</td>
<td></td>
<td>Cortisol: 4.1 µg/dl</td>
</tr>
<tr>
<td>ALP</td>
<td></td>
<td>ADH: 3.67 pg/ml</td>
</tr>
<tr>
<td>LDH</td>
<td></td>
<td>GH: 7.04 ng/ml</td>
</tr>
</tbody>
</table>


warrant immediate intervention to relieve the mass effect. Although such surgery in LHx leads to rapid relief of neurological symptoms, it is deleterious on the pituitary function. Further, because the patient hoped to conceive another infant, we decided to perform surgery only if she did not respond to steroid therapy. The patient agreed with treatment plan. Therefore, we administered HDMPT (1 g methylprednisolone daily for three days). One-day status-post HDMPT initiation, the patient's visual sensation become clear and her headache was dramatically improved. MRI taken 3 days later revealed marked mass reduction (Fig. 1B). We confirmed LHx, and a pharmacological dose of prednisolone (30 mg daily) was initiated. Her visual acuity was improved to 0.15 in the right eye and 0.3 in the left eye, and CFF was also improved (right 43 Hz, left 35 Hz). When the dose of prednisolone was tapered to 25 mg daily, the patient complained of the return of poor vision. Subsequent MRI revealed pituitary re-enlargement (Fig. 1C). Therefore, methylprednisolone pulse therapy (0.5 g daily for two days) was initiated, resulting in vision improvement and MRI-confirmed pituitary mass reduction (Fig. 1D). High doses of prednisolone (50 mg daily) were initiated and tapered gradually without recurrence of the disease on low-dose prednisolone (10 mg daily) (Fig. 3).

Endocrine assessment prior to the initiation of steroid therapy revealed low free thyroxine (0.6 µg/dl), low thyrotropin (0.25 µU/ml), and a low, blunted thyrotropin response to thyrotropin releasing hormone (TRH) (Fig. 2A). Cortisol and adrenocorticotropin (ACTH) were low, and ACTH response to corticotropin releasing hormone was blunted. Follicle stimulating hormone (FSH) and luteinizing hormone (LH) responses to LH releasing hormone were blunted. Growth hormone (GH) and prolactin responses proved to be blunted during provocative testing. Posterior pituitary function was deemed normal because she had normal urine output with a urinary osmolality of 638 mOsm/kg H₂O, and antidiuretic hormone was 3.67 pg/ml. Furthermore, she had normal urine output even after initiation of steroid therapy. Neither anti-thyroid nor anti rat pituitary antibodies were detected. Endocrinological examination 6 months after initiation of steroid therapy revealed normalization of thyroid function and normal TSH and ACTH responses to provocative testing. The GH response to GH releasing hormone (GRH) was marked (Fig. 2B).

Discussion

LHx is a rare autoimmune disease, usually diagnosed by pituitary biopsy or unexpectedly during the work-up for a presumed pituitary adenoma. Recently, it has been proposed that the diagnosis of LHx can be made without pathological confirmation in a high proportion of patients (3). In this setting, the differential diagnosis includes pituitary adenoma, sarcoidosis, tuberculosis, syphilis, and primary granulomatous hypophysitis. The present patient was diagnosed as having LHx without pituitary biopsy for the following reasons.

In most cases of LHx, as with our patient, initial clinical
symptoms occur in young women in the third trimester of gestation or in the postpartum period. It has been reported that neuron-specific enolase, which is expressed in normal human pituitary, is localized in normal human placenta, thus establishing a direct link between pituitary and placental autoantigens. This link provides a theoretical basis for the strong predilection of LHy to occur during or after pregnancy (4).

It has been reported that MRI studies are useful for the differentiation of LHy from pituitary adenoma. Marked and homogeneous contrast enhancement of the pituitary gland is characteristic of LHy, while pituitary macroadenomas typically show only moderate enhancement (5). In the present case, pituitary adenoma was unlikely because gadolinium uptake by the pituitary gland was intense and homogeneous. Furthermore, rapid regression of the pituitary mass immediately following high-dose HDMPT made the diagnosis of pituitary adenoma even less likely. Medical history, laboratory findings (angiotensin-converting enzyme for sarcoidosis, treponema pallidum test for syphilis), and chest radiography
Figure 2. Response of pituitary and adrenal hormones to intravenous injection of CRH (100 µg), GRH (100 µg), TRH (500 µg), and LH-RH (100 µg) before (A) and after (B). CRH: corticotropin releasing hormone, GH: growth hormone, GRH: GH releasing hormone, TRH thyrotropin releasing hormone, LH: luteinizing hormone, FSH: follicle stimulating hormone, LH-RH: LH releasing hormone, TSH: thyrotropin, ACTH: adrenocorticotropin.
Yamagami et al

Methylprednisolone
1 g/day

Methylprednisolone
0.5 g/day

Prednisolone
30 mg/day
20 mg/day

50 mg/day
40 mg/day
10 mg/day

Visual field defect,
headache

Visual field defect,
headache

Day
1
5
10
15
20
25

Date
1/15
1/20
1/25
1/30
2/4
2/9

Figure 3. Clinical course.

(tuberculosis and sarcoidosis) were helpful for rule out sarcoidosis, tuberculosis, and syphilis. While it is impossible to completely differentiate primary granulomatous hypophysitis from LHy without pituitary biopsy, it has been suggested that LHy and primary granulomatous hypophysitis may, in fact, be different manifestations of the same disease (6). We suggest that response to high dose HDMPT may help to confirm the diagnosis of LHy by inducing rapid mass regression, thereby avoiding useless surgery.

Antipituitary antibody testing by immunofluorescence using pituitary tissue from a rat was negative in the present case. However, this testing cannot be a positive marker for LHy because it has been reported that this testing is nonspecific and the antibody is believed to be of low titer. Recently, it has been reported that autoantibodies to a 22-kDa human pituitary cytosolic protein by immunoblotting could be a marker for LHy, and this diagnostic method certainly shows promise (7).

Corticosteroid therapy appears to be the logical treatment of LHy, as it has been used with success in various autoimmune diseases. However, controversy still surrounds the duration of treatment and appropriate dosage. Although surgery for mass effect in LHy leads to rapid relief of neurological symptoms, it is deleterious to pituitary function. Therefore, surgery should be avoided when LHy is suspected clinically. Initiation of corticosteroid therapy should be considered. Although a replacement dose or a high dose of corticosteroid (1 mg/body weight of prednisolone) has been used thus far, it may take more time to prompt a favorable response. The present patient’s visual impairment was so severe that we had to relieve the mass effect more quickly.

Therefore, we chose to administer HDMPT. Our patient had an extremely favorable response to this plan of action. Questions remain regarding the necessity of HDMPT in this case, because previous reports have discussed the efficacy of a replacement dose or high doses of corticosteroid for pituitary mass reduction. However, considering that our patient’s symptoms and MRI findings relapsed upon tapering the dose of prednisolone to 25 mg daily, there appears to be a great likelihood that our patient would not have had an adequate response to high dose prednisolone, such as 50 mg/day.

The effect of corticosteroid treatment on pituitary function remains uncertain. Some patients have experienced improvement in pituitary function following corticosteroid therapy (8, 9). It has been suggested that corticosteroids may improve pituitary function in the early stages of this disease, when the pituitary has become edematous, inflamed, and enlarged (10). On the other hand, when pituitary tissue has been destroyed and replaced by fibrosis, corticosteroids may not induce an adequate response (11, 12). In our patient, endocrinological examination 6 months after the start of steroid therapy revealed normalization of response of TSH and ACTH levels to provocative testing. We believe that the improvement of pituitary function in this patient can be attributed to successful steroid therapy. However, this is not definitive since some patients demonstrate spontaneous remission without therapy (13).

In summary, we have reported a case of LHy with gross visual disturbance whose neurological symptoms and MRI findings improved remarkably 3 days after the start of HDMPT, and whose pituitary function recovered 6 months after the start of corticosteroid therapy. This case report
suggests that methylprednisolone pulse therapy was effective for mass reduction of severe LHy and could allow patients to avoid useless surgery.

References