Use of a clinicoradiological score to determine the presurgical diagnosis of autoimmune hypophysitis in a teenage girl

Case report

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The distinction between autoimmune hypophysitis and other non–hormone secreting pituitary masses is often difficult to determine with certainty without pituitary biopsy and pathological examination. To aid in this distinction, the authors recently published a clinicoradiological scoring system, which they used in the case of a 15-year-old girl presented here. The patient presented with headache, visual field defects, polydipsia, and polyuria, and she was found to have secondary hypogonadism and hypoadrenalism. Magnetic resonance imaging showed a pituitary mass of approximately 2 cm in diameter. Application of the clinicoradiological parameters gave a score of −6, which favored a diagnosis of hypophysitis over that of adenoma. The presence of pituitary autoantibodies substantiated the diagnosis of hypophysitis. The patient was treated conservatively with high-dose prednisolone, and her symptoms improved markedly. This case illustrates the utility of using a clinicoradiological score when autoimmune hypophysitis is suspected since it can identify patients who can be treated without the need for pituitary surgery. (http://thejns.org/doi/abs/10.3171/2012.11.PEDS12432)

Key Words • hypophysitis • radiological score • pituitary antibody • pituitary surgery

A ut oimmune hypophysitis, although relatively rare, enters in the differential diagnosis of all non–hormone secreting pituitary masses, of which the most common is the nonsecreting pituitary adenoma. Autoimmune hypophysitis was initially described in 1962 as a disease typically found in women, especially occurring in late pregnancy and the early postpartum period. In recent years the epidemiological spectrum of autoimmune hypophysitis, including the sex bias, has changed dramatically, mainly due to the reports, the first in 2005, that autoimmune hypophysitis develops with significant frequency in oncology patients treated with a CTLA-4 blocking antibody.

Autoimmune hypophysitis shares a similar clinical presentation and radiographic appearance with other non–hormone secreting pituitary masses, so that it is often difficult to establish a diagnosis of certainty of hypophysitis without pituitary surgery and pathological examination of the resected pituitary tissue. Approximately half of the patients with autoimmune hypophysitis undergo unnecessary surgery for a presumptive diagnosis of pituitary adenoma. The best diagnostic tool we have at the moment to obtain a presurgical diagnosis for autoimmune hypophysitis is cranial MRI. Recently, we developed a diagnostic score based on 2 clinical parameters (age and relation to pregnancy) and 7 MRI parameters.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.
to help distinguish an autoimmune hypophysitis from a nonsecretory pituitary adenoma. The MRI parameters include pituitary mass volume, symmetry, signal intensity after Gd administration, signal homogeneity, presence of a posterior pituitary bright spot, stalk size, and mucosal swelling of the sphenoid sinus. Each of the 9 parameters has a weighted value (Table 1), and a cumulative score is calculated by summing these 9 numbers. The score ranges from a minimum of −13 to a maximum of +8. A score of 1 or more correctly distinguishes nonsecretory adenoma from autoimmune hypophysitis in 97% of the patients with a sensitivity of 92%, specificity of 99%, and positive and negative predictive values of 97%.

The goal of the present study was to report the case of a 15-year-old girl in whom autoimmune hypophysitis was diagnosed using this score and who benefited from conservative therapeutic management and avoided surgical pituitary exploration.

Case Report

Presentation and Examination. This 15-year-old girl was admitted to our Department of Neurosurgery, Gutenberg Medical University, Mainz, Germany, in October 2011 for a chief complaint of retroorbital headache, lasting permanently for more than 2 years (Table 2). The patient’s history was also significant for a diagnosis of hypothyroidism caused by Hashimoto thyroiditis (since 2008) treated with replacement L-thyroxine, untreated secondary amenorrhea (since 2010), and an increased fluid intake, which at admission was about 5 L per day. The patient did not report any visual disorders. Ophthalmological examination showed a visual acuity of 1.0 but a bitemporal hemianopia for the upper quadrants.

Serum endocrine tests confirmed the secondary hypothyroidism and revealed low serum cortisol, but otherwise normal hormone levels. Serum electrolytes were normal, but owing to the large amount of daily fluid intake, 0.2 mg of desmopressin was given daily.

Treatment. Magnetic resonance imaging showed a 2.0 × 2.3 × 1.1–cm symmetrical, intra- and suprasellar mass, elevating the optic chiasm. The pituitary stalk could not be identified, and the posterior pituitary bright spot was lost. The pituitary mass showed medium rimlike contrast enhancement, extending toward the hypothalamus (Fig. 1). Based on the clinical data and MRI findings at admission, we obtained a hypophysitis score of −6 (Table 1) and favored the diagnosis of autoimmune hypophysitis over pituitary adenoma. Consequently, despite the large pituitary mass compressing the optic chiasm, which usually leads us to perform transsphenoidal surgery immediately, we placed the patient on a regimen of high-dose prednisolone (60 mg/day). The patient’s headache improved significantly 2 days later, and the amount of fluid intake decreased. On Day 4 of prednisolone therapy, MRI already showed a significant reduction in the pituitary mass, and ophthalmological control revealed intact visual fields. The patient was discharged on Day 5 after admission and was instructed to taper prednisolone gradually over a period of 6 weeks.

A serum sample obtained on Day 3 of high-dose prednisolone therapy was sent to the Hypophysitis Research Center at the Department of Pathology, The Johns Hopkins University, Baltimore, Maryland, for the determination of pituitary antibodies. Antibodies were assessed by indirect immunofluorescence using a human pituitary gland collected at autopsy as the substrate. The procedure was carried out as previously described and showed perinuclear positivity in a subset of anterior pituitary cells (Fig. 2).

Posttreatment Course. Upon completion of the prednisolone medication after 6 weeks, the patient again was seen in our outpatient clinic. She reported feeling well despite gaining 10 kg; she was without headaches, signs of diabetes insipidus, and visual problems, although her secondary amenorrhea persisted (Table 2). Her daily medication at this time included 50 μg of L-thyroxine, 10 mg of hydrocortisone, and 0.2 mg of desmopressin. A second follow-up MRI study was performed, which demonstrated complete regression of the pituitary lesion and showed a normal pituitary stalk and physiological contrast enhancement (Fig. 3). A posterior pituitary bright spot was still absent. With the patient still on a regimen of hydrocortisone and L-thyroxine therapy, testing in December 2011 revealed normogonadotropic hypogonadism and low serum cortisol, but otherwise normal hormone levels (Table 3). Desmopressin medication was withdrawn.

At a recent clinical follow-up visit after 8 months, the patient was still feeling well and had lost 8 kg of the weight she had gained during her high-dose prednisolone treatment. She denied headaches, visual disturbances, and increased fluid uptake. Magnetic resonance imaging revealed a normally configured pituitary and pituitary stalk, no signs of tumor, and no signs of pathological Gd enhancement, but the posterior pituitary bright spot was still missing (Fig. 2).

Hormone testing revealed normogonadotropic hy-
Diagnosing autoimmune hypophysitis with a clinicoradiological score

**TABLE 2: Clinical features pre- and posttreatment***

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>On Admission</th>
<th>6 Wks After HD Prednisolone Therapy</th>
<th>6 Mos After HD Prednisolone Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>headache</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>fatigue</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>bitemporal hemianopia</td>
<td>+</td>
<td>−</td>
<td>−</td>
</tr>
<tr>
<td>secondary amenorrhea</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>diabetes insipidus</td>
<td>+</td>
<td>−†</td>
<td>−</td>
</tr>
<tr>
<td>hypoadrenalism</td>
<td>+</td>
<td>−‡</td>
<td>−‡</td>
</tr>
</tbody>
</table>

* HD = high-dose; + = presence; − = absence.
† Less than 0.2 mg desmopressin per day.
‡ Less than 10 mg of hydrocortisone per day.

Pogonadism and still slightly low serum cortisol levels; the pituitary hormones were all within reference ranges (Table 3). Substitution with gonadotropins was started.

**Discussion**

In this report we demonstrate the usefulness of a simple clinicoradiological diagnostic score to provide a high percentage of certainty in diagnosing autoimmune hypophysitis over nonsecreting pituitary adenoma.12 In our neurosurgical routine, this score helps us correctly classify those pituitary masses that most likely do not necessitate surgery but instead can be treated conservatively.

**Symptoms of Autoimmune Hypophysitis**

The size of our patient’s pituitary mass with compression of the optic chiasm and upper quadrantanopia led to serious discussion in our department of whether to operate. Autoimmune hypophysitis has a characteristic presentation, that is, headache, hypopituitarism, and, if suprasellar extension of the pituitary mass compresses the optic chiasm, visual disorders. Diabetes insipidus, which has been described as another indicator of autoimmune hypophysitis1,5 and is rarely seen in pituitary adenomas,6 may give the only clinical hint for a nonadenomatous origin of the pituitary mass. Furthermore, our patient presented with a history of autoimmunity, as she had already suffered from Hashimoto thyroiditis, making autoimmune hypophysitis even more likely.2

**Magnetic Resonance Imaging**

Magnetic resonance imaging features typical of autoimmune hypophysitis include a symmetrical, homogeneous mass with medium to intense Gd enhancement.12 Moreover, thickening of the pituitary stalk and loss of the posterior pituitary bright spot is more than indicative of autoimmune hypophysitis. In contrast, pituitary adenomas are typically asymmetrical, show a heterogeneous enhancement,7 and have a lower Gd uptake than the normal adenohypophysis.14

**Score and Practicability**

The cumulative hypophysitis score of −6 made us establish a diagnosis of autoimmune hypophysitis, with-

**TABLE 3: Endocrinological analyses pre- and posttreatment***

<table>
<thead>
<tr>
<th>Analyte</th>
<th>On Admission</th>
<th>6 Wks After HD Prednisolone Therapy</th>
<th>7 Mos After HD Prednisolone Therapy</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH basal (micro-IU/ml)</td>
<td>0.04</td>
<td>0.52</td>
<td>2.29</td>
<td>0.4–4.0</td>
</tr>
<tr>
<td>FT3 (pg/ml)</td>
<td>3.38</td>
<td>1.55</td>
<td>2.03</td>
<td>1.8–4.5</td>
</tr>
<tr>
<td>FT4 (ng/dl)</td>
<td>1.32</td>
<td>1.29</td>
<td>1.08</td>
<td>0.9–1.8</td>
</tr>
<tr>
<td>IGF-1 (ng/ml)</td>
<td>255.90</td>
<td>179.00</td>
<td>134.4</td>
<td>98–505</td>
</tr>
<tr>
<td>STH (ng/ml)</td>
<td>1.83</td>
<td>0.06</td>
<td>0.30</td>
<td>0.06–5</td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>16.10</td>
<td>6.15</td>
<td>14.0</td>
<td>&lt;5–46</td>
</tr>
<tr>
<td>FSH (milli-IU/ml)</td>
<td>0.71</td>
<td>1.82</td>
<td>2.41</td>
<td>LP 1.2–9.0; OP 5.5–21</td>
</tr>
<tr>
<td>LH (milli-IU/ml)</td>
<td>0.16</td>
<td>0.37</td>
<td>0.92</td>
<td>FP 1.1–11.6; OP 17–77</td>
</tr>
<tr>
<td>estradiol (pg/ml)</td>
<td>21.60</td>
<td>&lt;20</td>
<td>&lt;20.0</td>
<td>FP 20–298; LP 26–195</td>
</tr>
<tr>
<td>progesterone (μg/L)</td>
<td>&lt;0.2</td>
<td>&lt;0.2</td>
<td>&lt;0.2</td>
<td>FP 0.2–0.81; LP 4.1–25</td>
</tr>
<tr>
<td>cortisol (μg/dl)</td>
<td>1.28</td>
<td>1.30</td>
<td>3.69</td>
<td>5–25</td>
</tr>
<tr>
<td>prolactin (ng/ml)</td>
<td>10.7</td>
<td>11.4</td>
<td>12.4</td>
<td>4.6–33</td>
</tr>
</tbody>
</table>

* ACTH = adrenocorticotropic hormone; FP = follicular phase; FSH = follicle-stimulating hormone; FT = free thyroxine; IGF-1 = insulin-like growth factor–1; LH = luteinizing hormone; LP = luteal phase; OP = ovulatory phase; STH = somatotropic hormone; TSH = thyroid-stimulating hormone.
hold surgery, and begin a treatment with high-dose prednisolone. The prompt clinical and radiological response of the patient to prednisolone confirmed our diagnostic suspicion of autoimmune hypophysitis. In addition, the presence of pituitary antibodies in the patient’s serum contributed to establishing a medical diagnosis without the need for pituitary surgery.

It is important to note that our clinicoradiological score was built on a multivariate analysis that compared autoimmune hypophysitis with nonsecreting pituitary adenomas. Therefore, the score’s utility in distinguishing pituitary antibodies in the patient’s serum contributed to establishing a medical diagnosis without the need for pituitary surgery.

It is important to note that our clinicoradiological score was built on a multivariate analysis that compared autoimmune hypophysitis with nonsecreting pituitary adenomas. Therefore, the score’s utility in distinguishing autoimmune hypophysitis from other, rarer, pituitary diseases such as germinoma, lymphoma, or histiocytosis remains to be validated. The current detection of pituitary antibodies is based on indirect immunofluorescence.

Corticosteroids are recommended as first-line management for autoimmune hypophysitis and are usually successful. Relapses requiring additional therapy, however, are not uncommon. In such cases, transsphenoidal surgery or other forms of immunosuppressive therapy (for example, azathioprin or radiosurgery) can also be performed. In our patient, high-dose prednisolone, given as introduced by Kristof et al., showed an immediate regression of the intrasellar mass and cleared all signs of headache and visual disturbances within 48 hours. In the absence of histological analysis, the response to immunosuppressants can serve as an accurate confirmation of an autoimmune hypophysitis diagnosis. At the end of the prednisolone therapy, 6 weeks after the initial dose of 60 mg, MRI analysis showed complete remission of the pituitary mass, and the patient did not have any medical complaints.

Long-Term Follow-Up

Nevertheless, since there have been reports about the transient nature of pituitary recovery, long-term endocrinological and radiological follow-up is necessary. In case of tumor relapse after immunosuppressive therapy, one must have other even rarer differential diagnoses in mind that might show an initial response to glucocorticoids, such as pituitary lymphoma or germinoma.

Conclusions

This report confirms the diagnostic value of our re-
Diagnosing autoimmune hypophysitis with a clinicoradiological score

cently developed clinicoradiological score\(^2\) that differentiates autoimmune hypophysitis from nonsecreting pituitary adenoma. Other additional clinical features, such as the presence of diabetes insipidus, and other autoimmune diseases, such as Hashimoto thyroiditis, may reinforce the diagnosis of autoimmune hypophysitis.

**Disclosure**

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