Pseudotumoral Lymphocytic Hypophysitis Successfully Treated by Corticosteroid Alone: First Case Report

Nathalie Beressi, M.D., Régis Cohen, M.D., Jean-Paul Beressi, M.D., Jean-Luc Dumas, M.D., Maggy Legrand, M.D., Marie-Thérèse Iba-Zizen, M.D., Elisabeth Modigliani, M.D.

Departments of Endocrinology (NB, RC, J-PB, ML, EM) and Radiology (J-LD), Hopital Avicenne, Bobigny and Neuro-Radiology (M-TI-Z), Hôpital XV-XX, Paris, France

Since 1962, more than 40 cases of lymphocytic hypophysitis have been described, all histologically proven. Lymphocytic hypophysitis is characterized by lymphocytic infiltration of the pituitary, which occurs mostly during or after pregnancy. Such an infiltration usually leads to pituitary dysfunction and to hypophyseal surgery because the putative diagnosis is that of pituitary adenoma. Until recently, all cases of pseudotumoral hypophysitis led to surgical exploration, which does not cure this medical disease. We report here the case of a woman in whom autoimmune lymphocytic hypophysitis was diagnosed without surgery because of suggestive clinical, biological, and radiological aspects.

CASE REPORT

A young woman, aged 27 years, had been suffering from chronic headache that appeared 13 months after giving birth; she had no significant symptoms during pregnancy. Twenty-one months later, amenorrhea, visual symptoms, and persistent headache led her to seek medical advice (June 1990). At this time, galactorrhea was observed. An ophthalmological examination was normal. Cranial tomodensitometry and magnetic resonance imaging (MRI) revealed a pituitary gland increased in size, with suprasellar extension, but without any erosion of the dorsum sellae. Because mild hyperprolactinemia was evidenced, bromocriptine (Parlodel; Sandoz Ltd., Basel, Switzerland) treatment was prescribed at a dose of 5 mg daily and was soon followed by the transient appearance of menstruation.

Our patient was lost for follow-up until her admittance to our endocrinological unit 2 years later (March 1992) because of adrenal insufficiency. Biological features showed a panhypopituitarism without hyperprolactinemia (Table 1). At the time of admission, the patient underwent MRI on a 1.5 MR Unit (Magneton, Siemens, Erlangen, Germany). Coronal T1-weighted images and coronal gadolinium diethlenetriamine-pentaacetic acid (Gd-DTPA)-enhanced T1-weighted images were obtained: a large, pituitary lesion was identified with a su-

Key words: Autoimmunity, Corticoid, Hypopituitarism, Lymphocytic hypophysitis, Magnetic resonance imaging, Pituitary gland

Neurosurgery, Vol. 35, No. 3, September 1994
TABLE 1. Endocrine Investigation Before and After Steroid Treatment (60 mg/d) of Prednisone during 3 mo and Progressively Decreasing Dose for 6 mo: Basal Values and Response of LH, FSH, ACTH, Cortisol, and Prolactin to the Injection of LHRH, CRH, and TRH

<table>
<thead>
<tr>
<th>Hormones</th>
<th>Before Treatment</th>
<th>After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>June 1990</td>
<td>March 1992</td>
</tr>
<tr>
<td>LH</td>
<td>(n = 1–7 U/L)</td>
<td>1.6</td>
</tr>
<tr>
<td>Peak after LHRH</td>
<td>5</td>
<td>3.2</td>
</tr>
<tr>
<td>FSH</td>
<td>(n = 3–8 U/L)</td>
<td>5</td>
</tr>
<tr>
<td>Peak after LHRH</td>
<td>6.8</td>
<td>6.8</td>
</tr>
<tr>
<td>Estradiol</td>
<td>(n = 37–730 pM/L)</td>
<td>68</td>
</tr>
<tr>
<td>Peak after TRH</td>
<td>0.2–4.5 µg/ml</td>
<td>0.88</td>
</tr>
<tr>
<td>TSH</td>
<td>(n = 10–50 pg/ml)</td>
<td>11.8</td>
</tr>
<tr>
<td>Peak after CRH</td>
<td>24</td>
<td>134</td>
</tr>
<tr>
<td>Cortisol</td>
<td>(n = 345–662 nM/L)</td>
<td>32</td>
</tr>
<tr>
<td>Peak after CRH</td>
<td>107</td>
<td>107</td>
</tr>
<tr>
<td>Prolactin</td>
<td>(n = 130–700 mU/L)</td>
<td>1440</td>
</tr>
<tr>
<td>Peak after TRH</td>
<td>342</td>
<td>342</td>
</tr>
</tbody>
</table>

* LH, luteinizing hormone; FSH, follicle-stimulating hormone; ACTH, adrenocorticotropic hormone; TSH, thyroid-stimulating hormone; TRH, thyroid-releasing hormone; LHRH, luteinizing hormone-releasing hormone; CRH, corticotropin-releasing hormone; FT4, free thyroxine.

* After treatment means withdrawal of levothyroxine after 30 days, of prednisone after 15 days, and without hydrocortisone after 1 day.

The occurrence of hypopituitarism with transient hyperprolactinemia a few months after pregnancy, associated with previously described radiological aspects, led us to consider the diagnosis of hypophysitis. We did not find any positivity in antinuclear antibodies or other autoantibodies. Antibodies directed against the pituitary gland could not be assessed. Human leukocyte antigen serological Class II typing was DR3/DR4.

Because of the absence of any visual complications and patient refusal of surgical treatment, steroid therapy was attempted: 60 mg/d of prednisone were given for the first 3 mo. The dose was then progressively decreased for the next 6 mo. Clinical improvement consisted of the disappearance of headache and the appearance of menstruation. Hormonal tests (Table 1) pointed out that thyroid function was back to normal; the luteinizing hormone–releasing hormone test was positive. The basal cortisol level was low but reactive, as was the adrenocorticotropic hormone level, after corticotropin releasing hormone injection. Interestingly, a disruption in corticoid treatment for 15 days at the sixth month of follow-up did not induce clinical adrenal insufficiency. Furthermore, repetition of the MRI after 3 mo showed a substantial reduction of the pituitary mass, reaching 70% after 6 months and sustained at 9 months (January 1993) (Fig. 1C).

Five months later, the patient relapsed with amenorrhea, headache, and asthenia (April 1993). Biological explorations confirmed hypopituitarism, and a radiological examination showed the same pituitary volume as in Figure 1. She underwent steroid therapy, and a transphenoidal pituitary biopsy was performed, confirming the diagnosis of autoimmune hypophysitis, without giant cell granuloma. The patient still received steroid therapy.

**DISCUSSION**

Lymphocytic hypophysitis is a newly discovered disease. Thus, its frequency is not well established. The natural history and pathogenesis of lymphocytic hypophysitis remain poorly understood. The histological examination usually shows lymphocytic pituitary infiltration, confirming the diagnosis. In this report, we present the first case diagnosed with...
out histological data of pituitary infiltration diminishing under steroid therapy and confirmed after relapse by histological examination. Several characteristic features (clinical, radiological, and therapeutic) directed us toward hypophysitis.

As in our case, the first clinical symptoms usually occur in a young woman in the last trimester of gestation or in the postpartum period (1, 3–6, 8, 10, 14, 17). Panhypopituitarism symptoms occurring after gestation could lead one to suspect Sheehan’s syndrome. However, MRI eliminated this diagnosis, showing a hypothalamic mass mimicking a pituitary adenoma (2–6, 8, 10–14, 16–18). Hypophysitis can present confusing radiological signs, leading the physician to indicate medical or surgical adenoma treatment. The upper triangular shape of the pituitary and the homogenous signal before and after gadolinium injection are unusual signs in pituitary adenoma, but they are often reported in tumoral intrasellar hypophysitis (8, 10, 12, 13, 17); a global and symmetrical mass effect of the entire gland is also in favor of a diffuse, inflammatory pituitary infiltration rather than of a pituitary adenoma, which is usually more localized. Furthermore, this homogenous mass on MRI or cranial tomodensitometry contrasts with the normal floor of the sellae turcica and the absence of bone erosion on plain x-ray film. These radiological aspects, even if not entirely specific, appear to be very suggestive of lymphocytic hypophysitis.

The mild increase in prolactin in this case could not be related to prolactin adenoma because of the discrepancy between plasma prolactin levels and adenoma size. The probable explanation was local compression of the stalk, interrupting the inhibiting regulation of prolactin release by hypothalamic dopamine. Anyway, hyperprolactinemia subsided spontaneously even after the interruption of bromocriptine. The panhypopituitarism features seem in accordance with those from previous reports (5–8, 14, 18). Corticotropin, thyrotropin, and gonadotropin deficiencies were evidenced. Gonadotropin deficit associated with menstrual disturbance is observed in 30% of cases (5).

Because hypophysitis is thought to be of immunological origin, we tried to find other immunological abnormalities (9). Antigen antibodies were negative. Some authors described antipituitary antibodies (12, 19). This marker does not seem to be sensitive or specific. Mayfield et al. (12) found antipituitary antibodies in one of five patients suffering from hypophysitis. Conversely, antipituitary antibodies were positive in 18% of women in the postpartum period (15). These antibodies were not measured in our patient. There was no clinical or histological finding of other hypophyseal granulomatous diseases such as sarcoidosis, granulomatous hypophysitis, or syphilis. Moreover, our patient did not display diabetes insipidus, which is frequently present in these cases.

In our case, an important argument in favor of hypophysitis was the therapeutic test of corticosteroids, which induced in our patient a significant tumoral reduction and hormonal improvement. Amelioration of the hormonal course was parallel to the reduction in tumoral volume. Thyroid function returned to normal and corticotropin deficiency improved significantly after steroid treatment. The reduction in tumoral volume obtained in 3 months in our patient can be attributed to steroid therapy, because the tumoral volume had been previously stable for 2 years. The possibility of a spontaneous reduction, as observed in pituitary adenoma, by hemorrhage or necrosis was eliminated by MRI (Fig. 2) and by the spontaneous relapse after corticoid discontinuation. The only explanation of the two-thirds volume reduction after 6 months of steroid therapy in this case is the disappearance of the lymphocytic infiltration of the pituitary. In the published cases, even if most patients underwent radical surgery, because of the preoperative diagnosis of pituitary adenoma, some cases received steroid therapy (6, 8, 12–14, 17). The treatment was often given at low doses and for a short time, explaining the absent or transient effect. However, with higher or more prolonged doses, beneficial effects have been observed (6, 8), but without hormonal recovery. In conclusion, this case report is the first evidence that the diagnosis may be suspected on the basis of clinical, imaging, and biological data without histological confirmation. Response to steroid therapy may help to confirm the diagnosis by inducing volume reduction and also by improving hormonal status, avoiding a useless surgery.

ACKNOWLEDGMENTS

We thank Dr. Jacqueline Mikol for the expert histological examination of the pituitary biopsy.

Received, August 5, 1993.
Accepted, March 18, 1994.
Reprint requests: Dr. E. Modigliani, Endocrinology, Hopital Avicenne, 125, Route de Stalingrad, 93009 Bobigny Cedex, France.

REFERENCES

The authors present the first case report of the successful treatment of a pituitary mass by corticosteroids alone. This observation has implications for the management of inflammatory disease with possible immunological origin that involves the pituitary gland. In fact, clinical and neuroradiological features can be suggestive of lymphocytic hypophysitis. In such a case, a therapeutic trial with corticosteroids is justified and a response can avoid surgical exploration. On the other hand, steroids offer a therapeutic option in the case of incomplete surgical removal or recurrence if histology reveals the diagnosis of lymphocytic hypophysitis.

The autoimmune origin of lymphocytic hypophysitis is well established. However, the autoimmune background of other inflammatory pituitary diseases (for example, isolated giant cell granuloma of the pituitary) has not been clearly proved. A therapeutic trial with steroids would be worthwhile.

The therapeutic approach to lesions of the pituitary is multidisciplinary, and an early role of medical therapy is anticipated. Medical therapy in pituitary adenomas (i.e., with dopamine agonists in prolactinomas and with somatostatin analogs in acromegaly) is on the rise. An alternative or supplementary therapy to surgery in autoimmune disease involving the pituitary is lacking so far. Steroid therapy could close this gap and could enlarge the scope of therapeutic options in pituitary-related disease.

On the other hand, this conservative approach should not be extended too long if patients with suspected autoimmune disease of the pituitary do not respond to steroids. In these cases, transphenoidal surgery allows definite histological confirmation of the diagnosis and offers the chance of a surgical cure in many pathologies, especially in pituitary adenomas, which prevail among pituitary lesions.