A PITUITARY MASS AND HYPOPITUITARISM: IMPROVEMENT AFTER CORTICOSTEROID THERAPY

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ABSTRACT. Lymphocytic hypophysitis of the anterior pituitary is a rare autoimmune disease, invariably diagnosed either by surgical biopsy of the adenohypophysis or at autopsy. The current report describes the rapid development of hypopituitarism in a 42-year-old nulliparous woman with a large sellar mass, who did not undergo pituitary surgery. Transient regression of the sellar mass and partial improvement of the hypopituitarism was induced by treatment with corticoids. We suggest that the diagnosis of lymphocytic hypophysitis can be established clinically and that conservative treatment with corticoids should be considered prior to surgical intervention.


Keywords: hypopituitarism; pituitary mass; corticosteroids

LYMPHOCYTIC hypophysitis of the anterior pituitary is a rare cause of hypopituitarism of autoimmune pathogenesis. It develops rapidly, and presents as a large intrasellar mass extending superiorly. The disease is often associated with other autoimmune diseases, including Hashimoto’s thyroiditis (1,2), autoimmune adrenalitis (3,4), lymphocytic infiltration of the parathyroid glands (3) and pernicious anemia (5,6). This inflammatory process, characterized by diffuse lymphocytic and plasma cell infiltration of the adenohypophysis, clinically mimics a pituitary tumor (7-9). Initially, the diagnosis was established histologically at postmortem examination (4,10), while more recently it has been detected as an antemortem diagnosis during pituitary exploration for sellar masses (6-8,10-14).

This report describes the case of a woman with a clinical presentation compatible with lymphocytic hypophysitis who responded to corticosteroid therapy with regression of a pituitary mass, thus obviating the need for pituitary surgery.

CASE REPORT

A nulliparous unmarried woman aged 42 sought medical attention in September 1993 for severe recurrent headaches, fever, weakness, myalgia and amenorrhea of 2 months’ duration. Familial Mediterranean fever (FMF) had been diagnosed many years earlier, but she had not taken colchicine treatment regularly. Family history included diabetes mellitus in her mother and FMF in her brother. Physical examination revealed a woman suffering from severe diffuse headache, fever up to 39.1°C with no meningeal signs. Blood pressure was 140/80 mm Hg without orthostatic hypotension, and the neurologic examination was normal. There was no galactorrhea, and the ophthalmologic examination, including visual fields assessment, was normal.

Laboratory assessment revealed a white blood cell count of 8,600/mm³ (with normal differential count), hemoglobin 11.2 g/dl, platelet count 176,000/mm³ and

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erythrocyte sedimentation rate (ESR) of 100 mm/h. Serum glucose, electrolytes, liver enzymes and renal function were within normal range.

Computerized tomography (CT) scan of the sella turcica, performed in September 1993, demonstrated an intrasellar mass that measured 12 mm in diameter and extended superiorly. Magnetic resonance imaging (MRI) done 1 month later, disclosed an enlarged sella with a 15 mm pituitary mass, extending into the suprasellar cistern and displacing the infundibulum to the left without damage to the optic chiasm (Fig. 1). Laboratory evaluation revealed mild hyperprolactinemia of 690 mU/l (normal <460 nmol/l), secondary hypothyroidism with serum thyroxine level of 54 nmol/l (normal 64–154 nmol/l) and serum thyroid-stimulating hormone (TSH) of 2.1 mU/l (normal 0.5–4.0 mU/l); severe secondary hypocortisolism with a morning adrenocorticotropic hormone (ACTH) level of 1.43 pmol/l (normal 2.2–15.4 pmol/l) and serum cortisol of <193 nmol/l (normal 193–690 nmol/l); and hypogonadotropic hypogonadism with low serum levels of follicle-stimulating hormone (FSH) 1.5 IU/l, and luteinizing hormone (LH) <1.0 IU/l, as well as low 17-OH-estradiol <75 pmol/l. The growth hormone (GH) level was less than 1.0 nag g/l and diabetes insipidus was ruled out after water deprivation. The free α-subunit level was 0.25 mU/l (normal <0.25 mU/l).

The response of cortisol to intravenous ACTH was absent (193 nmol/l after 60 min), and steroid replacement therapy with prednisone 10 mg/day was therefore begun. During the next few days, the fever vanished and her general condition improved with resolution of the headache and weakness. Intravenous thyrotropin-releasing hormone (TRH) test revealed TSH hyperresponsiveness to 30 mU/l after 30 min. Serum thyroid microsomal and thyroglobulin anti-bodies were negative.

In November 1993, 10 days after the initiation of steroid replacement therapy, a second MRI was done, which demonstrated a normal pituitary gland, 4–6 mm height, again with infundibular displacement to the left (Fig. 2). In December 1993, she began menstruating after 6 months of amenorrhea. The FSH and LH levels were 6.8 and 6.3 IU/l respectively, and the prolactin gradually decreased to 265 mU/l. The ESR decreased to the normal range, 25 mm/h.

In January 1994, a gonadotropin-releasing hormone (LHRH) stimulation test was performed and judged to be normal: the maximal increase of LH was 39 IU/l after 30 min, and the FSH level increased up to 8.1 IU/l after 60 min. Intravenous growth hormone-releasing hormone (GHRH) test revealed normal GH response (GH increased from baseline level of 1.4 to 32 µg/l, after 15 min), but intravenous corticotropin-releasing hormone (CRH) did not stimulate ACTH secretion (basal and maximal ACTH levels <2.2 pmol/l). The prolactin level was less than 115 mU/l. The patient decided to discontinue her prednisone treatment as she felt well.

In March 1994, a third MRI examination was done which demonstrated re-expansion of the intrasellar mass to 18 mm height, with suprasellar extension and mild pressure on the optic chiasm (Fig. 3). She did not have headaches and visual fields were normal, but her
Figure 2. MRI of the sella with gadolinium – (A sagittal, B coronal). Marked decrease in the size of the sellar mass, with homogeneous changes in relaxation following gadolinium. Minimal shift of the infundibulum to the left. The chiasma is "V" shaped and pulled down by the shrinkage of the mass.

Figure 3. MRI of the sella with gadolinium – (A sagittal, B coronal). A repeat study after discontinuing steroid treatment. Relapse of the intra- and suprasellar mass, appearing hyperintense and even larger than in the initial study. On the right side of the figure – pressure on the chiasma, which is deformed.

menses ceased again. A second LHRH test revealed attenuated response of gonadotropins as compared with the test performed 2 months earlier. Prolactin was less than 115 mU/l. Repeated TRH stimulation test showed a very poor response (peak level 5.2 mU/l after 60 min). High dose prednisone (30 mg/day) and replacement thyroid hormones were given.

In May 1994, after 3 weeks of augmented prednisone dose (30 mg/day), the sellar mass shrunk significantly as demonstrated by MRI (Fig. 4). There was minimal central suprasellar extension but no chiasmal damage. Clinically, there was no evidence of improvement of the pituitary dysfunction. The steroid dose was tapered off slowly, and was continued at a replacement dose of 7.5 mg/day. In December 1995 – two years after the onset of the disease – the patient was still on replacement therapy with 7.5 mg of prednisone, no signs of other disease (such as sarcoidosis, etc) were found and MRI of the pituitary was normal.
DISCUSSION

Lymphocytic hypophysitis is a rare disease of the pituitary gland, reported almost exclusively in women, and is often associated with pregnancy or with the 14 months after childbirth (9,11,15,16). Only a few male patients or women not in their peripregnancy period have been described (12,13,16,17). The disease usually presents with varying degrees of pituitary dysfunction and/or with symptoms of an expanding intrasellar mass. The natural history of this disease is unknown, as it is usually interrupted by surgical intervention for diagnosis, which is made histologically (6--9,11,13,18--22) or at autopsy (4,20).

The clinical presentation of lymphocytic hypophysitis (10,12,13,19--21) is insidious and nonspecific, copresenting with other autoimmune endocrinopathies in 30% of the patients (15). Pituitary autoantibodies have not been found in the majority of cases (1,9,13,16,20).

Our patient’s presenting symptoms were dramatic and included fever, headache, secondary amenorrhea, hypocortisolism and increased ESR. This presentation is compatible with an inflammatory process of the anterior hypophysis. Prolactin levels were mildly increased at this stage because of compression of the pituitary stalk by the inflammatory mass, as was described in previous cases (19,20,23). MRI with gadolinium showed a contrast enhancement of the pituitary mass (Fig. 3), a characteristic feature for lymphocytic hypophysitis (24). Treatment with corticosteroid-induced regression of the sellar mass (Fig. 2) ruled out an alternative diagnosis of pituitary adenoma and supported the diagnosis of lymphocytic hypophysitis (16), although dexamethasone therapy failed in one case of hypophysitis (25).

The majority of patients with hypophysitis do not recover from pituitary dysfunction, even after regression of the sellar mass, although partial or complete improvement has been reported in a few cases (1,2,23).

Granulomatous hypophysitis, another rare entity that presents with hypopituitarism, is accompanied by radiologic evidence of minimal sellar enlargement only (23) or the pituitary-hypothalamic lesions are involved together with other organ systems (26).

In our patient, an inflammatory process of the pituitary was suspected, and, since there was no evidence of a symptomatic expanding mass, the patient did not undergo surgical intervention and managed on medical treatment with corticosteroids. Thus, histologic confirmation of our clinical diagnosis was not possible. Only a few cases have been previously reported without pathologic studies (1,2,27). Our report supports these rare cases which indicate that a high index of clinical suspicion can lead to detection of this rare condition, thus allowing a therapeutic trial with corticoids which can prevent unnecessary surgery (28).

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