Brief report

Lymphocytic hypophysitis in a 43-year-old woman

G.M. Steup-Beekman, E.J.K. Zweers *

Department of Internal Medicine, Bronovo Hospital, Bronovolaan 5, 2597 AX The Hague, The Netherlands

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Abstract

A woman with sarcoidosis and primary hypothyroidism presented with partial hypopituitarism without pituitary gland enlargement. A clinical diagnosis of lymphocytic hypophysitis was established after exclusion of other possibilities, since a definitive diagnosis can only be made after histological studies. This rare form of chronic inflammation and destruction of the anterior pituitary gland is discussed. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

Lymphocytic hypophysitis is a rare inflammatory cause of hypopituitarism, occurring mainly during pregnancy and in the postpartum period. Since it was first described in 1962 by Goudie and Pinkerton [1], the suggested autoimmune pathogenesis has been supported by several authors [2–6]. Diagnosis, which is difficult because specific tests are not available, can only be confirmed by histological studies. A patient with autoimmune hypothyroidism and sarcoidosis and a clinical diagnosis of lymphocytic hypophysitis is described.

2. Case report

A 43-year-old woman was admitted to our hospital in December 1995 with reduced consciousness, malaise, anorexia, a weight loss of 9 kg and severe hypoglycaemia.

In 1991 sarcoidosis had been diagnosed on the basis of pulmonary interstitial abnormalities, hilar lymphadenopathy and elevated serum levels of angiotensin-converting enzyme (ACE). She took prednisone until 1994. No systemic manifestations of sarcoidosis have been seen since then. In April 1995 primary autoimmune hypothyroidism was diagnosed on the basis of positive thyroid autoantibody tests and high levels of thyroid-stimulating hormone (TSH). Thyroid hormone replacement was begun with normalisation of TSH levels. In June 1995 she was referred to the neurologist for Bell’s palsy. The patient used oral contraceptives and had grown-up children. Deliveries had been uncomplicated.

Physical examination revealed a cachectic woman; height 165 cm and weight 50 kg. Blood pressure was 130/90 mmHg and temperature 36.6°C. There were no signs of orthostatic hypotension or abnormal pigmentation. Physical examination was otherwise normal.

* Corresponding author. Tel.: +31-70-3124-681; Fax: +31-70-3262-706

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Laboratory determinations included a serum sodium level of 131 mmol/l, potassium 3.3 mmol/l and glucose 1.6 mmol/l. Because of the unexplained hypoglycaemia, cortisol was assessed at 08.00 h; the level was low: 84 nmol/l (normal 138–635 nmol/l). The cosyntropin test was abnormal with a basal cortisol of 75 nmol/l increasing to 130 nmol/l 30 min after intravenous administration of 250 μg synthetic adrenocorticotropic hormone (ACTH) (normal > 400 nmol/l). Assuming adrenal insufficiency, treatment with hydrocortisone (eventually 20 + 10 mg per day) and fludrocortisone (0.1 mg per day) was started. The patient improved markedly within 24 h. The level of ACTH before cosyntropin testing was low: 9 ng/l (normal 7–50 ng/l), suggesting secondary adrenal insufficiency. Fludrocortisone was discontinued. After discontinuation of oral contraceptives, the menstrual cycle resumed. Further hormonal studies were performed to evaluate anterior pituitary gland function. Prolactin levels were not detectable (normal 0–20 ng/ml). Growth hormone (GH) level was 0.9 mE/l (normal < 35 mE/l) and Somatomedin C level was 46 μg/ml (normal 144–252 μg/ml). Analysis thus showed hypopituitarism, including ACTH deficit and possibly insufficient GH production. A magnetic resonance imaging (MRI) scan revealed no pituitary enlargement and a normal median pituitary stalk (Fig. 1). There was no clinical evidence of systemic sarcoid activity; serum level of ACE was 52 nmol/min/ml (normal 23–67 nmol/min/ml), that of lysozyme 77% (normal 55–145%). Chest films showed no abnormalities. A clinical diagnosis of lymphocytic hypophysitis was made, supported by the recent diagnosis of autoimmune hypothyroidism. Antibodies against adrenal cortex were not detectable.

During follow-up the hydrocortisone doses were gradually reduced without symptoms. However, at 2.5 mg hydrocortisone daily, the patient deteriorated clinically with very low serum levels of cortisol (< 27.6 nmol/l) and ACTH (3 ng/l), confirming permanent incomplete hypopituitarism. Adequate hormone replacement was continued and her symptoms subsided.

3. Discussion

The symptoms and laboratory values for this 43-year-old patient were compatible with partial anterior pituitary gland insufficiency (insufficient ACTH and GH production).

Since the MRI scan of the pituitary gland was normal, pituitary adenoma was considered unlikely. Granulomatous hypophysitis due to sarcoidosis was suggested. Sarcoidosis, which has a predilection for the posterior pituitary gland, is associated with dia-

Fig. 1. Coronal (a) and Sagittal (b) T1 weighted MRI scans through the sella turcica showing a normal pituitary gland and stalk.
betes insipidus and hypopituitarism. Since this patient exhibited no signs of either posterior pituitary gland insufficiency or systemic sarcoid activity, sarcoidosis of the sella seemed unlikely. Sheehan’s syndrome (postpartum pituitary necrosis) should always be considered since it has been described even 15–20 years post partum [7]. However, this was believed unlikely because the patient did not have a history of complicated delivery with shock or hypotension. After excluding these causes of hypopituitarism and in view of the recently diagnosed autoimmune hypothyroidism, lymphocytic hypophysitis was suspected. This rare form of hypophysitis usually develops peripartum and is associated with autoimmune diseases such as Hashimoto’s thyroiditis [2–6]. Since the first report in 1962 [1] about 60 patients have been described; most cases were confirmed histologically by biopsy or at autopsy [8,9]. There were also a few postmenopausal women, nulliparae and men. Presenting symptoms are related to mass effects or adenohypophysial hypofunction. In 83–95% of all cases an enlarged pituitary mass is seen on the computed tomographic (CT) or MRI scan which is indistinguishable from a pituitary tumour [8,9]. It has been reported that depending on the phase of the disease, the pituitary gland can also be normal or small. Various combinations of hormone deficiencies occur, but ACTH-producing cells seem to be the most and FSH/LH-producing cells the least affected [2,10]. Prolactin levels are variable. Certain pituicytes seem to be more susceptible to cellular destruction. The posterior pituitary gland is usually unaffected, but cases of involvement have been reported [8,11]. The definitive diagnosis of lymphocytic hypophysitis is based on histological studies. Only in a minority of histologically proven cases was the diagnosis suspected preoperatively [8,12]. Pathological studies have demonstrated polyclonal infiltration of B and T cells [8]. In previous reports, 20–25% of patients had a history of other autoimmune diseases, usually primary hypothyroidism [7,8]. The strong association of the disease with pregnancy and the immunological changes occurring in this period are also suggestive of autoimmunogenesis. Antipituitary autoantibodies are not found consistently and are non-specific. The natural history is variable; complete pituitary dysfunction may develop. Since spontaneous normalisation of pituitary function and size has also been described, surgical intervention should be avoided unless symptoms of compression are present. Attempts can be made to withdraw hormonal substitution gradually 6 to 12 months after presentation [2]. Patients have also been reported to improve on glucocorticoid therapy alone [13].

In conclusion, lymphocytic hypophysitis does not only occur in patients with hypopituitarism and a sellar mass peripartum, it should also be considered when patients present with hypopituitarism and a history of autoimmune disease, regardless of the size of the pituitary gland. A clinical diagnosis is difficult, since a definitive diagnosis can only be made after histological studies.


References

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