LETTER TO THE EDITOR

Lymphocytic hypophysitis and autoimmune thyroid disease

Dear Sir,
Bayram *et al.* (1) reported a case of a patient with Graves' disease and lymphocytic hypophysitis (LIH) presenting with pituitary mass. Pituitary mass is usually but not invariably present (2, 5) 4 and in our experience we have had two cases of chronic thyroiditis and hypothyroidism who subsequently developed "idiopathic" hypopituitarism with atrophy of the pituitary gland (6).
The two patients (white females aged 70 and 72) had been affected for many years by chronic thyroiditis (ultrasonography with typical and marked hypoechoic pattern and antithyroperoxidase antibodies elevated) with hypothyroidism and they were treated with L-T4. They subsequently slowly developed symptoms and signs of hypoadrenalism (weight loss, anorexia). Basal and dynamic tests showed hypopituitarism: very low values of GH (<0.1 ng/ml) and IGF-1 (<10 ng/ml), low gonadotropin (rispectively LH<1.0 mU/ml and FSH 1.5 mU/ml, LH 1.2 mU/ml and FSH 2.2 mU/ml), low basal cortisol (1.7 and 2.2 µg/dl h 8:00) with impaired response to rapid ACTH test (net increase of cortisol between 4.5 and 6.1 µg/dl), normal response after prolonged ACTH iv infusion, and no response in ACTH and cortisol after CRH test, PRL was low (4-6 ng/ml). There was no sign of diabetes insipidus.
Magnetic resonance imaging showed a primary empty sella with a very thin pituitary residue on the bottom of the sellar floor. In the first patient antinuclear, antimithocondrial and anti-smooth muscle antibodies were present, while the second patient had a positive test for antibodies to gastric parietal cell.
In these patients we couldn't have a firm diagnosis of LIH since obviously we did not perform a surgical biopsy. However the diagnosis of LIH appeared highly suggestive for the association with chronic thyroiditis, for the other laboratory tests positive for autoimmunity and for no apparent reason which could explain the hypopytuitarysm.
In conclusion we agree with the authors that LIH should be born in mind in patients with autoimmune desease of the thyroid and we wish to remark the wide spectrum of clinical presentation of LIH, which shows surprisingly analogies with autoimmune thyroiditis since LIH may be associated with mass or atrophy of the pituitary gland, it can occur in post-partum period and it may be transient.

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This letter has been sent to the authors cited (Bayram et al.*) whose reply follows:*

Dear Sir,
I have read, with interest, the letter of D. Barbaro and G. Loni. They present two patients with chronic thyroiditis and hypothyroidism who subsequently developed "idiopathic" hypopituitarism with at-

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rophy of the pituitary gland and they agree with us that lympocytic hypophysitis should be born in mind in patients with autoimmune diseases of the thyroid. The authors give no information about thyroid function tests of the patients. For this reason, it is not clear whether the patients had primary or secondary hypothyroidism before hypopituitarism developed.

In my opinion, the most interesting issue raised by the authors is about the relation between lymphocytic hypophysitis and empty sella. The patients slowly developed panhypopituitarism and MRI showed empty sella which has been suggested as primary empty sella. But, it is difficult to say that empty sella is primary or secondary in origin by MRI alone in these patients. On the other hand, primary empty sella is not a reasonable radiologic diagnosis for a patient with presumed lymphocytic hypophysitis. I think that secondary empty sella is a more likely diagnosis.

What about the causes of the empty sella in this condition? Three possibilities may be suggested;

1) If the patients had primary hypothyroidism, whatever its origin is, it would be expected that pituitary gland may be enlarged because of thyrotroph and/or lactotroph cell hyperplasia and thyroxine replacement therapy may result in empty sella, as we have previously descrebed (1).

2) If the patients had secondary hypothyroidism, Sheehan's syndrome, which occurs as a result of ischemic pituitary necrosis due to severe post-partum hemorrhage and is characterized by various degrees of hypopituitarism and empty sella, should be taken account in the differential diagnosis. The authors give no positive medical history (post-partum hemorrhage) suggesting Sheehan's syndrome. Some autoantibodies including antinuclear, antimithocondrial, anti-smooth muscle and gastric parietal cella have been found as positive in the patients and this finding is in favor of autoimmune etiology. But definitive diagnosis of lymphocytic hypophysitis without surgical biopsy which may be unsuccessful in the presence of atrophic pituitary gland is problematic.

3) The third possibility is empty sella developed as a result of lymphocytic hypophysitis. Although more than 100 patients with lymphocytic hypophysitis were reported in the literature, there is only little information about the relationship between lymphocytic hypophysitis and empty sella. Okada *et al.* reported a case of partial hypopituitarism with empty sella following normal course of pregnancy and delivery (2). Nishiyama *et al.* also pointed out that there may be a possible relation between empty sella and lymphocytic hypophysitis (3). To suggest that empty sella may be a final outcome in patients with lymphocytic hypophysitis, prospective follow-up of the patients is necessary.

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