J. Endocrinol. Invest. 25: 93-94, 2002

LETTER TO THE EDITOR

Lymphocytic hypophysitis and diabetes insipidus in non-pregnant women

We have read with interest the report by Durán Martínez *et al.* in the March 2001 issue of the *Journal of Endocrinological Investigation* (1) concerning the development of diabetes insipidus in a non-pregnant woman with lymphocytic hypophysitis. They reported a 36-year-old-woman with bilateral hemianopia, diabetes insipidus, hypopituitarism, and hyperprolactinemia. Magnetic resonance imaging (MRI) showed an intrasellar mass with supra-and retrosellar extension with an absence of hyperintense signal of the posterior lobe. Histologic examination of the pituitary gland revealed an inflammatory infiltrate composed of lymphocytes and plasma cells. The authors stated that this is the 11th reported case of lymphocytic hypophysitis with diabetes insipidus not related to pregnancy. Last year we had the opportunity to report the case of a menopausal woman presenting with diabetes insipidus as a primary clinical manifestation of lymphocytic hypophysitis (2). She was a 53-year-old woman referred to us because of polyuria, nocturia, and polydipsia. The diagnosis of diabetes insipidus was confirmed with the water deprivation test and subsequent arginine vasopressin (AVP) administration. The endocrinologic evaluation of the anterior hypophyseal function showed only a GH deficiency and a modest hyperprolactinemia. MRI study showed homogeneous enlargement of the whole pituitary gland, without evidence of supra-or parasellar extension, absence of hyperintense signal of the neurohypophysis and a thickened pituitary stalk. Histologic study of the pituitary revealed anterior pituitary cells with diffuse infiltration of lymphocytes with no evidence of granulomatous or giant cell disease.

It must be emphasized that the majority of these cases with this triple association have been observed in the Japanese population (3). In our country, Spain, another non-pregnant woman with lymphocytic hypophysitis and diabetes insipidus had been previously reported (4). She was a 25 year-old woman with a one-year history of amenorrhea and polyuria. Partial central diabetes insipidus was confirmed by Miller's test. Evaluation of the anterior pituitary function showed hypopituitarism with hyperprolactinemia. MRI revealed an intrasellar mass with suprasellar extension, thickened pituitary stalk and minimal neurohypophyseal signal. Pathological examination of the pituitary revealed abundant lymphocytic infiltrate, with no giant cells or granulomas.

Lymphocytic hypophysitis is an infrequent inflammatory disorder of the pituitary gland. There have been three clinical forms of this described entity (Table 1). The first one is the classical lymphocytic adenohypophysitis, in which the lymphocytic infiltration is limited to the adenohypophysis (5). This form occurs in young women and is predominantly related to pregnancy or delivery. Clinically, it usually presents with partial or panhypopituitarism. Central diabetes insipidus has not been considered a distinctive clinical entity of this disorder. Morphological imaging shows a large pituitary mass. The second form of lymphocytic hypophysitis, lymphocytic infundibuloneurohypophysitis, is caused by lymphocytic infiltration of the posterior lobe, pituitary stalk, and/or hypothalamus (6). It has been considered as a common cause of what was previously considered to be idiopathic diabetes insipidus. MRI study shows thickening of the pituitary stalk, enlargement of the neurohypophysis, and/or loss of the normal hyperintense signal of the neurohypophysis with normal anterior pituitary. The third form of lymphocytic hypophysitis has been named lymphocytic infundibulohypophysitis with diabetes insipidus (3). In this case the lymphocytic infiltration affects both anterior and posterior lobes and extends to the pituitary stalk and, sometimes, to the hypothalamus. Lymphocytic infundibulohypophysitis is not usually related to pregnancy or delivery and it has also been described in men. Apart from diabetes insipidus, adenohypophyseal function can also be affected. MRI study shows similar morphological characteristics of lymphocytic adenohypophysitis and lymphocytic infundibuloneurohypophysitis. The absence of relation to pregnancy or postpartum period, the association of diabetes insipidus with adenohypophyseal dysfunction, and the mor-

Accept: June 1, 2001.

Table 1- Main clinical and radiological features of the clinical forms of lymphocytic hypophysitis.

	LAH	LIN	LIH
Affected population	Young women	Menopausal women and men	Menopausal women and men
Relationship with pregnancy or puerperium	Yes	No	No
Anterior pituitary function	Partial or total hypopituitarism	Usually normal or blunted GH response to insulin	Partial or total hypopituitarism
Diabetes Insipidus	No	Yes	Yes
Magnetic resonance imaging	Large pituitary mass	Thickened pituitary stalk, absence of hyperintense signal of posterior lobe	Similar findings in both LAH and LIN
Lymphocytic Infiltration	Anterior lobe	Posterior lobe, pituitary stalk, and/or hypothalamus	Anterior and posterior lobes, pituitary stalk, and/or hypothalamus

LAH: lymphocytic adenohypophysitis; LIN: lymphocytic infundibuloneurohypophysitis; LIH: lymphocytic infundibulohypophysitis.

phologic and histological findings indicate that reported clinical cases are consistent with new cases of lymphocytic infundibulohypophysitis with diabetes insipidus.

P. Iglesias* and
J. J. Díez**

Departments of Endocrinology,
*Hospital General de Segovia and
**Hospital Ramón y Cajal,
Madrid, Spain

REFERENCES

1. Durán Martínez M., Santonja C., Pavón de Paz I., Monereo Megías S.
Lymphocytic hypophysitis: Report of an unusual case of a rare disorder.
J. Endocrinol. Invest. 2001, *24*: 190-193.
2. Iglesias P., Díez J.J.
Diabetes insipidus as a primary clinical manifestation of lymphocytic hypophysitis in a postmenopausal woman.
Endocrinologist 2000, *10*: 127-130.
3. Miyagi K., Shingaki T., Ito K., Koga H., Mekaru S., Kinjo T., Arakaki Y., Nakasone S.
Lymphocytic infundibulo-hypophysitis with diabetes insipidus as a new clinical entity: a case report and review of the literature.
No Shinkei Geka 1997, *25*: 169-175.
4. Paja M., Estrada J., Ojeda A., Ramón y Cajal S., García-Uría J., Lucas T.
Lymphocytic hypophysitis causing hypopituitarism and diabetes insipidus, and associated with autoimmune thyroiditis, in non-pregnant woman.
Postgrad. Med. J. 1994, *70*: 220-224.
5. Cosman F., Post K.D., Holub D.A., Wardlaw S.L.
Lymphocytic hypophysitis. Report of 3 new cases and review of the literature.
Medicine (Baltimore) 1989, *68*: 240-256.
6. Imura H., Nakao K., Shimatsu A., Ogawa Y., Sando T., Fujisawa I., Yamabe H.
Lymphocytic infundibuloneurohypophysitis as a cause of central diabetes insipidus.
N. Engl. J. Med.,1993, *329*: 683-689.