LYMPHOCYTIC INFUNDIBULOHYPOPHYSISITIS PRESENTING IN THE POSTPARTUM PERIOD: CASE REPORT

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Lymphocytic adenohypophysitis is considered to be an autoimmune disease predominantly occurring in women during pregnancy or during the postpartum period [1,5,6,13]. Cases unrelated to pregnancy and occurrence in male patients have also been reported [4,12,14,25]. This disorder is characterised by lymphocytic infiltration and destruction of the anterior pituitary gland. Patients usually present with partial or complete hypopituitarism [5,6].

Lymphocytic hypophysitis as a cause of central diabetes insipidus, is rare; it was first suggested by Imura et al. in 1993 [10].

This so-called lymphocytic infundibuloneurohypophysitis is now being regarded as the etiology of idiopathic central diabetes insipidus and should not be confused with the formerly described lymphocytic adenohypophysitis. MRI of the brain shows a normal anterior pituitary gland but clear thickening of the neurohypophysis or stalk with variable enhancement. Neuroradiologic involvement of the infundibulum is less common [10,13].

The natural course of this disorder is thought to progress from inflammatory enlargement of the pituitary stalk or posterior pituitary gland to subsequent fibrosis and atrophy [2,5,10]. No cases of spontaneous recovery have been reported. These findings support the theory of an autoimmune disorder. A definite diagnosis can only be made by biopsy and pathologic examination [5]. We present a case of lymphocytic infundibuloneurohypophysitis presenting with central diabetes insipidus in a woman in the postpartum period with clear radiologic and histologic findings.
### Results of Endocrine Tests during Follow-up

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<tr>
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### CASE REPORT

This 32-year-old Caucasian woman presented 6 months after a fourth uncomplicated delivery with important polyuria and polydipsia. The patient had no other medical problems. She had always had regular menstrual periods and had had four normal uncomplicated pregnancies. One of her children suffered a congenital CMV infection with mental retardation.

In June 1993, after a 3-month period of breastfeeding her fourth child, the patient had galactorrhea that was treated successfully with bromocryptine for 2 months. Menses returned on a regular basis 6 weeks after delivery.

In October 1993 the patient presented with polyuria and polydipsia. Physical examination was normal. During hospitalization urinary production of 9–10 L/24 hours was recorded under restricted intake of 1800 mL of fluid/24 hours. A fluid deprivation test was performed and proved positive showing plasma osmolality of 304 mosm/kg H2O, urine osmolality of 166 mosm/kg H2O, and serum sodium concentration of 151 mmol/L. No other endocrine abnormalities were found (Table 1).

Pulmonary investigation (including X ray of the chest, CT of the chest, lung diffusion tests, and angiotensin-converting-enzyme concentration) was normal. MRI of the brain showed a slight thickening of the pituitary stalk with inhomogeneous enhancement with gadolinium.

The patient was treated with vasopressin 3 × 0.05 mg/d intranasally. Four months later the patient complained of progressive bifrontal headache. She was readmitted for observation. A raised prolactinemia with suppressed FSH, LH, and somatomedine C levels were found. Growth hormone, cortisol, and ACTH levels were normal (Table 1). Pulmonary investigation was negative and lumbar puncture with CSF analysis was normal. A new MRI of the brain showed a clear thickening of the infundibulum with homogeneous gadolinium enhancement extending into the hypothalamic region (Figure 1).

A differential diagnosis was made of hypothalamic glioma, optic nerve glioma, pituitary adenoma, histiocytosis, sarcoidosis, or other granulomatous mass, and hypophysitis.

A right pterional craniotomy was performed for exploration and biopsy of the thickened infundibulum. Frozen section examination showed granulomatous tissue. Light microscopic examination revealed widespread lymphocytic infiltration with islets of fibrosis and small rests of normal infundibular tissue (Figure 2).

There was an uncomplicated postoperative recovery. The patient was given glucocorticoid substitution for 2 months for safety. As soon as maintenance of adrenal function was established, glucocorticoids were discontinued. Vasopressin administration was obviously still required. After surgery the patient was found to have moderate hy-
perprolactinemia with decreased estrogen and progestogen levels and borderline low gonadotrophic hormones. There was a normal response to LRH. The latter was treated with estrogen substitution.

Four months after surgery MRI of the brain showed a marked decrease in the thickening of the pituitary stalk and infundibulum. There was still a homogeneous enhancement of these structures. Eight months after the diagnosis the endocrine control revealed the known moderate hyperprolactinemia and a slightly depressed plasma growth hormone concentration (Table 1). The response to growth hormone-releasing hormone was normal but subnormal to the insulin-induced hypoglycemia. New MRI of the brain showed a further decrease of the thickening of the infundibulum with poor enhancement (Figure 3).

At this time the patient is taking desmopressin and estrogen substitution. The MRI of the brain with a small volume increase of infundibulum and pituitary stalk gland remained unchanged 1 year after diagnosis.

**DISCUSSION**

Lymphocytic adenohypophysitis is a rare disorder. Since the first case reported by Goudie and Pinkerton in 1962 [7] about 60 cases have been described in the literature [6]. All except six were women [8,12,17,18,25]. Most of these patients presented during pregnancy or immediately postpartum [5]. Only 13 cases unrelated to pregnancy were reported [4,6,26].

There is an involvement of the anterior pituitary gland with consequent isolated or combined hypoadrenalism, hypothyroidism, and hypogonadism. Spontaneous recovery has been reported [3,15]. Hyperprolactinemia is a less common feature and is explained by stalk compression by pituitary mass or residual lactotroph hyperplasia from recent pregnancy [4,5].

Diabetes insipidus in lymphocytic adenohypophysitis has only been reported in two cases and always presented in combination with anterior pituitary gland dysfunction [17,22,26]. Isolated cen-
Lymphocytic infundibulohypophysitis in relation to lymphocytic infiltration of the pituitary stalk or infundibulum is rare [10,11,21]. This so-called lymphocytic infundibuloneurohypophysitis as a cause of central diabetes insipidus was first proposed by Imura et al. in 1993 [10]. This author presented 17 cases of which only two had a biopsy of the pituitary stalk or neurohypophysis with proven lymphocytic infiltration.

In the literature we can find only three additional cases of lymphocytic infundibuloneurohypophysitis [9,11,21]. None of these cases (five histologically proven, 15 with typical endocrine presentation and clear MRI findings) presented in women in the postpartum period.

In view of the radiologic and clinical evolution, as well as the histologic findings, it is thought to be an autoimmune disorder [16,19,23].

Our case also presents with an isolated diabetes insipidus suggesting a dysfunction of the hypothalamic neurohypophysial system. This suggestion is supported by the neuroradiologic findings on the MRI of the brain showing an enlargement of the pituitary stalk and infundibulum, with abnormal enhancement extending into the hypothalamus. The lesion has isointense characteristics on T1 weighted images [10,13].

Endocrine tests clearly show a central type of diabetes insipidus with a normal anterior pituitary gland function during a follow-up period of more than 1 year. We only found a moderate and probably postoperative hyperprolactinemia with secondary gonadal insufficiency. The plasma growth hormone response to growth hormone-releasing factor is normal but there is a decreased growth hormone response to insulin-induced hypoglycemia. Identical findings have been reported by Imura et al. [10].

Since only a few cases have been described, diagnosis can be difficult [24]. These lesions have to be differentiated from other mass lesions in the hypothalamic and pituitary stalk region such as sarcoidosis or hypothalamic glioma.

Although the clinical and radiologic picture strongly matched Imura’s findings, we preferred a clear and definite diagnosis by biopsy through craniotomy. The histologic examination showed widespread lymphocytic infiltration with islets of fibrosis and histiocytes in between small rests of normal infundibular tissue. The lymphocytic infiltration was dominated by T lymphocytes, as is usually the case. We found a low CD4/CD8 fraction, the importance of which is still unclear. Antipituitary or antithyroid antibodies were not found [16].

Treatment should consist of close follow-up and hormonal substitution. Since the disorder is thought to be an autoimmune disease, corticoste-

roid therapy could be suggested as it was for the more common lymphocytic adenohypophysitis, but there are no data to support the efficacy of such treatment [20].

The natural history of this disease is probably self-limiting but is still unclear. We present a case of histologically proven lymphocytic infundibulohypophysitis with a clear clinical and radiologic picture. In view of the autoimmune pathophysiology the occurrence in the postpartum period is not surprising even though it has not been reported before.

Lymphocytic infundibulohypophysitis must be differentiated from the more common lymphocytic adenohypophysitis. Our data support Imura’s findings and emphasize the autoimmune character of this disorder.

REFERENCES

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COMMENTARY

The authors present a most interesting case of a patient who developed lymphocytic infiltration of the pituitary stalk very similar to the more common lymphocytic hypophysitis that affects the anterior pituitary gland and is fairly common in women in the postpartum period. This particular specific focal inflammatory condition primarily affecting the pituitary stalk is quite unusual, although the pathologic manifestations seem to be very similar to those that occur with hypophysitis. As expected, the patient presented with diabetes insipidus and responded nicely to treatment with DDAVP. The illustrations are quite clear in demonstrating a lesion that affects the pituitary stalk in the area of the tuber cinereum, and the diagnosis was clearly proven by the craniotomy and biopsy. It is interesting that the disease ran a benign course and that the patient apparently does not require cortical or thyroid replacement medication. The clearly-described imaging and clinical features of this case might be important in avoiding surgery in future cases that present in a similar fashion.

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IF HELP AND SALVATION ARE TO COME, THEY CAN ONLY COME FROM THE CHILDREN, FOR THE CHILDREN ARE THE MAKERS OF MEN.

MARIA MONTESSORI (1870–1952)
"THE ABSORBENT MIND," CH. 1