CASE REPORT

Lymphocytic infundibuloneurohypophysitis presenting as diabetes insipidus in a man

N. Kamel*, Ş. Dağcı Ilgin*, D. Çorapçıoğlu*, H. Deda**, and S. Güllü*
*Department of Endocrinology and Metabolic Diseases, **Department of Neurosurgery, Ankara University, Medical School, Ankara, Turkey

ABSTRACT. We report a patient with diabetes insipidus, whose sella magnetic resonance imaging revealed a normal hypophysis with a focal nodular thickening of the infundibulum and lack of hyperintense signal of the normal neurohypophysis. The histopathologic examination of the lesion showed a lymphoplasmacytic, predominantly lymphocytic, infiltration. A diagnosis of lymphocytic infundibuloneurohypophysitis was made, by the exclusion of other infiltrative, granulomatous diseases.

INTRODUCTION

Central diabetes insipidus (DI) is a chronic disorder, characterized by polyuria and polydipsia due to vasopressin deficiency. The disorder may be familial, idiopathic or secondary to hypothalamic or pituitary disorders (1). Idiopathic DI which is speculated to be an autoimmune disorder, accounts for 10-30 percent of central DI cases (1, 2). Besides the reported few patients with lymphocytic (adenohypophysitis who also had DI (1, 3, 4), only a few reports have described patients with lymphocytic infiltration confined to the hypothalamo-neurohypophysial system (1, 5). Apart from the abnormalities of thickening of the stalk and/or enlargement of the neurohypophysis, loss of hyperintense signal on T1-weighted images of magnetic resonance imaging (MRI) was also described in the lymphocytic infundibuloneurohypophysitis (LI) patients who had had DI for less than two years. During follow-up while the abnormalities disappear, the absence of the normal hyperintense signal precipitates (1). Here we report a case of LI, presenting as a nodular infundibular lesion, producing DI in a man. This case is interesting because of presenting with an isolated nodular infundibular enlargement which could be confused with the other masses of this region.

CASE REPORT

A 27-year-old man was admitted to our hospital with a two months history of polydipsia, polyuria - up to 8 litres a day - and fatigue. He had had a diagnosis of major depression three years ago and he had used amitriptyline and lithium for two years but stopped the medication over six months before the presenting complaints. There was no history of head trauma, operation or family history of DI. On physical examination, his blood pressure was 130/90 mm Hg, pulse was 82 beats/min and regular. He was obese with a BMI of 35.6 kg/m². His visual field evaluation, done by a campimeter, was normal. No abnormality could be found on other systemic examinations. He had no lymphadenopathies.

Laboratory evaluation demonstrated a normal white blood cell count. Hematocrit was 48% and erythrocyte sedimentation rate was 6 mm/hour. Besides hypernatremia (158 mEq/L), whole biochemical tests, including calcium, phosphorus, alkaline phosphatase were found to be normal. His ppo was 10 mm. His urine volume was 10.5 l/day and plasma - urine osmolalities were 302.8 and 52.7 mOsm/kg, respectively. He had elevated prolactin levels (on two measurements 22.3 ng/ml and 48.0 ng/ml). His free T3, free T4 and TSH levels were normal and he was negative for thyroid antibodies (anti microsomal antibody and antithyroglobulin antibody). Other endocrinological evaluations revealed normal levels of adrenocorticotropic hormone, plasma cortisol, growth hormone, follicle stimulating hormone, luteinizing hormone, free and

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Correspondence: Dr. Şen Dağcı Ilgin, Yüksek Caddesi Kışla Sokak No: 29/14, Yenişehir, Ankara 06420, Turkey.
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total testosterone (Table 1). Partial hypopituitarism was excluded by means of insulin-induced hypoglycemia testing with adequate plasma cortisol and growth hormone responses. Thyrotropin releasing hormone stimulation test responses were also normal.

On water deprivation test, plasma osmolality elevated from 303 to 320 mOsm/kg with a simultaneous urine osmolality of 73 at the beginning and 123.2 mOsm/kg at the end of the test. Urine osmolality showed a further elevation to 503 mOsm/kg while plasma osmolality was 321.5 mOsm/kg, after intranasal administration of 20 μg desmopressin, indicating a partial central DI.

Radiological studies
His plain lateral sella turcica and chest roentgenograms were normal. T1-weighted magnetic resonance imaging (MRI) revealed a focal nodular thickening of infundibulum and a normal hypophysis. Loss of “bright spot” signal intensity was observed. The nodular lesion enhanced after IV gadolinium administration (Fig. 1).

Operation
The patient received desmopressin acetate 20 μg/day, bid via intranasal route before operation by which daily urine output decreased to 1.5 l. Because the patient was thought to have a tumor of the stalk region, he underwent neuromicrosurgery. A rightpterional craniotomy was performed under general endotracheal anesthesia. The pituitary stalk was thicker than normal and the mid part had a nodular appearance. Surrounding arachnoidal structures of the pituitary stalk were normal. The nodular mass was hard and adherent to the surrounding tissue but it was dissected from other structures of the pituitary stalk. The 3x3x4 mm gray-white mass was excised, protecting the pituitary stalk.

Postoperative course
The patient’s postoperative course was uneventful and there was no neurological deficit. His diabetes insipidus persisted after operation, but no anterior pituitary hormonal deficiency developed. His postoperative hormonal profile is given in Table 1.

![Fig. 1 - Coronal view of MRI of the case. Focal nodular thickening of the stalk and a normal hypophysis, enhanced after IV gadolinium administration.](image-url)
Pathological and immunohistochemical studies

By light microscopy, hematoxylin and eosin stained sections exhibited a diffuse lymphoplasmocytic (mainly lymphocytic) infiltration. These cells gathered particularly around the vessels. There were neither diffuse nor compact granulomas (especially suggest to sarcoidosis) or giant cells. There was no histological evidence of a neoplasm.

Immunohistochemical analysis was also performed. The inflammatory cells were polyclonal populations of T and B cells with positivity for CD45RO (80-85%) (Fig. 2) and CD20 (15-20%), respectively. The specimen did not contain S-100 protein of Langerhans cells. There was no evidence of caseous necrosis or granulomas. No meningopithelial components could be seen.

The patient’s outpatient course was good and he is being followed-up on desmopressin acetate treatment, 20 μg/day, for 17 months. There is no recurrence of the lesion on control MR images.

DISCUSSION

Lymphocytic (adenohypophysial) hypophysitis (LHy) is a rare inflammatory disease of the pituitary. It commonly affects women but also can be seen in men with a female to male ratio of 8:5:1, 7:1 in different series. The clinical presentation of LHy includes four categories of symptoms and signs (5):

1. Mass effects, such as headaches and visual field impairments.
2. Partial or total adenohypophysial hypofunction
3. Hyperprolactinemia
4. Neurohypophysial involvement manifesting as DI.

The pathogenesis of LHy and LI are both thought to be autoimmune because about 25% of affected patients have either thyroiditis, adrenalitis, pernicious anemia, parathyroiditis or retroperitoneal fibrosis (5-9).

Specific subtypes of the major histocompatibility complex (MHC) human leukocyte antigens (HLA) can be correlated with a number of autoimmune endocrine disorders, such as A29, B8, Bw35, DR1, DR5, DR3, DRw53, DRw57, DQw2. Our patient’s major histocompatibility complex - human leukocyte antigen (HLA) types were A1, B35, B7, Bw4, Bw6, Cw4, DR3, DR1, DR53, DQw1, DQw2.

Imura et al. in 1993, reported 17 central DI cases with LI (1). Only two of them revealed prominent pituitary stalk thickening while five patients had mild stalk enlargement. In 1995 Thodou et al., described the clinicopathological features of 16 patients with LH (5). One of them (Case 2) had normal sella with stalk lesion. She had DI and hyperprolactinemia, probably attributable to stalk effect. Reported lymphocytic infiltration cases limited to stalk as stalk thickening are very few. Our case is interesting as he did not show diffuse thickening of the stalk but nodular infundibular enlargement, mimicking tumoral involvement on MRI.

The differential diagnosis of a thickened pituitary infundibulum includes Langerhans-cell histiocytosis, sarcoidosis, tuberculosis, germinoma, infiltrations from pituitary adenoma, hypothalamic glioma or teratoma and mass lesions such as craniopharyngioma, Rathke pouch cyst, tumors of the pituitary infundibulum and metastasis (5, 10). Our patient’s pathological examination showed predominancy of lymphocytic infiltration with some plasma cells. Tuberculosis and sarcoidosis were ruled out by the absence of granuloma, presence of normal chest x-ray and pdd of 10 mm, indicating lack of anergy. His Kweim test result was negative. He had no signs of histiocytosis in other tissues and histopathologically the lesion was lacking of histiocytic infiltration and the specimen did not contain S-100 protein. So Langerhans-cell histiocytosis was ruled out. In addition, no tumor formation and no cellular components of the above mentioned malignancies could be detected in biopsy specimens, LI was diagnosed.

The pathological diagnosis in the present case was made by surgical intervention. Since LI can simulate tumoral processes as in our case, in order to avoid unnecessary major operations, stereotactic biopsy of suspected lesions should be considered in such patients. Evaluation of the obtained material by both light microscopy and immunocytochemical staining will make the differential diagnosis accurate.
In conclusion, nodular enlargement of the stalk detected by computerized tomography or MRI scans leading to central DI can be caused by LI. Our case is interesting because of presenting with an isolated nodular infundibular enlargement which could be confused with the other masses, especially tumors of this region. We suggest that LI should be kept in mind in the differential diagnosis of pituitary region masses.

REFERENCES


