Bilateral Dacryoadenitis Complicated by Lymphocytic Hypophysitis

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Abstract: Three patients developed dacryoadenitis (DA) or lymphocytic pneumonitis before the diagnosis of lymphocytic hypophysitis (LyH). There were two previous reports of concurrence of DA and LyH. Our patients add support to the idea that DA and LyH are manifestations of a systemic autoimmune disease. We suggest that the discovery of DA should prompt imaging and endocrine investigation of LyH.

(Dacryoadenitis (DA) is one of most common anatomic subtypes of idiopathic orbital inflammation (IOI) (1). Patients typically present with a painful, firm, upper temporal orbital mass, often associated with ptosis. The differential diagnosis of this presentation requires the exclusion of systemic diseases such as sarcoidosis and Sjögren syndrome, as well as lymphoma and primary lacrimal gland tumor (2).

Lymphocytic hypophysitis (LyH), also called autoimmune hypophysitis (AH), was first described in 1962 and is believed to have an autoimmune basis (3). The defining pathologic feature is infiltration of the pituitary gland by lymphocytes, particularly around the acini and ducts. Although LyH is usually considered a primary process, it may develop in response to viral, bacterial, or fungal infection or in Langerhans cell histiocytosis, sarcoidosis, Wegener granulomatosis, Crohn disease, Takayasu disease, or ruptured cysts (4).

About 400 cases of LyH have been reported (5) and can be divided into three subtypes: lymphocytic adenohypophysitis (LAH), lymphocytic infundibuloneurohypophysitis (LINH), and lymphocytic panhypophysitis (LPH). LAH is more common in women and is associated with pregnancy and the postpartum period. LINH appears to show no gender bias, and LPH is slightly more common in women. Neither LINH nor LPH shows an association with pregnancy.

The most common ophthalmic manifestations of LyH are visual field defects and decreased visual acuity due to compression of the optic chiasm by the upwardly expanding pituitary mass. On rare occasions, patients develop diplopia because of the lateral expansion of the process into the cavernous sinus, with compression of the third, fourth, or sixth cranial nerves and subsequent ocular misalignment (6–8).

There is a single case report of DA and LyH coexisting in the same patient (9), but the LyH was diagnosed before the DA. We report 3 patients who developed DA or lymphocytic pneumonitis before the diagnosis of LyH.

Case Reports

Case 1

A 50-year-old man presented with loss of libido for 1 year and polydipsia and polyuria for 3 months. He had been found to have enlarged lacrimal glands bilaterally 2 years earlier. Our examination confirmed enlarged lacrimal glands on both sides. Otherwise the ophthalmic examination was normal.

MRI disclosed bilateral lacrimal gland enlargement (Fig. 1A), but also that the pituitary gland was symmetrically enlarged and compressing the optic chiasm. The pituitary stalk was obviously thickened, measuring 7mm at the level of the median eminence of the hypothalamus. It appeared to enhance pathologically (Fig. 1B).

The levels of triiodothyronine (T3), thyroxine T4, free thyroxine (FT4), thyroid-stimulating hormone (TSH), luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estradiol (E2) were lower than normal.

Stimulation with gonadotropin-releasing hormone (GnRH) (gonadotropin secretion test) or with insulin (hypoglycemia stimulation test) showed that LH and FSH
increased by less than 20% of the expected amounts, so we concluded that the patient’s pituitary gland had poor hormonal reserve. The results of the adrenocorticotropic hormone (ACTH) stimulation test were normal.

Laboratory tests detected no signs of vasculitis. Results of a chest x-ray were normal. All hematologic parameters were within normal limits, including the protein electrophoretic profile and immunoglobulin fraction analysis. Serologically there was no evidence for human immunodeficiency virus, syphilis, or viral hepatitis type B.

Lacrimal gland biopsy showed that the acini were infiltrated with lymphocytes (Fig. 2A). Transsphenoidal biopsy of the pituitary gland showed lymphocytes and scattered monocytes and plasma cells (Fig. 2B).

The patient was treated with 600 mg/day methylprednisone orally for 3 days, following by a gradual tapering. The appearance of the orbit gradually returned to normal. The patient showed no recurrence within a 4-year follow-up period.

**Case 2**

A 55-year-old woman consulted us with an 8-year history of persistently dry eyes and swollen lacrimal glands, coupled with polydipsia and polyuria for 2 months. Seven years earlier, she had reported that both lacrimal glands had become swollen with no obvious predisposing cause. She had been treated with an initial dose of 60 mg/day prednisone slowly tapered over a 3-month period.

Three years before her visit to us, she had received a diagnosis of "pseudotumor of the lacrimal glands" and had undergone bilateral lacrimal sac resections elsewhere. Two years later, she developed recurrent polydipsia and polyuria and swollen parotid glands without pain and fever.

Our ophthalmic examination disclosed bilateral proptosis and symmetrical enlargement of the lacrimal glands. We diagnosed Sjögren syndrome and prescribed 30 mg/day prednisone, 400 mg/day hydroxychloroquine, and 10 mg/week methotrexate.

Ultrasound showed that both parotid glands were diffusely swollen. A labial gland biopsy showed lymphocytic and plasmacytic infiltration. The histological findings were consistent with Sjögren syndrome. Biopsy of the lacrimal gland showed marked lymphocytic infiltration (Fig. 3).

Brain MRI showed a symmetrically enlarged pituitary gland and thickened stalk (Fig. 4). Antinuclear

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**FIG. 1.** Case 1. Postcontrast axial MRI (A) shows enlarged lacrimal glands bilaterally (oblique arrows). Axial (A) and coronal views (B) show an enlarged pituitary stalk (vertical arrows).

**FIG. 2.** Case 1. A. Lacrimal gland biopsy shows lymphocytic infiltration between the acini. B. Pituitary gland biopsy shows infiltration mostly of lymphocytes with scattered mononuclear and plasma cells.

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antibodies (ANA), double-stranded DNA, RNA, SM, SSA, SSB, Scl-70, JO-1, and C-reactive protein levels (CRP) were normal, suggesting that there was no systemic rheumatologic condition. The results of the GnRH-stimulated gonadotropin secretion test were normal. However, GH, ACTH, and prolactin (PRL) reserve levels were deficient as tested by insulin-induced hypoglycemic (IIH) stimulated GH and ACTH secretion, which suggested that pituitary function was poor.

We prescribed 0.1 mg desmopressin acetate twice daily to treat the diabetes insipidus, as well as 600 mg/day methylprednisolone orally for 3 days, followed by gradual tapering, and 0.6 g/2 weeks cyclophosphamide and 200 mg/day hydroxychloroquine sulfate. The patient experienced no recurrence of polydipsia and polyuria within a 1-year follow-up period.

Case 3

A 56-year-old man presented with acute hearing loss and malaise. There were no associated visual disturbances, headaches, or vomiting. However, the patient gave a history of lymphocytic interstitial pneumonia for more than 1 year and had been treated intravenously with 200 mg/day methylprednisolone for 3 days and orally with 100 mg/day for 3 days and then 30 mg/day followed by gradual tapering (half-dose per 10 days and a maintenance dose of 4 mg/day for 1 year). Our ophthalmic examination showed right lacrimal gland enlargement without other abnormalities.

Brain and orbit MRI confirmed the right lacrimal gland enlargement (Fig. 5) and symmetrical enlargement of the pituitary gland to 1.2 cm in height and thickening of its...
stalk without displacement (Fig. 6). Thyroid function test results were normal.

Right dacryoadenectomy showed normal acini that were heavily infiltrated with lymphocytes and plasma cells (Fig. 7).

Treatment with 64 mg/day methylprednisolone for 6 months brought pituitary function under control.

**DISCUSSION**

We have reported 3 patients in whom the diagnosis of DA or lymphocytic pneumonitis preceded the diagnosis of LyH. Our Cases 1 and 2 showed a pan pituitary deficiency. Most of the anterior pituitary hormones were deficient, namely TSH, GnRH, and GH in Case 1, and ACTH, TSH, GnRH, GH, and PRL in Case 2. In Case 1, a PRL deficiency manifested itself in the postpartum period as an inability to lactate.

Joussen et al. (9) reported a case of LyH associated with lymphocytic DA in 1999. The patient reported in that case study differed from our Cases 1 and 2 in 2 ways. First, she developed DA 1 year after trans-sphenoidal hypophysectomy. Second, she had an acutely swollen lacrimal gland only on one side. Our Cases 1 and 2 had swollen lacrimal glands for several years and had bilateral rather than unilateral DA. In our Case 3, DA was diagnosed by imaging performed as part of a broader health examination after the development of lymphocytic pneumonitis. He had

**FIG. 6.** Case 3. Postcontrast T1 sagittal (A) and coronal (B) MRI studies show diffuse enhancement of the pituitary gland and its stalk without stalk displacement.

**FIG. 7.** Case 3. Histology from dacryoadenectomy shows extensive lymphocytic infiltration.
imaging evidence of pituitary infundibular enlargement but no pituitary hormone deficiency. We presume that the LyH had just begun.

Our report adds further support to the idea that there might be a relationship between DA and LyH, reflected by pathophysiologic changes that occur simultaneously within the pituitary gland, the pituitary stalk, and lacrimal glands as part of a common autoimmune illness. The discovery of DA should prompt consideration of the diagnosis of LyH and appropriate imaging and endocrine investigation.

REFERENCES


