Lymphocytic Adenohypophysitis with Sudden Onset of Diabetes Insipidus in Menopausal Female

—Case Report—

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Abstract

A rare case of a postmenopausal (60-year-old) female with lymphocytic adenohypophysitis manifesting as a sudden onset of diabetes insipidus is reported. Magnetic resonance imaging with gadolinium-diethylenetriaminepenta-acetic acid enhancement showed a spherical lesion, approximately 1 cm in diameter, in the sella turcica and a thickened, deviated pituitary stalk. The abnormal tissue was totally removed. Histological examination showed marked infiltration of lymphocytes and plasma cells. Postoperatively, the pituitary stalk became normal. Preoperative differentiation of lymphocytic adenohypophysitis from pituitary adenoma is extremely difficult, and biopsy is essential.

Key words: electron microscopy, lymphocytic adenohypophysitis, magnetic resonance imaging, pituitary tumor, transsphenoidal surgery

Introduction

Lymphocytic adenohypophysitis (LAH) is mainly associated with pregnancy, and/or hyperprolactinemia are present in the postpartum period. LAH is difficult to differentiate from pituitary adenoma by neuroimaging. No specific antibodies have been detected, but LAH is possibly an autoimmune disease.

Here, we describe a postmenopausal female presenting with only polyuria and polydipsia. The problems of diagnosis and the etiology of LAH are discussed.

Case Report

A 60-year-old female complaining of thirst and polydipsia was admitted. She had no headaches or other symptoms, and no detected autoimmune disease. Menopause began at 50 years old.

Physical and neurological examinations revealed no abnormalities. Her visual field was normal. Urine volume was almost 5,000 ml/day, and the specific gravity was 1.003.

Plain skull x-ray films found no abnormalities. Computed tomographic (CT) scans demonstrated a pituitary mass. Coronal and sagittal magnetic resonance (MR) images demonstrated a 10 x 10 x 10 mm mass occupying the sella turcica. The mass was homogeneously isointense with the brain parenchyma on the T1-weighted image. The optic chiasma was not compressed. The coronal image showed the pituitary stalk to be enlarged and deviated to the right. Gadolinium-diethylenetriaminepenta-acetic acid (Gd-DTPA) enhanced the pituitary and pituitary stalk (Fig. 1). These findings, except for the stalk enlargement, are consistent with a pituitary adenoma.

Laboratory investigations are shown in Table 1. Immunological studies found negative reactions to antibodies for antinuclear, ribonucleoprotein, microsomal, smooth muscle, and mitochondrial antigens, OKT4 35.4% (normal, 22-55%), OKT8 42.8% (11-48%), OKT4/OKT8 ratio 0.83 (0.5-2.7),

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and histocompatibility antigen A2B7Cw1Cw3.

Transsphenoidal exploration of the sella totally removed abnormal yellowish, elastic hard tissue behind the normal pituitary gland. Histological examination revealed extensive infiltration of reactive lymphocytes, plasma cells, and some eosinophilic cells to the pituitary gland (Fig. 2). Electron microscopy revealed abundant infiltration of lymphocytes, plasma cells, and adenohypophysial cells (Fig. 3).

Postoperative MR images showed that the pituitary stalk returned to normal size, and the deviation disappeared (Fig. 4). Pituitary gland in the sella turcica was isointense on the T1-weighted image. The diabetes insipidus was controlled by desmopressin acetate nasal spray. No endocrine dysfunctions of the anterior pituitary lobe were noted.

At 3-year and 5-month follow-up, she was well, except for diabetes insipidus. Desmopressin acetate nasal spray is still in use.

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Fig. 3 Electron micrographs, showing lymphocytes (L), one with a lysosome (•) (left); a plasma cell (P) with prominent granular endoplasmic reticulum (R) (center); and a lymphocyte, and an adenohypophysial cell (A) with abundant secretory granules (S) (right). Bar = 1 μm.

Fig. 4 Postoperative T<sub>1</sub>-weighted MR images, midline sagittal (left) and coronal (right) sections, showing the diminished tumor. The pituitary gland is visible on the floor of the sella turcica in the sagittal section. Deviation of the stalk has disappeared.

Discussion

Goudie and Pinkerton<sup>3</sup> first described LAH as a pathological entity in 1962. However, the first case diagnosed antemortem was not reported until 1980.<sup>6</sup> The majority of LAH cases are diagnosed during the early postpartum period based on an enlarged pituitary gland or hypopituitarism.<sup>7</sup> All cases reported to date except one<sup>6</sup> have been females. LAH typically presents with diffuse lymphocyte and plasma cell infiltration to the pituitary gland, occasionally lymphoid follicles with germinal centers, destruction of adenohypophysial cells, and/or fibrosis. Electron microscopy may show interdigitation by lymphocytes and adenohypophysial cells, fusion of lysosomes with secretory granules, and...
swollen mitochondria indicating oncocytic transformation. The two reported cases of electron microscopic study showed no evidence of immune complex deposits or vascular injury. Our case clearly demonstrated infiltrated plasma cells and lymphocytes.

The macrophagic features of LAH resemble those of autoimmune thyroiditis, adrenitis, oophoritis, orchitis, and gastritis, which are presumably caused by delayed or cellular immune mechanisms. Some LAH patients demonstrate another prominent feature of autoimmune disease: the lesion affecting multiple organs in the same individual. Several LAH patients have had associated autoimmune-type diseases such as Hashimoto's thyroiditis, silent thyroiditis, idiopathic adrenitis, and pernicious anemia, all considered to have autoimmune causes. Engelberth and Jezkova were the first to associate anti-tpituitary antibodies with the development of hypopituitarism in postpartum females. Botazzo et al. identified the autoantibodies reacting with anterior pituitary tissue in LAH patients, using immunofluorescent staining. They found anti-prolactin cell antibodies in 19 of 287 patients with other autoimmune diseases. Although no pituitary antibodies were found in patients with panhypopituitarism, isolated hormone deficiency may be caused by specific antibodies.

Pregnancy is associated with the remission of autoimmune disorders. The loss of fetal suppressor activity postpartum may enhance the potential for autoantigenicity, allow an autoimmune reaction to manifest, or worsen pre-existing autoimmune disease. Such an event might trigger lymphocytic hypophysitis. Maternal antibodies responding to fetal antigens and antibody may lead to cross reaction with maternal antigens. Our case was a postmenopausal female without autoimmune disease. This case is rare, so another mechanism should be considered. However, we could not verify the etiology in our case.

Most patients have various degrees of hypopituitarism and/or slight hyperprolactinemia. Our case demonstrated hyperprolactinemia. Postoperatively, the prolactin levels decreased to within the normal range. Portocarrero et al. suggested several mechanisms for the elevated prolactin levels in LAH cases unrelated to pregnancy: 1) distortion of the portal system with enlarged pituitary gland and reduced dopamine delivery; 2) inflammation mediators stimulating prolactin secretion or blocking dopamine receptors; and 3) the presence of a prolactin stimulating antibody.

Three cases presented persistent diabetes insipidus, recognized pre- and postoperatively. In our case, diabetes insipidus was diagnosed preoperatively. Diabetes insipidus occurring postoperatively is thought to result from surgery. The etiology of diabetes insipidus presenting preoperatively is unknown, but may be due to inflammation extending to the posterior lobe and stalk of the pituitary gland.

Plain skull x-ray films frequently show sellar enlargement and/or thinning of the floor in LAH cases. Postcontrast CT scans show a homogeneously enhanced mass. These findings are similar to those of pituitary adenomas. In some cases, the lesion extends to suprasellar regions and compresses the optic chiasm. In one case, T1-weighted MR images demonstrated a 1 x 1.2 cm homogeneously intense mass in the sella turcica, consistent with a pituitary adenoma. In our case, plain skull x-ray films found no abnormalities. However, CT scans and MR images showed a bulging mass without compression of the optic chiasm. MR images showed that the pituitary mass and stalk were homogeneously enhanced by Gd-DTPA, and the pituitary stalk deviated anteriorly to the right. The enhanced pituitary mass and stalk probably resulted from inflammation.

Preoperative differentiation of LAH from pituitary adenoma is extremely difficult, and biopsy is essential. In LAH cases, the pituitary mass disappears spontaneously postpartum and hypopituitarism resolves within 1 year, so further removal is unnecessary. Since most cases demonstrate spontaneous improvement of the inflammation, and total removal of the mass often results in hypopituitarism, we recommend a biopsy to diagnose the tumor histologically and to improve the complications.

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References


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