Lymphocytic Hypophysitis in a Patient with Testicular Feminization Syndrome

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Lymphocytic hypophysitis is a rare inflammatory disease of the pituitary gland that is one of the causes of hypopituitarism. The majority of cases occur in women during the peripartum period, and it is rare in men. Testicular feminization syndrome is a genetic disorder presenting a 46,XY karyotype, but a normal female phenotype. We report a case of lymphocytic hypophysitis in a 23-year-old woman with testicular feminization syndrome.

KEY WORDS: Lymphocytic hypophysitis • Testicular feminization syndrome.

Introduction

Lymphocytic hypophysitis is an unusual inflammatory disorder of the pituitary gland. Most cases occur in pregnant women, and patients typically present during the peripartum period with dysfunction of the adrenohypophysis and visual complaints. Recently there are reports of cases in non-pregnant females and in males. Testicular feminization syndrome is a genetic disorder that makes XY fetuses insensitive to androgens. They are born looking externally like normal girls.

The authors report a rare case of lymphocytic hypophysitis in a patient with testicular feminization syndrome.

Case Report

A twenty-three-year-old woman presented with headache, vomiting and diplopia for two weeks. She had been amenorrheic since birth. Neurological examination showed an adduction of the left eye, but no impairment of eye movement.

Endocrinological examination showed triiodothyronine (T3) and 3, 5, 3'-, 5'-tetraiodothyronine (free T4) levels within the normal range. Thyroid stimulating hormone (TSH) was 0.19U/ml (normal 4.3~22.4IU/ml), and serum cortisol was 1.41ug/dl (normal 4.3~22.4ug/dl). Adrenocorticotropic hormone (ACTH) was 3.93pg/ml (normal 6~60pg/ml). Testosterone, androstenedione, growth hormone, and prolactin levels were all within the normal range. Somatotropin, lutecinizing hormone (LH), and follicle-stimulating hormone (FSH) were within the normal range, but estradiol was 15.42pg/ml (normal 35.5~570.8pg/ml).

Magnetic resonance imaging (MRI) of the sella revealed a 10×25mm suprasellar mass of triangular shape with peripheral rim enhancement. After oral administration of 15mg/day of methylprednisolone for 2 weeks, computed tomography (CT) showed a significant reduction of the mass (Fig. 1).

Fig. 1. Preoperative coronal magnetic resonance images (MRI) showing the suprasellar mass. A and B: Coronal T1-weighted (A) and T2-weighted (B) MRI showing the hypointense and hyperintense signals, respectively. C: Coronal T1-weighted Gd-enhanced MRI showing the dense peripheral rim enhancement with triangular shape (arrow). D: Brain computed tomography showing the mass reduced (circle) after oral administration of steroid for 2 weeks.

* Received: May 10, 2006 • Accepted: September 22, 2006
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To prevent recurrence, and to make a histologic diagnosis, the mass was surgically removed using the transsphenoidal approach with C-arm and the Navigator system (Stealth plus®, Medtronic®, USA). The mass appeared yellowish-gray in color with sticky mucus. Gross total excision of the mass was achieved. Histology of the specimen showed infiltration of mildly atypical lymphocytes, plasma cells, and histiocytes. There was destruction of the pituitary tissue with dense stromal fibrosis (Fig. 2). At 2 weeks after the operation, the patient was discharged without any neurological deficits.

In post-operative evaluation, the karyotype of the patient was 46XY. Pelvic ultrasonography revealed a short, blind-pouch vagina, and there were testes in the abdomen but no uterus, fallopian tubes or ovaries. After gonadectomy and biopsy by the department of obstetrics and gynecology, the tissue was found to be seminiferous tubules containing only dysgenetic Sertoli cells surrounded by Leydig cells. These findings were compatible with testicular feminization syndrome.

Discussion

Lymphocytic hypophysitis is an inflammatory process of the pituitary gland first reported in 1962. The condition is rare, accounting for 0.38% to 1.1% of sellar lesions excised during transsphenoidal surgery. Although it typically affects young, pregnant women, lymphocytic hypophysitis has been documented with increasing frequency in men and in menopausal females.

The cause of lymphocytic hypophysitis remains obscure, but has been attributed to an underlying autoimmune disorder by some investigators, and autoantibodies against pituitary-specific proteins have been described.

The clinical presentation is variable and comprises four categories of symptoms: sellar compression, hypopituitarism, diabetes insipidus, and hyperprolactinemia. Symptoms of sellar compression, represented by headache and visual disturbances, are the most common and usually the initial complaint. The next most common are symptoms due to a partial or complete deficit of the anterior pituitary hormones, mainly ACTH followed by TSH, gonadotropins, and prolactin. These defects are considered the direct result of an autoimmune attack on the pituitary acinar cells. Next are symptoms due to a deficit of the posterior pituitary (diabetes insipidus), which can be attributed either to direct immune destruction or to compression of the posterior lobe and infundibular stem. Least common are manifestations of hyperprolactinemia, mainly represented by amenorrhea/oligomenorrhea and galactorrhea.

Imaging studies play a crucial role in the diagnosis of inflammatory hypophysitis. A global and symmetrical mass affecting the entire gland is indicative of a diffuse, inflammatory pituitary infiltration rather than of a pituitary adenoma, which is usually more localized. Marked contrast enhancement in MRI and CT is also typical of inflammatory lesions of the pituitary. A comparison of MR findings between lymphocytic hypophysitis and pituitary macroadenoma are described in Table 1.

The natural history of inflammatory hypophysitis is not completely understood, and its treatment is controversial.

Spontaneous resolution of the lesion on MR images following

<table>
<thead>
<tr>
<th>Table 1. The comparisons of Magnetic resonance(MRI) findings between the lymphocytic hypophysitis(LAH) and the pituitary macroadenoma</th>
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<tbody>
<tr>
<td><strong>MRI finding</strong></td>
</tr>
<tr>
<td>Symmetric mass</td>
</tr>
<tr>
<td>Pre-contrast homogeneous signal</td>
</tr>
<tr>
<td>Infact sellar floor</td>
</tr>
<tr>
<td>Suprasellar extension</td>
</tr>
<tr>
<td>Stalk thickening</td>
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<tr>
<td>Stalk displacement</td>
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<tr>
<td>Homogeneous enhancement</td>
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<tr>
<td>Loss of posterior hypointensity</td>
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LAH: Lymphocytic pitrophritis
steroid therapy has been described. When lymphocytic hypophysitis is the presumptive diagnosis in pregnant and postpartum patients, and in those with evidence of an autoimmune process, some advocate an initial trial of therapeutic corticosteroid administration, except in the face of progressive and severe vision loss. Poor responses or recurrences following steroid withdrawal have been described, and the significant side effects of long-term steroid therapy are also a major concern.

Surgical resection through the transphenoidal approach is a safe and effective treatment for inflammatory hypophysitis.

In our case, even though the size of the mass was markedly reduced after steroid administration, surgical removal was performed via the transphenoidal approach to prevent the recurrence of the mass and to confirm the diagnosis.

Testicular feminization syndrome is a genetic disorder that makes XY fetuses insensitive (unresponsive) to androgens. They are born looking externally like normal girls. Internally, there is a short blind-pouch vagina and no uterus, fallopian tubes or ovaries. There are testes in the abdomen or the inguinal canal. The incidence is 1/20,000–64,000 at male birth, and 10% in cases of primary amenorrhea. The gene for the syndrome is on the X chromosome in band Xq11-q12. This gene codes for the androgen receptor (also called the dihydrotestosterone receptor), and is mutated in the complete androgen insensitivity syndrome. Because of the mutation, the cells cannot respond to androgen.

Initially, we focused on the pituitary mass found in a non-pregnant woman. However, while evaluating the patient we found that although the phenotype was female, the karyotype was 46 XY, indicating testicular feminization syndrome. To our knowledge, this is the first case of lymphocytic hypophysitis in a patient with testicular feminization syndrome.

This coincidence of two rare disorders may be a helpful clue in explaining the pathogenesis and female preponderance of lymphocytic hypophysitis. We suggest that a full obstetric and gynecologic evaluation should be undertaken in patients with lymphocytic hypophysitis.

Conclusion

We herein report the first case of lymphocytic hypophysitis in a patient with testicular feminization syndrome, and suggest that full obstetric and gynecologic evaluation should be performed in cases of lymphocytic hypophysitis. Further study of the relationship between these two diseases would be valuable.

References