Giant Cell Granulomatous Hypophysitis Manifesting as an Intrasellar Mass with Unilateral Ophthalmoplegia
—Case Report—

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Abstract

A 62-year-old female presented with giant cell granulomatous hypophysitis manifesting as subacute unilateral ophthalmoplegia. Neuroimaging revealed a mass lesion expanding in the pituitary fossa. The mass was totally removed through the transsphenoidal approach. The histological diagnosis was giant cell granuloma. The oculomotor nerve paresis resolved completely 10 days after the operation. Giant cell granulomatous hypophysitis is symptomatically and radiologically indistinguishable from non-functioning pituitary adenoma, but is less likely to cause visual disturbance than pituitary adenoma. Giant cell granulomatous hypophysitis should be considered in the differential diagnosis of sellar and suprasellar lesions, particularly if oculomotor nerve paresis is observed without impaired visual field or acuity.

Key words: pituitary gland, ophthalmoplegia, giant cell granuloma

Introduction

Giant cell granulomatous hypophysitis is a rare disease of the pituitary gland, presenting as hypopituitarism and the symptoms of an expanding mass lesion.1,13,15,21,24,27,30-32) The histological characteristics are multinucleated giant cells and epithelioid cells coexisting with accumulations of plasma cells and lymphocytes. Granulomatous lesion of the pituitary gland is usually associated with systemic granulomatous diseases such as sarcoidosis, tuberculosis, syphilis, mycosis, and histiocytosis X.8,14,19,20,24) These systemic disorders should be excluded before the diagnosis of idiopathic giant cell granulomatous hypophysitis is established.

Giant cell granulomatous hypophysitis is not rare in autopsy cases,34) but only 12 surgically treated cases have been reported2,13,15,21,24,27,30-32) We describe the case of a 62-year-old female who developed left ophthalmoplegia due to giant cell granulomatous hypophysitis, and discuss the clinical symptoms, radiological findings, and treatment of this disease.

Case Report

A 62-year-old female was referred to our hospital for evaluation of ophthalmoplegia of the left eye. She had been in good health until 10 days prior to admission, when she suddenly felt giddy and experienced ptosis of the left eye and diplopia. Over the next 10 days she became unable to raise her left eyelid. In addition, she found she could not move her left eye except for the abduction. Her family history and past history were unremarkable.

Physical examination found she was healthy, but had left oculomotor nerve paresis with mydriasis and complete ptosis of the left eyelid. The pupillary response to light was absent in the left eye. Visual fields were full, and visual acuity was not impaired. There was no pain in or behind the eyes. The ocular fundus was clear. General physical examination was otherwise unremarkable. The complete blood count, routine urinalysis, serum electrolyte, and biochemical profile examinations were normal. Preoperative endocrinological studies showed normal basal levels
of thyroid-stimulating hormone, luteinizing hormone, follicle-stimulating hormone, prolactin, growth hormone, and adrenocorticotropic hormone. However, a blunt response to administration of thyrotropin-releasing hormone, luteinizing hormone-releasing hormone, and insulin was observed. Preoperative serum hormone values are summarized in Table 1. Skull radiography revealed a slightly enlarged sella turcica and erosion of the dorsum sellae. Computed tomography (CT) displayed an isodense mass in the sella turcica (Fig. 1 left), which was enhanced slightly (Fig. 1 right). Magnetic resonance (MR) imaging showed an intrasellar mass with no upward extension. The mass was isointense on the T1-weighted image (Fig. 2 A, C), hyperintense

Table 1 Preoperative serum hormone values

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Basal value (normal range)</th>
<th>Response value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH (mU/ml)</td>
<td>2.5 (0.5-5.0)</td>
<td>5.9 5.5 4.5</td>
</tr>
<tr>
<td>ACTH (pg/ml)</td>
<td>30 (9-52)</td>
<td>24 42 35</td>
</tr>
<tr>
<td>PRL (ng/ml)</td>
<td>4.3 (1.4-14.6)</td>
<td>15 11 6.8</td>
</tr>
<tr>
<td>GH (ng/ml)</td>
<td>0.59 (0.66-3.08)</td>
<td>1.2 5.6 2.1</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>6.3 (8.7-38.0)**</td>
<td>11 15 18</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>29 (26.2-113.9)**</td>
<td>31 35 41</td>
</tr>
</tbody>
</table>

*Response values are measured by intravenous injection of thyrotropin-releasing hormone (0.5 mg), luteinizing hormone (LH)-releasing hormone (0.1 mg), and regular insulin (2.5 U). **Normal ranges of LH and follicle-stimulating hormone (FSH) in menopause. ACTH: adrenocorticotropic hormone, GH: growth hormone, PRL: prolactin, TSH: thyroid-stimulating hormone.

Ten days after total removal of the intrasellar mass, the left oculomotor nerve paresis resolved completely. The basal levels of pituitary hormones were unchanged after the operation. Histological examination showed extensive well-formed non-caseating granulomas without Schaumann bodies, cholesterol crystals, or necrosis.

Fig. 1 Axial computed tomography scans showing an isodense mass in the sella turcica (left) and after administration of contrast medium showing slight enhancement of the mass (right).

Fig. 2 T1-weighted magnetic resonance images, axial (A, B) and sagittal (C, D) views, showing an intrasellar isointense mass (A, C) and after administration of gadolinium-diethylene triamine penta-acetic acid showing homogeneous enhancement of the mass (B, D).

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The granulomas were composed of multinucleated giant cells and epithelioid cells coexisting with accumulations of plasma cells and lymphocytes. There were several areas where the normal glandular structure of the hypophysis was destroyed by granulomatous inflammation (Fig. 3). Epithelial element such as stratified squamous cells or ciliated columnar cells was not found. There was no evidence of the presence of craniopharyngioma or Rathke's cleft cyst. Acid-fast staining and periodic acid-Schiff staining failed to demonstrate tubercle bacilli and fungi.

All follow-up clinical and serological examinations for tuberculosis were negative. Although the patient showed a moderately increased value in the serum Treponema pallidum hemagglutination assay, she had never been treated for syphilis. She may have been infected by syphilis serologically through her husband, but the disease did not develop to show clinical signs. Chest radiography and tomography revealed clear lungs and no mediastinal adenopathy. There was no pathological change in her skin. Levels of angiotensin-converting enzymes in the serum and cerebrospinal fluid were normal. Since no systemic granulomatous disease was detected, the intrasellar mass was diagnosed as a giant cell granulomatous hypophysitis of unknown etiology. She was healthy and leading a normal life as a housewife 5 years after the operation.

**Discussion**

Serological and histological examinations are helpful in distinguishing idiopathic giant cell granulomatous hypophysitis from tuberculosis, syphilis, and mycosis. There is no definite histological difference between giant cell granuloma and pituitary sarcoidosis, but sarcoidosis, unlike giant cell granulomatous hypophysitis, is characterized by various systemic lesions in the hilar lymph node, lung, skin, and eye. In addition, increased levels of angiotensin I-converting enzyme in serum or cerebrospinal fluid are indicative of sarcoidosis.

Giant cell granulomatous hypophysitis manifests as symptoms of hypopituitarism and an expanding sellar mass. However, it rarely causes diabetes insipidus unlike pituitary sarcoidosis and histiocytosis X, as only two of the 13 surgically resected cases and two of the 23 autopsy cases indicated diabetes insipidus. Histologically, the anterior lobe of normal pituitary gland is aggressively invaded by inflammatory cells in giant cell granulomatous hypophysitis, corresponding to the clinical symptoms of this disease.

Lymphocytic adenohypophysitis is another type of inflammatory disease of the pituitary gland which typically occurs in females in the puerperium or during pregnancy, and is thought to be an autoimmune disease. Lymphocytic adenohypophysitis often causes visual disturbance in addition to hypopituitarism. Likewise, impaired visual field or acuity is exhibited by 60–80% of patients with non-functioning pituitary adenomas. In contrast, visual disturbance is rarely associated with giant cell granulomatous hypophysitis as only one autopsy and two surgical cases showed symptoms of chiasmal involvement. Giant cell granulomatous hypophysitis may tend to cause hypopituitarism before reaching the optic chiasm. Interestingly, three of the 13 surgically resected giant cell granulomas were associated with oculomotor nerve paresis, but none with visual disturbance. Ocular nerve paresis occurs in 1–8% of patients with pituitary tumors. Patients who present with an isolated ocular nerve paresis are even less common. Oculomotor nerve paresis without visual field defect is a rare complication of pituitary adenomas. Therefore, giant cell granulomatous hypophysitis may be more likely to extend in the lateral direction than pituitary adenoma. Furthermore, oculomotor nerve paresis without visual field defect is sometimes caused by pituitary apoplexy. Giant cell granulomatous hypophysitis should be considered as a differential diagnosis of pituitary apoplexy.

CT has frequently been performed in cases of granulomatous diseases of the pituitary gland, but no specific findings have been identified.

Fig. 3 Photomicrograph of the surgical specimen showing a granulomatous area with multinucleated giant cells, histiocytes, and lymphocytes. Arrow indicates normal hypophyseal cells. HE stain, ×200.
MR imaging has been performed in two cases of giant cell granulomatous hypophysitis including the present case. In both cases, the masses were isointense on the T1-weighted image, and hyperintense on the T2-weighted image. The intrasellar mass was homogeneously enhanced with Gd-DTPA in the present case, but no contrast study was performed previously. Although MR imaging has frequently shown hypothalamo-hypophyseal involvement in pituitary sarcoidosis, this was unclear in the two cases of giant cell granulomatous hypophysitis. Recently, it has been considered that contrast-enhanced MR imaging enables the preoperative differentiation between pituitary adenoma and lymphocytic adenohypophysitis. In the present case, diffuse swelling and intense enhancement of pituitary mass may be suggestive of lymphocytic adenohypophysitis rather than pituitary adenoma. However, in the cases of giant cell granulomatous hypophysitis in which contrast-enhanced CT had been performed, intense or homogeneous enhancement was not always noted. We conclude that giant cell granulomatous hypophysitis is indistinguishable from pituitary adenoma and lymphocytic adenohypophysitis by neuroimaging methods.

The optimum treatment for giant cell granulomatous hypophysitis has not been established. The mass was removed by a transsphenoidal procedure in most cases. The symptoms of an expanding mass lesion, such as headache or cranial nerve paresis, improved after removal of the mass. However, hypopituitarism due to the mass lesion was frequently prolonged or deteriorated postoperatively, since the granulomatous lesion was mixed with normal hypophyseal elements. In contrast, some granulomatous diseases such as sarcoidosis and Tolosa-Hunt syndrome are usually treated by steroid therapy. 

Administration of steroid has been effective for the improvement of clinical symptoms caused by giant cell granulomatous hypophysitis. However, steroid therapy is rarely used for the treatment of this disease because of the difficult preoperative diagnosis. In the absence of clinical symptoms due to an expanding mass lesion, minimum removal of the giant cell granuloma is necessary to prevent the deterioration of hypopituitarism. Furthermore, steroid therapy should be considered as postoperative treatment.

**References**


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