Xanthogranuloma of the Sellar Region
—Case Report—

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Abstract
A 55-year-old woman presented with a rare xanthogranuloma of the sellar region after complaining of severe headache and visual disturbance 3 months previously. Clinical examination showed she was alert with early signs of bitemporal hemianopsia. Endocrinological examination revealed hypopituitarism. Magnetic resonance imaging showed an intrasellar mass extending into the suprasellar region and compressing the optic chiasma, which appeared homogeneously hyperintense on T1-weighted images. Endonasal transsphenoidal resection of the tumor was performed. Histological examination disclosed granulomatous tissue with cholesterol clefts, hemosiderin deposits, fibrous tissues, and macrophages containing rich fat. The histological diagnosis was xanthogranuloma of the sellar region. Her visual symptoms recovered postoperatively although the hypopituitarism remained. Xanthogranuloma of the sellar region is rare, but must be considered in the differential diagnosis of tumors of the sellar region.

Key words: xanthogranuloma of the sellar region, sellar tumor, hypopituitarism, craniopharyngioma, pituitary adenoma

Introduction
Xanthogranuloma of the sellar region is rare, and clinically and pathologically distinct from classical adamantinomatous craniopharyngioma. Thirty-seven cases of xanthogranuloma of the sellar region were reported in 1999, which differed from classical adamantinomatous craniopharyngiomas with respect to the preferential occurrence in adolescents and young adults, predominant intrasellar location, smaller tumor size, more severe endocrinological deficits, longer preoperative history, lower frequency of calcification and visual disturbances, better resectability, and more favorable outcome.9) Xanthogranuloma of the sellar region was added to the World Health Organization (WHO) brain tumor classification in 2000.12)

Here, we report a case of xanthogranuloma of the sellar region and discuss the radiological and clinical findings.

Case Report
A 55-year-old woman complained of severe headache and visual disturbance 3 months previously. Clinical examination found she was alert with early signs of bitemporal hemianopsia. She had received a short course of corticosteroid therapy (prednisolone 2.5 mg/day) for chronic arthritis 20 years previously. Blood examination showed abnormal hormonal values: growth hormone (GH) <0.15 ng/ml (normal range 0–3), follicle-stimulating hormone (FSH) 3.3 mIU/ml, luteinizing hormone (LH) 0.2 mIU/ml, prolactin (PRL) 16.6 ng/ml (6.1–30.5), adrenocorticotropic hormone (ACTH) <5.0 pg/ml (0–46), cortisol <0.4 μg/dl, thyroid-stimulating hormone (TSH) 1.015 mIU/ml (0.4–3.8), free triiodothyronine 1.4 μg/ml (2.2–3.4), and free thyroxine 0.64 ng/dl (0.8–1.2). GH-releasing factor, LH-releasing hormone, TSH-releasing hormone, and ACTH-releasing hormone tolerance tests showed low responses. These endocrinological findings suggested hypopituitarism with secondary adrenal insufficiency. Hormone replacement therapy with corticosteroid (cortisol 10 mg/day) and thyroid hormone (thyroxine 25 μg/day) was started.

Computed tomography demonstrated isodense intrasellar masses without calcification. Magnetic resonance (MR) imaging showed an intrasellar mass extending into the suprasellar region that compressed the optic chiasma. The lesion was homogeneously hyperintense on T1-weighted images and hypo- and hyperintense on T2-weighted images. The tumor intensity was not enhanced with gadolinium (Fig. 1). MR angiography revealed no cerebral aneurysms. As her clinical signs were
similar to those of pituitary apoplexy, our preoperative diagnosis was hemorrhagic pituitary adenoma or Rathke’s cleft cyst.

The tumor was approached via an endonasal transsphenoidal approach under the operating microscope with a frameless neuronavigation system (BrainLAB AG, Feldkirchen, Germany). When the capsule was opened, a yellow-brown fluid together with a crystal-like material flowed out. The main component of the mass was yellowish soft tissue and was almost completely removed. The pituitary gland was found at the posterior side of the mass.

Histological examination revealed granulomatous tissue with cholesterol clefts, hemosiderin deposits, fibrous tissues, and macrophages containing rich fat, as well as cell infiltrates of mainly lymphocytes as a sign of chronic inflammatory reactions (Fig. 2A, B). No nodule of compact wet keratin or strands of squamous epithelium, which are typical for craniopharyngioma, were observed. No ciliated cuboidal epithelial cells were observed. However, immunohistochemical staining for cytokeratin and epithelial membrane antigen showed only a small part of the lesion showed evidence of epithelial cells (Fig. 2C). Furthermore, immunohistochemistry revealed no expressions of GH, PRL, FSH, LH, TSH, and ACTH. No mitosis or necrosis was seen. Ki-67 labeling index was lower than 1%. The histological diagnosis was xanthogranuloma of the sellar region.

The postoperative course was uneventful except for the presence of transient diabetes insipidus. Her severe headache disappeared rapidly, and her visual disturbance improved gradually. Her endocrinological dysfunction did not recover, so hormonal replacement was continuously required. Postoperative MR imaging revealed no residual tumor. There has been no sign of recurrence for 18 months (Fig. 3).

**Discussion**

Xanthogranulomatous tissue contains cholesterol clefts and occurs secondary to hemorrhage, infarction, inflammation, or necrosis. Nineteen cases of cholesterol granuloma reaction among 211 sellar tumors. This change is often observed in craniopharyngiomas. Xanthogranuloma of the sellar region shows distinct histological features with cholesterol clefts, lymphocytic infiltrates, marked hemosiderin deposits, multinucleated foreign body giant cells around cholesterol clefts, accumulation of macrophages, and only small epithelial cell clusters. Xanthogranulomas may represent a degenerative form of craniopharyngioma based on the intraoperative aspect and the occasional presence of epithelial components.

The differential diagnoses for xanthogranuloma of the sellar region include craniopharyngioma, Rathke’s cleft cyst, and pituitary adenoma. Pituitary adenomas that occur in the majority of cases appear as hypo- to isointense lesions on T1-weighted imaging and iso- to hyperintense on T2-weighted imaging, and show marked contrast en-
Table 1 Reviewed cases of xanthogranuloma of the sellar region

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author (Year)</th>
<th>Age (yrs)/Sex</th>
<th>Magnetic resonance imaging appearance</th>
<th>Clinical findings</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Reithmeier et al.</td>
<td>51/M</td>
<td>high</td>
<td>heterogeneous</td>
<td>NA</td>
</tr>
<tr>
<td>2</td>
<td>Yonezawa et al.</td>
<td>67/M</td>
<td>high</td>
<td>no</td>
<td>RHR after 3 mos</td>
</tr>
<tr>
<td>3</td>
<td>Burt et al.</td>
<td>29/M</td>
<td>heterogeneous</td>
<td>rim-enhanced</td>
<td>NA</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>26/M</td>
<td>high</td>
<td>no</td>
<td>doing well after 18 mos</td>
</tr>
<tr>
<td>5</td>
<td>Murao et al.</td>
<td>57/F</td>
<td>mainly high, partially low</td>
<td>heterogeneous</td>
<td>NA</td>
</tr>
<tr>
<td>6</td>
<td>Jung et al.</td>
<td>5/NA</td>
<td>high</td>
<td>no</td>
<td>NA</td>
</tr>
<tr>
<td>7</td>
<td>Chen et al.</td>
<td>5/NA</td>
<td>high</td>
<td>no</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>Liu et al.</td>
<td>32/M</td>
<td>high</td>
<td>no</td>
<td>NA</td>
</tr>
<tr>
<td>9</td>
<td>Moriya et al.</td>
<td>54/M</td>
<td>high</td>
<td>no</td>
<td>RHR after 12 mos</td>
</tr>
<tr>
<td>10</td>
<td>Sugata et al.</td>
<td>26/M</td>
<td>iso</td>
<td>heterogeneous</td>
<td>NA</td>
</tr>
<tr>
<td>11</td>
<td>Present case</td>
<td>55/F</td>
<td>high</td>
<td>no</td>
<td>RHR after 18 mos</td>
</tr>
</tbody>
</table>

NA: not available, RHR: required hormonal replacement.

hancement. Pituitary apoplexy appears as hyperintense on T₁-weighted imaging. Cranioopharyngiomas are solid tumors with cystic components and often show calcification, appearing heterogeneously iso- and hyperintense on T₁- and T₂-weighted imaging. Rathke’s cleft cysts can be hypo- or hyperintense on T₁- and T₂-weighted imaging, but show neither signs of calcification nor contrast enhancement. MR imaging was performed in all 10 reviewed cases (Table 1). For nine of the 11 cases including our present case, the lesions appeared homogeneously or mainly hyperintense with or without contrast enhancement. The cholesterol clefts of xanthogranuloma characteristically appear as hyperintense on T₁-weighted imaging. However, xanthogranuloma is difficult to differentiate from craniopharyngioma, Rathke’s cyst, or pituitary adenoma with hematoma using only the appearance on T₁-weighted imaging. In the 10 reviewed cases, the lesions revealed variable signal intensity on T₂-weighted imaging. Therefore, definitive preoperative diagnosis is still difficult. Previous preoperative diagnoses have included craniopharyngioma or Rathke’s cleft cyst.

Nine of the 11 cases including our present case reported since xanthogranuloma of the sellar region was added to the WHO brain tumor classification in 2000 showed some degree of endocrinological deficits. However, no visual field defect was revealed in five of these nine cases. The characteristics include smaller tumor size and more severe endocrinological deficits. Severe inflammatory changes leading to granulomatous degeneration may result in serious damage to the hypothalamo-pituitary axis. Headache was described in some cases including ours. Pituitary apoplexy and hemorrhagic Rathke’s cleft cyst are usually suggested by clinical findings such as headache, decreased visual acuity, visual field defects, and hypopituitarism. The present case showed similar symptoms to those of pituitary apoplexy, so our preoperative diagnosis was hemorrhagic pituitary adenoma or Rathke’s cleft cyst.

Surgical removal is necessary to obtain the correct diagnosis and to reduce the mass effects on the anatomy such as the optic nerves. In the 10 reviewed cases of xanthogranuloma, no recurrence was noted, and the surgical outcome appeared favorable. Six of the nine patients with hormonal deficits were followed up after surgery. In five of these six cases, the hormonal deficits did not recover after surgery, and hormonal replacement was continuously required as in our present patient. While visual deficits and headache recover after resection of the tumor, endocrinological deficits are difficult to cure.

Xanthogranuloma of the sellar region is rare, but should be considered in the differential diagnosis of tumors in the sellar region. Preoperative diagnosis of xanthogranuloma of the sellar region is still difficult, but a good clinical course except for endocrinological insufficiency may be obtained by complete resection. Therefore, surgical treatment must be performed in all cases. Further experience is needed with the clinical features of this new entity.

References


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