Chronic Sclerosing Dacryoadenitis
- Report of 2 Cases -

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Chronic sclerosing dacryoadenitis is a rare and under-recognized chronic inflammatory dis-
ease of the lacrimal gland. We describe 2 patients with a localized type of chronic sclerosing
dacryoadenitis. Both patients presented with a slowly growing painless mass of the eyelid
mimicking a tumorous lesion. The morphologic findings of the masses excised under the
clinical diagnosis of lymphoma closely recapitulate those of chronic sclerosing sialadenitis
(Küttner tumor). Immunohistochemical staining demonstrated an increased population of
IgG4-positive plasma cells confirming that this disease also belongs to the spectrum of a
recently described IgG4-related sclerosing disease.

Case Report

Case 1

A 55-year-old man presented with a 6-month history of visual
disturbance of the right eye. His past medical history was insignif-
icient except for hypertension. The results of full blood count,
differential white blood cell count, and liver function test were
within normal range. Physical examination and magnetic reso-
nance imaging of the brain and orbit revealed a 2.5 × 2 × 1.5
cm-sized right lacrimal gland mass. Computed tomography of
the neck, abdomen, and chest demonstrated no lymphadenopa-
ythy. Under the clinical diagnosis of lymphoma, orbitotomy and
mass excision were performed. Frozen section examination sug-
gested the diagnosis of extranodal marginal zone B-cell lym-
phoma of mucosa-associated lymphoid tissue (MALT). After
the surgery his vision improved without further therapy.
Case 2

A 72-year-old woman presented with bilateral painless firm eyelid masses of 1 month duration. A computerized tomography scan revealed well-demarcated ovoid masses in bilateral eyelids (Fig. 1), measuring 1.8 cm and 1.3 cm in the right and left sides, respectively, in maximal diameter. The results of full blood count, differential white blood cell count, and liver function test were all within normal range and her past medical history was insignificant. Under the clinical diagnosis of lymphoma, an excision of the left upper eyelid lesion was done. No further therapy was performed and the right eyelid mass has demonstrated no change.

Morphologic findings

Grossly, both lesions were well-encapsulated and the cut surfaces were similar to that of a lymph node except for traversed fibrous bands. Microscopically, both lesions were characterized by dense lymphoplasmacytic infiltration with scattered lym-
phoid follicles containing germinal centers, marked parenchymal atrophy and dense peri ductal and septal fibrosis (Fig. 2A-C). The normal lobular pattern of the lacrimal gland was vaguely retained. Many mature plasma cells were scattered among small lymphoid cells (Fig. 2D). There was no evidence of marginal zone cell proliferation or lymphoepithelial lesions. Eosinophil infiltration and obliterative phlebitis were not observed.

Immunohistochemical stain results

Immunohistochemical staining using monoclonal antibodies against human IgG (DakoCytomation, Glostrup, Denmark; 1:1,000) and human IgG4 (Zymed Laboratories Inc, San Francisco, CA, USA; 1:500) demonstrated abundant IgG-positive and IgG4-positive plasma cells in both lesions (Table 1, Fig. 3). The proportions of IgG4-positive/IgG-positive plasma cells were 54.4% and 72.4% for cases 1 and 2, respectively.

Table 1. Number of IgG4-positive and IgG-positive plasma cells per high-power field (HPF) and the proportion of IgG4-positive/IgG positive plasma cells in the 2 cases

<table>
<thead>
<tr>
<th>Case 1</th>
<th>IgG4 (HPF)</th>
<th>IgG (HPF)</th>
<th>IgG4/IgG (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>173</td>
<td>318</td>
<td>54.4</td>
</tr>
<tr>
<td>Case 2</td>
<td>472</td>
<td>652</td>
<td>72.4</td>
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</tbody>
</table>

Fig. 3. Immunohistochemical stains for IgG (A) and IgG4 (B) demonstrate a high proportion of IgG-positive plasma cells and IgG4-positive plasma cells (Case 2).

DISCUSSION

This report is based on two cases of a chronic inflammatory disease of the lacrimal gland with clinicopathologic similarities to CSS. CSS was originally described by Kuttner in 1896 and has also been referred as Kuttner tumor due to its usual clinical presentation as a mass lesion mimicking a salivary gland neoplasm. Although it is not an uncommon disease, pathologists sometimes experience difficulties in diagnosis because it is an under-recognized entity that rarely has been reported in the English literature.

Similar organotypic diseases occur in the lacrimal and salivary glands, probably because they share similar morphologic and physiologic features. Various types of salivary gland neoplasms commonly occur in the lacrimal glands. CSD can also be regarded as a lacrimal counterpart of CSS as the clinicopathologic findings are almost identical.

Unlike CSS, CSD has rarely been reported as a distinct entity, though lacrimal gland swelling has been described in patients with autoimmune pancreatitis or Kuttner tumor. In Korea, Roh and Kim reported a case of Kuttner tumor presenting with bilateral involvement of the lacrimal and submandibular glands. Ocular pathology textbooks currently do not contain descriptions of this disease and thus most clinicians and pathologists are not aware of its existence. Recently, Cheuk et al. described the clinicopathologic findings of 6 cases of CSD as a distinct entity for the first time. According to their data, there was a female predominance and the mean age of the patients was 45.5 years. Five cases presented as bilateral lesions and three cases were accompanied by salivary gland involvement. Two cases were associated with generalized lymphadenopathy and one patient lost her vision due to entrapment of the optic nerve by the disease process. Our two cases occurred in old patients. The first case which presented with blurred vision was a localized CSD demonstrating no other organ involvement by imaging studies. The second case presented with bilateral disease, and seemed
to be a localized CSD based on the symptoms and physical examination findings although meticulous systemic imaging studies were not performed.

The morphologic findings of CSD are distinct and a pathologic diagnosis is usually not difficult if the pathologist is aware of this entity. Although CSS and CSD share microscopic findings, phlebitis - a common feature of CSS - has been reported to be absent in CSD. Our two cases also did not show phlebitis. CSD should be differentiated from a variety of other diseases including benign lymphoepithelial lesions, Kimura’s disease, sclerosing variant of follicular lymphoma and extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue. Although these diseases can be easily excluded by the absence of distinct lymphoepithelial lesions, eosinophil infiltration, neoplastic follicles with back-to-back arrangement or marginal zone cell proliferation, frozen section diagnosis can be difficult as in our first case.

In 2005, Kitagawa et al. described for the first time that CSS, the salivary gland counterpart of CSD, belongs to a group of IgG4-related sclerosing diseases. IgG4 is the rarest IgG subclass occupying less than 6% of the total IgG fraction in the serum of normal subjects. IgG4-related sclerosing disease is a recently documented entity and a systemic disease characterized by high levels of serum IgG, lymphoplasma cell infiltration with high proportions of IgG4-positive plasma cells, sclerotic changes and good response to steroid therapy. The prototypic lesion of this entity is autoimmune (sclerosing) pancreatitis which is occasionally associated with other extrapancreatic sclerosing lesions such as sclerosing cholangitis, retroperitoneal fibrosis and sclerosing sialadenitis, and these lesions share common features of elevated serum IgG4 levels and marked IgG4-positive plasma cell infiltration. Several investigators placed all of these sclerosing lesions listed above in the spectrum of IgG4-related sclerosing disease. Recently, Cheuk et al. suggested that CSD may also be one of these lesions by demonstrating high serum IgG4 levels and abundant IgG4-positive plasma cell infiltration in their review of 6 cases of CSD. In their report, the ratio of IgG4-positive plasma cells out of IgG-positive plasma cells and the number of IgG4-positive plasma cells/HPF ranged from 44% to 99% and from 170 to 799/HPF, respectively. To confirm the validity of CSD as an IgG4-related sclerosing disease, we analyzed the numbers of IgG4-positive plasma cells and the number of IgG4-positive plasma cells/HPF in the tissue sections of our two patients and showed that IgG4-positive plasma cells occupied a high proportion of IgG-positive plasma cells. There are no established quantitative criteria regarding the level of IgG4-positive plasma cells in tissue sections for IgG4-related sclerosing disease. However, according to the report by Kitagawa et al., in the case of CSS, the proportion of IgG4-positive to IgG-positive plasma cells was significantly higher than in sialolithiasis or Sjögren’s syndrome (45.8-92.8% vs 0-4.9%), and our results belonged to the range reported by Cheuk et al. and Kitagawa et al., thus suggesting that CSD may be an IgG4-related sclerosing disease.

It has also been suggested that Mikulicz disease-defined as bilateral symmetrical swelling of more than two lacrimal and major salivary glands with histologic features of prominent mononuclear infiltration-belongs to the spectrum of IgG4-related sclerosing disease due to a high IgG4 level in serum and tissue sections. IgG4-related sclerosing diseases have shown good responses to steroid therapy. Therefore, a high index of suspicion for CSD by clinicians and an increased awareness of the existence of CSD by pathologists could avoid unnecessary aggressive surgery.

**REFERENCES**


