

Chronic Sclerosing Dacryoadenitis

- Report of 2 Cases -

Ji Eun Kwon • Sang Kyum Kim
Sang-Ryul Lee¹ • Woo-Ick Yang
Haeryoung Kim²

Department of Pathology and Brain
Korea 21 Project for Medical Science,
¹Department of Ophthalmology, Yonsei
University Health System, Seoul;
²Department of Pathology, Seoul
National University Bundang Hospital,
Seongnam, Korea

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Corresponding Author

Haeryoung Kim, M.D.
Department of Pathology, Seoul National University
Bundang Hospital, 300 Gumi-dong, Bundang-gu,
Seongnam 463-707, Korea
Tel: 031-787-7715
Fax: 031-787-4012
E-mail: hkim759@snuh.org

Chronic sclerosing dacryoadenitis is a rare and under-recognized chronic inflammatory disease 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.

Key Words : Dacryocystitis; Lacrimal apparatus

We recently experienced two cases of a chronic inflammatory condition of the lacrimal gland demonstrating clinicopathologic similarities to chronic sclerosing sialadenitis (CSS). Clinically, they presented as painless firm eyelid masses mimicking neoplastic lesions and morphologically they were characterized by prominent atrophy of acini, dense lymphoplasmacytic infiltrates with scattered germinal centers, and bands of sclerosis with preservation of lobular architecture.

Recently, Cheuk *et al.*¹ reported 6 cases of chronic sclerosing dacryoadenitis (CSD) as a distinct entity for the first time and they suggested that CSD may be part of the spectrum of IgG4-related sclerosing disease which was described by Kitagawa *et al.*² We herein report on two cases of CSD and support the theory that CSD may be a type of IgG4-related sclerosing disease by demonstrating an increased population of IgG4 positive plasma cells in the lesion.

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 insignificant 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 resonance 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 lymphadenopathy. Under the clinical diagnosis of lymphoma, orbitotomy and mass excision were performed. Frozen section examination suggested the diagnosis of extranodal marginal zone B-cell lymphoma 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 sur-

faces 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-



Fig. 1. A computerized tomography scan of case 2 demonstrates well-demarcated bilateral ovoid mass lesions in both eyelids.

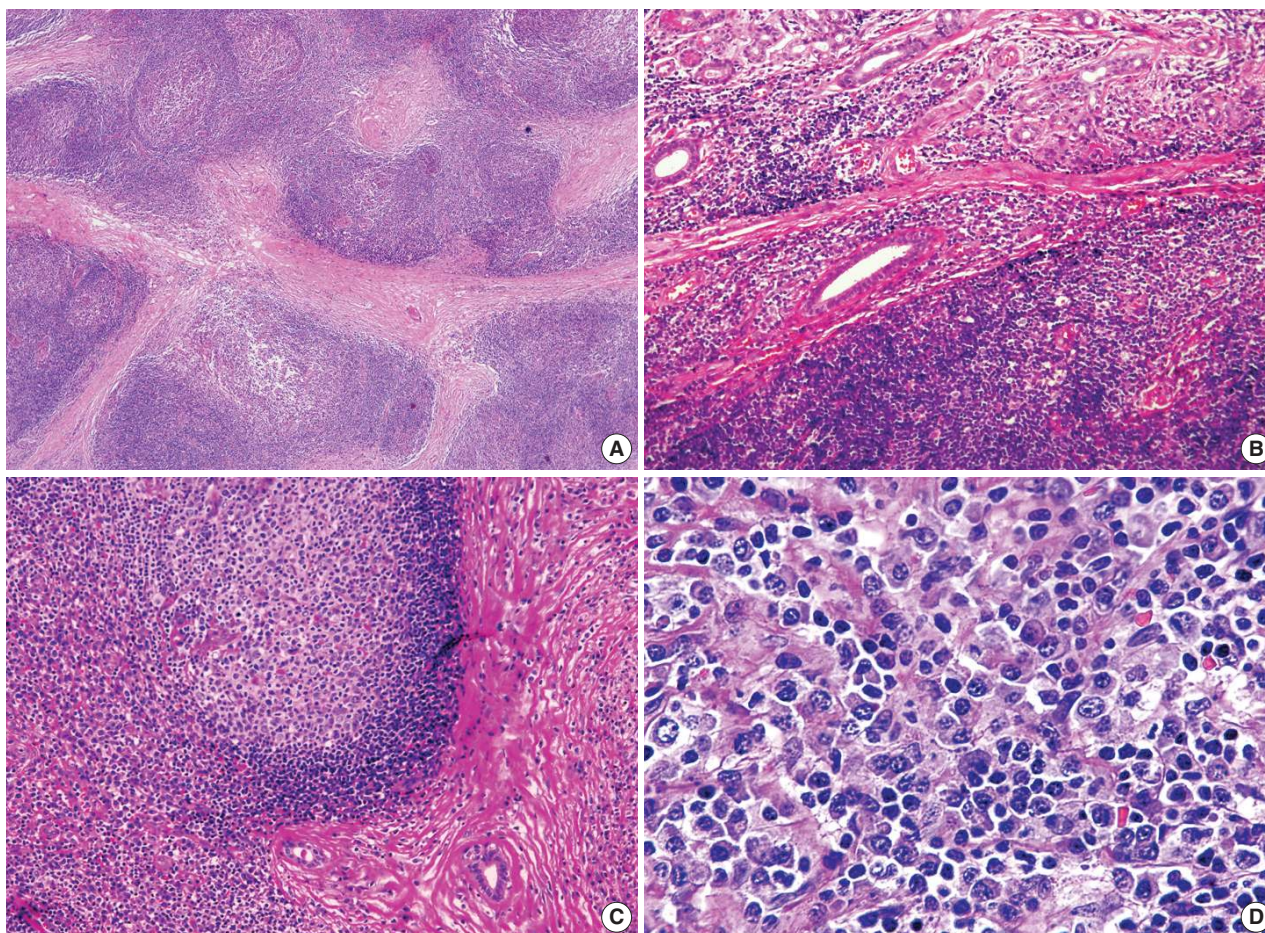


Fig. 2. (A) Low power microscopic findings of case 1 show dense lymphoplasmacytic infiltrates with scattered germinal centers, loss of acini and prominent septal fibrosis. (B) A residual lobule is seen at the periphery of the lymphoplasmacytic infiltrate on medium power microscopy of case 1. (C) Dense periductal sclerotic fibrosis and a germinal center are noted in case 2. (D) High power magnification of case 2 shows many mature plasma cells admixed with lymphocytes.

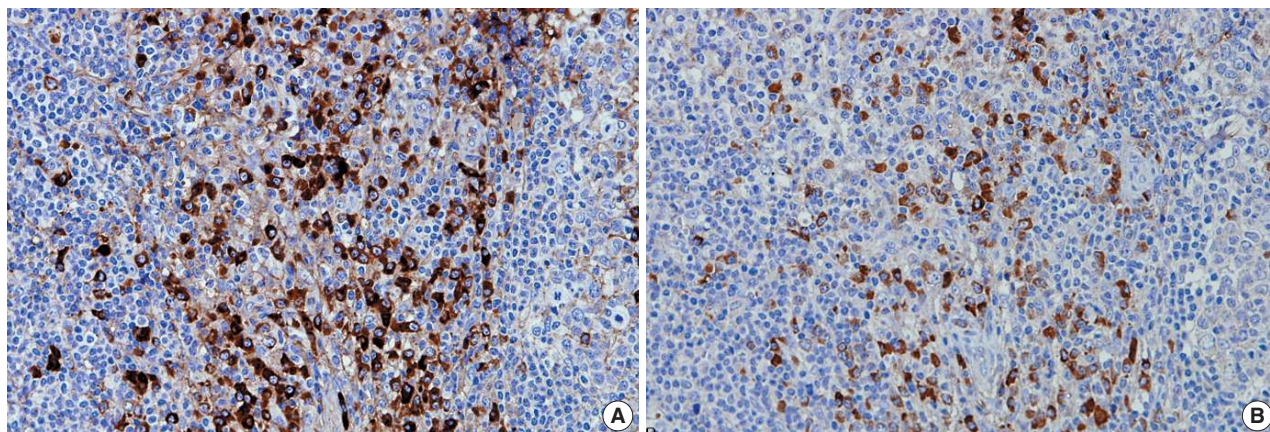


Fig. 3. Immunohistochemical stains for IgG (A) and IgG4 (B) demonstrate a high proportion of IgG-positive plasma cells and IgG4-positive plasma cells (Case 2).

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

	IgG4 (/HPF)	IgG (/HPF)	IgG4/IgG (%)
Case 1	173	318	54.4
Case 2	472	652	72.4

phoid follicles containing germinal centers, marked parenchymal atrophy and dense periductal 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.

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 Küttner³ in 1896 and

has also been referred as Küttner 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.^{4,5}

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 Küttner tumor.^{2,6-8} In Korea, Roh and Kim⁹ reported a case of Küttner 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.*¹ 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.¹ 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.*² 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.¹⁰ 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.^{7,8,11} Several investigators placed all of these sclerosing lesions listed above in the spectrum of IgG4-related sclerosing disease. Recently, Cheuk *et al.*¹ 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 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, accord-

ing to the report by Kitagawa *et al.*², 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.*¹ and Kitagawa *et al.*², 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.¹²⁻¹⁴

IgG4-related sclerosing diseases have shown good responses to steroid therapy.⁷ 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

- Cheuk W, Yuen HK, Chan JK. Chronic sclerosing dacryoadenitis: part of the spectrum of IgG4-related sclerosing disease? *Am J Surg Pathol* 2007; 31: 643-5.
- Kitagawa S, Zen Y, Harada K, *et al.* Abundant IgG4-positive plasma cell infiltration characterizes chronic sclerosing sialadenitis (Küttner tumor). *Am J Surg Pathol* 2005; 29: 783-91.
- Küttner H. Über entzündliche tumoren der submaxilla-speicheldrüse. *Bruns' Beitr Klin Chir* 1896; 15: 815-28.
- Seifert G. Tumor-like lesions of the salivary glands. The new WHO classification. *Pathol Res Pract* 1992; 188: 836-46.
- Chan JK. Küttner tumor (chronic sclerosing sialadenitis) of the submandibular gland: an underrecognized entity. *Adv Anat Pathol* 1998; 5: 239-51.
- Boccatto P, Blandamura S, Midena E, Carolla C. Orbital ectopic lacrimal gland tissue simulating a neoplasm. Report of a case with fine needle aspiration biopsy diagnosis. *Acta Cytol* 1992; 36: 737-43.
- Kamisawa T, Okamoto A. Autoimmune pancreatitis: proposal of IgG4-related sclerosing disease. *J Gastroenterol* 2006; 41: 613-25.
- Kamisawa T, Nakajima H, Egawa N, *et al.* IgG4-related sclerosing disease incorporating sclerosing pancreatitis, cholangitis, sialadenitis and retroperitoneal fibrosis with lymphadenopathy *Pancreatology* 2006; 6: 132-7.
- Roh JL, Kim JM. Küttner tumor: unusual presentation with bilateral involvement of the lacrimal and submandibular glands. *Acta Otolaryngol* 2005; 125: 792-6.
- Van der Zee JS, Aalberse RC. Immunohistochemical characteristics

- of IgG4 antibodies. *N Engl J Allergy Proc* 1988; 9: 31-3.
11. Kamisawa T, Funata N, Hayashi Y, *et al.* A new clinicopathological entity of IgG4-related autoimmune disease. *J Gastroenterol* 2003; 38: 982-4.
 12. Yamamoto M, Ohara M, Suzuki C, *et al.* Elevated IgG4 concentrations in serum of patients with Mikulicz's disease. *Scand J Rheumatol* 2004; 33: 432-3.
 13. Yamamoto M, Harada S, Ohara M, *et al.* Clinical and pathological differences between Mikulicz's disease and Sjogren's syndrome. *Rheumatology (Oxford)*. 2005; 44: 227-34.
 14. Yamamoto M, Takahashi H, Ohara M, *et al.* A new conceptualization for Mikulicz's disease as an IgG4-related plasmacytic disease. *Mod Rheumatol* 2006; 16: 335-40.