There were no corneal lesions. The dilated fundus examination findings were normal. Blood studies were negative for antinuclear antibodies and rheumatoid factors and showed a normal complete blood count and negative angiotensin-converting enzyme levels.

We diagnosed bilateral atypical Cogan syndrome in the patient. The bilateral iritis resolved with cycloplegics and topical steroid drops. The patient has been referred for a cochlear implant. He had another episode of bilateral iritis 3 months later, which also resolved with topical cycloplegic and steroid eye drops.

Case 2. A 10-year-old white boy had a history of bilateral red eyes for 1 month at initial examination. One year prior to this eye examination, he had acutely lost all of his hearing and had undergone a cochlear implant in his right ear. Visual acuity was 20/30 OD and 20/20 OS. He had bilateral iritis with posterior synechiae in the left eye. There were no corneal lesions and the dilated fundus examination findings were normal. Blood studies were performed and levels of rheumatoid factor, fluorescent treponemal antibody absorption, angiotensin-converting enzyme, and complete blood count were all normal. The iritis resolved quickly with topical dilating and corticosteroid drops. Six months later, the patient had another episode of bilateral iritis without corneal inflammation, which also resolved with topical drops. At the 2-year follow-up, there was no recurrence.

Case 3. A 13-year-old white boy had a history of red eyes off and on for the past 2 years, which were treated with topical antibiotic drops. He had lost all hearing acutely during a 2-week period 18 months previously. He had received a successful left cochlear implant. Visual acuity was 20/30 OU and bilateral iritis was present. There were no corneal lesions and the dilated fundus examination findings were also normal. Blood tests showed that levels of fluorescent treponemal antibody absorption, rheumatoid factor, complete blood cell count, and angiotensin-converting enzyme were all normal. The iritis resolved with topical cycloplegic and steroid drops. The patient had 1 recurrent episode of bilateral iritis 4 months later and now has been clear for 2 years.

Comment. Cogan syndrome mainly affects young adults but can appear from ages 3 to 40 years. Slightly more males are affected than females. The etiology is unknown, but in approximately 20% of cases, the onset is preceded by an upper respiratory infection. In 41% of cases, the eye is affected first; in 43%, the ear is affected first; and in 16% of cases, both organs are affected at the same time. The interval between ocular and ear involvement can be as short as 3 months in the typical syndrome or as long as 11 years in the atypical syndrome. Making the diagnosis of Cogan syndrome is important, not only because vision can be lost, but also because 10% of cases are complicated with aortic insufficiency, which can be life threatening. Polyarthralgias or arthritis can also accompany the disease.

Neurologic findings, such as epilepsy or encephalitis, can also be seen. Almost 90% of patients have severe hearing loss or total bilateral deafness. When deafness is not complete, high-dose corticosteroids can lead to hearing improvement in 50% of cases, but if deafness is already total, the corticosteroids do not help.

The atypical form of Cogan syndrome can be an overlooked cause of uveitis in children; the disease had been undiagnosed in our patients until their initial visit to our office. One patient had seen 9 physicians before we made the association between uveitis and sensorineural hearing loss. Many articles on pediatric uveitis do not even mention atypical Cogan syndrome as a cause of uveitis. While most cases of uveitis will not involve sensorineural hearing loss, the small percentage that will be seen with this serious complication warrants a recommendation to evaluate the patient’s hearing status when no etiology for the uveitis is found.

IgG4-Related Chronic Sclerosing Dacryoadenitis

Recent evidence suggests that Mikulicz disease is distinct from Sjögren syndrome and is an IgG4-related systemic disease. Herein we report 4 cases of Mikulicz disease in which the serum IgG4 concentrations were elevated and infiltration of IgG4-stained plasma cells with sclerosing fibrosis was pathologically observed in the lacrimal gland.

Report of Cases. Three women (aged 46, 47, and 64 years) and 1 man (aged 66 years) were referred with swelling of the lacrimal gland region (Table). Every patient had experienced a chronic episode (3 months to 5 years) of progressive eyelid swelling. The 64-year-old woman (patient 3) had a history of surgical resection of a subcutaneous mass in the upper eyelid, which was pathologically diagnosed as lymphoid hyperplasia at a different hospital 2 years prior to the initial visit. Magnetic resonance imaging depicted well-circumscribed masses including bilateral lacrimal glands in the lacrimal fossa (Figure 1). In ev-
ery patient, swelling of the salivary glands (submandibular or parotid) was also observed (Table). No patients showed symptoms or opthalmic findings of keratoconjunctivitis sicca. Laboratory data ruled out systemic diseases causative of so-called Mikulicz syndrome, such as sarcoidosis, leukemia, and lymphoma. Concentrations of the serum IgG (reference range, 870-1700 mg/dL; to convert milligrams per deciliter to grams per liter, multiply by 0.01) and IgG4 (reference range, <135 mg/dL) were obtained prior to treatment (Table). In all of the patients, the serum IgG4 concentration and the ratio of IgG4 to IgG were elevated. All of the patients underwent partial resection of the mass including the lacrimal gland.

Lacrimal glands resected from 4 cases pathologically showed severe lymphoplasmacytic infiltration with lymphoid follicles and irregular fibrosis (Figure 2). Inflammatory cells consisted of mature lymphocytes and plasma cells without any atypia. Glandular tissue was atrophied and associated with interacinar and intra-acinar sclerosing inflammation. Hyalinized dense fibrosis was also observed in cases 1 and 2 (Figure 2A and C). Immunostaining revealed that the lymphocytes were polyclonal and composed of B cells (positive for CD20 and CD79α) and T cells (positive for CD3) in all of the cases. Monoclonality was also not evident in the infiltrating plasma cells, which were composed of κ-positive cells and λ-positive cells (not shown). Immunostaining of IgG4 showed that numerous IgG4-positive plasma cells infiltrated the lacrimal glands in all of the cases (Figure 2). IgG4-positive plasma cells were commonly observed in inflammatory areas among lymphoid follicles (Figure 2D and H).

Based on these findings, we diagnosed these cases as chronic sclerosing dacryoadenitis, consistent with Mikulicz disease related to IgG4. No patients manifested evidence for IgG4-related sclerosing
disease in other organs except salivary glands. Oral prednisolone (starting at 30 or 40 mg) was administered to all but patient 2, who required the control of diabetes mellitus and had no further symptoms with the residual lacrimal glands. In the 3 patients receiving steroids, the symptoms of eyelid swelling and salivary gland enlargement improved. In addition, IgG4 levels improved after steroid treatment in 2 patients tested: 86 mg/dL in case 3 and 36 mg/dL in case 4.

Comment. Mikulicz disease is a disorder characterized by symmetrical enlargement of the lacrimal and salivary glands. Beginning with the report by Morgan and Castleman in 1953, Mikulicz disease had been considered to be a subtype of primary Sjögren syndrome owing to their resemblance pathologically. However, later studies suggested that these 2 diseases were distinctly different pathologically and clinically, ie, in Mikulicz disease, lacrimal gland acinar cells maintained their function and were not programmed for cell death. More recently, Mikulicz disease has been suggested to be a disorder involving IgG4, the rarest subclass of IgG in healthy subjects. The serum level of IgG4 is elevated in patients with Mikulicz disease and prominent infiltration of IgG4-stained plasma cells is observed pathologically, which are features not seen in Sjögren syndrome. Moreover, it has been proposed that Mikulicz disease belongs to the clinical entity IgG4-plasmacytic endocrinopathy, which includes IgG4-related sclerosing diseases such as autoimmune pancreatitis, sclerosing cholangitis, retroperitoneal fibrosis, and chronic sclerosing sialadenitis. These diseases are characterized by histopathological features that include dense lymphoplasmacytic infiltration intermixed with fibrosis, obliterator phlebitis, and prominent infiltration of IgG4-positive plasma cells. In IgG4-related chronic sclerosing sialadenitis, marked lymphoplasmacytic infiltration is associated with the destruction and atrophy of the salivary gland. These histopathological features are identical to those of the 4 cases of Mikulicz disease reported here. Another differential diagnosis would be extranodal marginal zone lymphoma of the mucosa-associated lymphoid tissue, which could, however, be excluded in all of the cases on the basis of histological and immunohistochemical findings of those lesions consisting of mature polyclonal lymphocytes and plasma cells. To our knowledge, no relationship between IgG4-related chronic inflammation and lymphoma of the mucosa-associated lymphoid tissue has been reported.

There was variability in the amount of fibrosis and destruction of acinar subunits (Figure 2). Fibro-
sis is one of the characteristic pathological findings of IgG4-related disease irrespective of the organ of origin. However, hyalized dense fibrosis as observed in cases 1 and 2 is not typical for IgG4-related diseases to our knowledge. We speculated that this difference might depend on anatomical characteristics of the lacrimal gland (eg, tightly surrounded by muscles and bone) or the duration of this disease. In addition, it is interesting that acinar subunits were considerably atrophied, although no patients showed lacrimal dysfunction such as keratoconjunctivitis sicca. Similarly, pancreas with autoimmune pancreatitis usually shows normal exocrine pancreatic function irrespective of acinar atrophy. This discrepancy has not been well documented until now, and further pathophysiologic examinations are mandatory for this issue.

In all of the cases, we performed unilateral resection of the lacrimal gland to make a diagnosis. However, surgery was also intended as part of the treatment in case 2 because steroid therapy was undesirable for the patient’s diabetes mellitus. The left eyelid swelling, his chief symptom, improved after surgery. Thus, excisions of enlarged lacrimal glands (occasionally bilateral) may be an alternative treatment for Mikulicz disease when steroid treatment is undesirable.

In conclusion, the 4 cases of Mikulicz disease reported here had chronic sclerosing inflammation of the lacrimal gland with IgG4-stained plasma cell infiltration. These findings support the theory that Mikulicz disease is within the clinical spectrum of IgG4-related sclerosing diseases.

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Spontaneous Filtration Bleb as a Consequence of Scleritis

Report of a Case. A 40-year-old woman with systemic lupus erythematosus was seen for evaluation of persistent redness and discomfort of variable intensity in the left eye during the previous 2 years. Her best-corrected visual acuity was 20/30 OD and 20/40 OS, with intraocular pressure of 10 mm Hg in the right eye and 11 mm Hg in the left eye. Slitlamp biomicroscopy showed mild dilatation of conjunctival and episcleral vessels of the right eye. The left eye demonstrated diffusely dilated episcleral vessels with a flat, superotemporal perilimbal avascular region with focal surrounding conjunctival edema. Magnetic resonance imaging performed to assess for orbital venous outflow disturbances was unrevealing. Topical corticosteroid therapy (1% prednisolone acetate) with subsequent tapering resulted in limited clinical improvement bilaterally.

At follow-up examination 2 years later, the patient reported substantial left eye pain. Visual acuity in both eyes was unchanged. Examination of the right eye demonstrated engorgement of both superficial vessels and the deeper scleral vascular plexus with a superotemporal perilimbal avascular patch (Figure 1). The left eye demonstrated apparent underly-

Figure 1. Right eye. Note engorgement of both superficial vessels and the deeper scleral vascular plexus with a superotemporal perilimbal avascular patch.