Dacryoadenitis Associated With Acanthamoeba Keratitis

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Objective: To report the incidence of dacyoadenitis as a symptom associated with Acanthamoeba keratitis.

Methods: We investigated all cases of Acanthamoeba keratitis (20 patients and 21 eyes) diagnosed and treated at Tokyo Dental College, Ichikawa General Hospital, Ichikawa, Japan, between May 1, 1994, and November 30, 2005. We recorded the incidence of dacryoadenitis diagnosed using clinical signs of lacrimal gland swelling and pain on pressure, computed tomography, magnetic resonance imaging, and histopathologic analysis.

Results: Eight eyes (38%) of 8 patients had dacyoadenitis simultaneously with Acanthamoeba keratitis. Dacryoadenitis was diagnosed using histopathologic analysis and computed tomography in 1 patient, histopathologic analysis and magnetic resonance imaging in 1, magnetic resonance imaging in 2, and clinical signs alone in 4. Histopathologic examination in 2 patients revealed moderate infiltration of lymphocytes and plasma cells in the lacrimal gland compatible with dacyoadenitis. No Acanthamoeba organisms were found in the lacrimal gland. The standard protocol for Acanthamoeba keratitis was performed without particular treatment of dacryoadenitis in all patients. Lacrimal gland swelling improved after a mean of 10 weeks (range, 4-17 weeks) in conjunction with symptoms of keratitis; however, 1 patient (patient 1) required levator muscle surgery and blepharoplasty for residual ptosis.

Conclusion: Dacryoadenitis is a clinical finding associated with Acanthamoeba keratitis.

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Acanthamoeba keratitis is associated with various clinical findings in the eye and the adnexa, including severe anterior and posterior scleritis, anterior uveitis, cataract, glaucoma, lid edema, and reactive pseudoptosis. Acanthamoeba organisms are not normally pathogens of the eye. Although an epithelial defect is necessary for infection to occur, the ability to bind to the corneal epithelium may also be a virulence factor. Once established, Acanthamoeba organisms are capable of progressive invasion into the stroma. They may eventually reach the deeper layers of the cornea and even the anterior chamber. However, to our knowledge, there have been no reports of dacyoadenitis associated with Acanthamoeba keratitis.

Dacryoadenitis is not a common disease, and it is usually caused by bacterial or viral infection. Bacteria are known to cause dacyoadenitis mainly by retrograde infection of the drainage duct; sepsis or another systemic infection may also cause dacyoadenitis. There are reports of Pseudomonas dacyoadenitis caused by lacrimal gland duct obstruction and of systemic tuberculosis or brucellosis causing bilateral or unilateral dacyoadenitis. In this article, we describe patients with dacyoadenitis who were observed to simultaneously have Acanthamoeba keratitis. The patients typically had swelling of the ipsilateral lacrimal gland, which resolved with treatment of the keratitis. Although we did not identify Acanthamoeba organisms in lacrimal tissue biopsy samples, the circumstantial evidence strongly suggests that the dacyoadenitis was caused by Acanthamoeba infection of the cornea. We propose that dacyoadenitis is another ocular symptom found in association with Acanthamoeba keratitis.

METHODS

We reviewed the medical records of 20 patients (21 eyes) with Acanthamoeba keratitis whose conditions were diagnosed and treated at Tokyo Dental College, Ichikawa General Hospital, Ichikawa, Japan, between May 1, 1994, and November 30, 2005. Acanthamoeba keratitis was diagnosed by means of slitlamp examination, corneal biopsy, or examination of contact lens preservation solution. We recorded the patient age, sex, history of contact lens wear, diagnostic method of keratitis and dacyoadenitis, stage of
corneal disease at the time of diagnosis, and therapy. Dacryoadenitis was diagnosed using signs of acute swelling and pain in the lacrimal gland, computed tomography, magnetic resonance imaging (MRI), and histopathologic examination.

**RESULTS**

**OVERALL**

Of 21 eyes diagnosed as having *Acanthamoeba* keratitis, 8 (38%) showed signs of dacryoadenitis. The 8 patients included 3 men and 5 women aged 16 to 32 years (mean age, 23 years). Four patients wore disposable soft contact lenses (DSCLs), 3 wore conventional soft contact lenses (SCLs), and 1 did not wear contact lenses (Table). Of the 4 DSCL users, 2 used 1-day DSCLs for a week (patients 2 and 8), 1 wore 2-week DSCLs extendedly (patient 5), and 1 used 2-week DSCLs (patient 6). Patient 4 belonged to a baseball club, and his conventional SCL solution was contaminated with muddy water. All the patients were otherwise healthy; patient 3 was pregnant. No patient had a medical history of other ocular disorders.

All the patients had severe ocular pain at the first examination at Ichikawa General Hospital. Visual loss was associated with corneal infiltration in 6 eyes. The mean period from the onset of subjective symptoms to examination was 7.8 weeks (range, 1-24 weeks).

Keratitis was diagnosed using corneal biopsy in 1 patient, corneal smear in 4, examination of contact lens solutions in 2, and slitlamp examination in 1 (Table). Dacryoadenitis was diagnosed by means of histopathologic examination and computed tomography in 1 patient, histopathologic examination and MRI in 1, MRI alone in 2, and clinical signs alone in the other 4. *Acanthamoeba* cysts and trophozoites were not found in lacrimal gland biopsy specimens (n=2). Clinically, all patients revealed swelling of the lacrimal gland associated with pain on pressure. Tearing was normal in all patients, who for the most part complained of increased lacrimation secondary to ocular pain.

All patients underwent the standard protocol for *Acanthamoeba* keratitis without particular treatment of dacryoadenitis. All patients were treated with antifungal eye drops, corneal epithelial debridement, and antibiotic eyedrops. All patients except patient 3 (owing to pregnancy) were treated with systemic antifungal drugs (Table). Lacrimal gland swelling improved after a mean of 10 weeks (range, 4-17 weeks) in conjunction with symptoms of keratitis. Resolution of dacryoadenitis was judged by clinical improvement in 6 patients and by MRI in 2 patients. One patient (patient 1) required levator muscle surgery and blepharoplasty for residual ptosis.

**PATIENT 1**

A 22-year-old woman experienced the onset of severe pain in the right eye associated with mild photosensitivity. She did not wear contact lenses and was originally diagnosed as having herpetic keratitis. One month later, the disease was confirmed by corneal biopsy to be *Acanthamoeba* keratitis.
patient was referred to Ichikawa General Hospital after antitherpetic therapy was not effective. Swelling and pain in the ipsilateral lacrimal gland were observed during the first examination (Figure 1A). Computed tomography confirmed swelling of the lacrimal gland. Histopathologic examination by means of lacrimal gland biopsy revealed moderate infiltration of lymphocytes in the lacrimal gland lobules compatible with dacryoadenitis. No *Acanthamoeba* organisms were found in the lacrimal gland (Figure 1B). *Acanthamoeba* cysts were found in corneal smear samples. The patient was treated for *Acanthamoeba* keratitis with antifungal eyedrops, antibiotic eyedrops, antiprotozoal eyedrops, corneal epithelial debridement, and systemic antifungal drugs. She underwent lamellar keratoplasty 9 months later for removal of residual disciform infiltration and a persistent corneal epithelial defect. *Acanthamoeba* cysts and lymphocyte infiltration were identified in the corneal stroma excised during surgery (Figure 1B, inset). There was no recurrence of *Acanthamoeba* keratitis after surgery. Three months after keratoplasty, phacoemulsification and intraocular lens implantation were performed for secondary cataract. No *Acanthamoeba* organisms were found in the lens cortex resected during surgery. Eight years after the first examination, optical penetrating keratoplasty was performed for residual corneal opacity. Although lacrimal gland swelling improved in conjunction with symptoms of keratitis, this patient underwent levator muscle surgery and blepharoplasty for the correction of residual ptosis and for cosmetic purposes.

**PATIENT 5**

A 32-year-old man experienced the onset of severe pain and visual loss in the left eye after wearing a 2-week DSCL continuously for 5 days. He was originally diagnosed as having infectious keratitis. Two days later, the patient was referred to Ichikawa General Hospital after antibiotic therapy was not effective. The left lacrimal gland showed signs of swelling simultaneously with corneal inflammation (Figure 2A). Swelling of the lacrimal gland was confirmed by means...
of MRI 1 month after the onset of symptoms (Figure 2B and C). No inflammation was observed in the surrounding tissue. The diagnosis of Acanthamoeba keratitis was confirmed by the presence of organisms in his contact lens solution. He was treated with antifungal eyedrops, antibiotic eyedrops, antiprotozoal eyedrops, chlorhexidine, corneal epithelial debridement, and systemic antifungal drugs. Two months later, keratitis and dacyroadenitis improved without any particular treatment for dacyroadenitis. Lacrimal gland swelling was no longer observed, and tearing was normal.

COMMENT

In this retrospective study, 38% of the patients with Acanthamoeba keratitis had associated signs of dacyroadenitis when first examined. All the patients with dacyroadenitis had lacrimal gland swelling and pain but did not experience dry eye symptoms. Instead, subjective tearing was increased because of pain and foreign body sensation. In this series, 2 histopathologic samples were examined, which showed moderate infiltration of lymphocytes in the lacrimal gland lobules similar to lacrimal gland biopsy samples from patients with Sjögren syndrome. However, the lobular architecture was intact in patients with Acanthamoeba keratitis, unlike the destruction of lobular tissue and intralobular fibrosis observed in patients with Sjögren syndrome.10,11

The mechanisms involved in dacyroadenitis associated with Acanthamoeba keratitis are not clear. Dacyroadenitis may be caused by direct invasion of Acanthamoeba organisms in the lacrimal gland. Although we did not obtain evidence of this in the gland, Acanthamoeba organisms are known to invade nerve fibers.12 Acanthamoeba meningoencephalitis is caused by the entry of organisms into the central nervous system through the olfactory neuroepithelium and invasion of the amyelinating nerve fibers.13 Dacyroadenitis may therefore be caused by Acanthamoeba organisms invading trigeminal nerve fibers, which are connected to nerve branches of the lacrimal gland. On the other hand, dacyroadenitis may be secondary to inflammation extending from the corneal lesion because the conditions of all patients with dacyroadenitis improved with the treatment of keratitis. We did not obtain biopsy samples after clinical improvement, and the level of residual tissue damage to the lacrimal gland is unknown. However, there does not seem to be any effect on tear function because none of the patients complained of dry eye symptoms after the episode of Acanthamoeba keratitis. Although all the patients in this series were diagnosed as having Acanthamoeba infection owing to clinical signs of keratitis, there is the possibility that Acanthamoeba dacyroadenitis may occur without signs of keratitis. This is worth considering because the incidence of dacyroadenitis was relatively high (38%) in our study. As long as the possibility of direct invasion of the lacrimal gland by trophozoites cannot be ruled out, Acanthamoeba infection should be considered as a differential diagnosis in dacyroadenitis.

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REFERENCES