Dacryoadenitis Associated With Acanthamoeba Keratitis

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Objective: To report the incidence of dacryoadenitis 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 dacryoadenitis 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 dacryoadenitis. 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 dacryoadenitis 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 dacryoadenitis mainly by retrograde infection of the drainage duct; sepsis or another systemic infection may also cause dacryoadenitis. There are reports of Pseudomonas dacryoadenitis caused by lacrimal gland duct obstruction and of systemic tuberculosis or brucellosis causing bilateral or unilateral dacryoadenitis. In this article, we describe patients with dacryoadenitis 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 dacryoadenitis was caused by Acanthamoeba infection of the cornea. We propose that dacryoadenitis 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 dacryoadenitis, 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

<table>
<thead>
<tr>
<th>Patient No./ Sex/Age, y</th>
<th>SCL Use</th>
<th>Method of Diagnosis of Keratitis</th>
<th>Method of Diagnosis of Dacryoadenitis</th>
<th>Corneal Lesion</th>
<th>Therapy</th>
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</thead>
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<tr>
<td>1/F/22</td>
<td>None</td>
<td>Biopsy</td>
<td>CT and biopsy</td>
<td>Disciform</td>
<td>TF, SF, DB, TA, AB</td>
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<td>2/F/24</td>
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<td>SCL solution</td>
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<td>Disciform</td>
<td>TF, SF, DB, CHL, AB</td>
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<tr>
<td>3/F/30</td>
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<td>Smear</td>
<td>Clinical</td>
<td>Subepithelial</td>
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<td>4/M/16</td>
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<td>MRI</td>
<td>Ring infiltrate</td>
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<tr>
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<td>Smear</td>
<td>MRI</td>
<td>Keratoneuritis</td>
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<tr>
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<tr>
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<tr>
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<td>Clinical</td>
<td>Keratoneuritis</td>
<td>TF, SA, DB, TA, CHL, AB</td>
</tr>
</tbody>
</table>

Abbreviations: AB, topical antibiotics; CHL, chlorhexidine; CT, computed tomography; DB, epithelial debridement; MRI, magnetic resonance imaging; SA, systemic antibiotics; SCL, soft contact lens; SF, systemic antifungal agents; TA, topical antiprotozoal agents; TF, topical antifungal agents.
patient was referred to Ichikawa General Hospital after antiviral 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

Figure 2. Patient 5. A, Swelling of the lacrimal gland is marked in black. Axial (B) and coronal (C) magnetic resonance images of the orbit show swelling of the lacrimal gland (arrows). No inflammation was observed in the surrounding tissue.
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 dacryoadenitis improved without any particular treatment for dacryoadenitis. Lacrimal gland swelling was no longer observed, and tearing was normal.

In this retrospective study, 38% of the patients with Acanthamoeba keratitis had associated signs of dacryoadenitis when first examined. All the patients with dacryoadenitis 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 dacryoadenitis associated with Acanthamoeba keratitis are not clear. Dacryoadenitis 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 amyoelastic submucosal nerve plexus.13,14 Dacryoadenitis 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, dacryoadenitis may be secondary to inflammation extending from the corneal lesion because the conditions of all patients with dacryoadenitis 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 dacryoadenitis may occur without signs of keratitis. This is worth considering because the incidence of dacryoadenitis 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 dacryoadenitis.

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