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A lacrimal drainage pathway disease-associated keratopathy (LDAK) case with non-infectious endophthalmitis

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ABSTRACT

Purpose: To report a case of lacrimal drainage pathway disease-associated keratopathy (LDAK) with endophthalmitis.

Observations: An 80-year-old man with diabetic retinopathy and nephropathy was referred to our hospital with endophthalmitis of the left eye. Slit-lamp examination revealed slight eye discharge, peripheral corneal ulcers, diffuse hyperemia of the conjunctiva, iris synechia, and a large amount of fibrin in the anterior chamber of the left eye. No puncta of the left eye were observed. The patient had undergone trabeculectomy for primary open-angle glaucoma 5 years previously. B-mode echo examination confirmed vitreous opacity in the left eye. We suspected endophthalmitis and performed a par-plana vitrectomy, bacterial culture, and polymerase chain reaction examination for eye discharge, aqueous humor, and vitreous humor. However, no bacteria or viruses were detected. The eye discharge and corneal peripheral ulcers did not improve following surgery. A lacrimal syringe test was performed two weeks after surgery, and bacterial concretion and discharge were observed. We detected *Actinomyces* in the bacterial concretions and performed dacryocystorhinostomy. After surgery, the corneal ulcer improved, and eye discharge disappeared.

Conclusions and importance: LDAK causes corneal perforation and endophthalmitis. In cases of intraocular inflammation with corneal ulcers, a lacrimal syringing test should be performed, even in the absence of lacrimal findings on slit-lamp examination.

1. Introduction

lacrimal drainage pathway disease-associated Keratopathy (LDAK) is characterized by non-infectious corneal ulcer (including corneal perforation) related to lacrimal drainage pathway disease.[1] According to reports, LDAK displays limited cellular infiltrations of the ulcerated area, suggesting that the ulcers in LDAK are not caused by corneal inflammation.[1–4] The most common location of corneal perforation is the nasal or inferior peripheral location of the ulcers and ocular discharge. Chronic dacryocystitis and lacrimal canaliculitis can cause lacrimal diseases.[1,4]

Bleb-related infections occur after filtration surgery following trabeculectomy or tube implant surgery in patients with glaucoma. In a prospective multicenter study, the five-year cumulative incidence of bleb-related infection was 2.2 ± 0.5 % in eyes treated with mitomycin C-augmented trabeculectomy or trabeculectomy combined with phacoemulsification and intraocular lens implantation.[5] Bleb leakage and younger age are the main risk factors for infection. A bleb-related infection is classified into stages[5], where Stage I presents with localized inflammation of the bleb, Stage II is characterized by an anterior chamber with cells, flare, or hypopyon, and Stage III includes vitreous involvement.

However, no LDAK cases with severe anterior chamber inflammation and vitreous or suspected bleb-related endophthalmitis have been reported. Herein, we report the case of a patient with LDAK who presented with severe inflammation resembling endophthalmitis.

2. Case report

An 80-year-old man with left eye endophthalmitis was referred to our hospital. He experienced a decrease in vision and an increase in discharge 3 days prior. The patient did not experience any ocular pain. He had been treated for diabetic retinopathy and had undergone panretinal photocoagulation in both eyes 2 years previously. Additionally, the patient had undergone trabeculectomy for primary open-angle glaucoma 5 years previously. He underwent dialysis 3 times per week

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for chronic renal failure due to diabetic nephropathy.

The best-corrected visual acuity was 20/40 in his right eye and 20/250 in his left eye. The intraocular pressure was 15 mmHg in his right and 23 mmHg in his left eye. Slit-lamp examination revealed conjunctival hyperemia, marginal corneal ulcers, corneal descemet's fold, iris synechia, and fibrin in the anterior chamber of the left eye (Fig. 1). A vascular bleb was observed in the left upper conjunctiva. There were no upper or inferior puncta findings on the slit-lamp examination. B-mode echo scan revealed high intensity area in the left vitreous. Blood tests showed an increase in Hemoglobin A1c of 7.5 %, similar to results from two months previously of 7.3 %. White blood cell count was 8290/μl, CRP was 0.42 mg/dl, and fasting blood sugar was 162 mg/dl. HLA-B27 and HLA-B51 were not detected in the present study.

Stage III bleb-related endophthalmitis was suspected, and a pars plana vitrectomy was performed immediately. Vitreous opacities were predominantly observed in the anterior vitreous, with no evident signs of vasculitis (Fig. 2A). Bacterial cultures were examined, and a multiplex polymerase chain reaction (PCR) test[6,7] was performed on eye discharge, aqueous humor, and vitreous samples. Microscopic examination revealed an abundance of neutrophils and a few lymphocytes in aqueous humor, and vitreous. However, neither bacteria nor viruses were detected in the bacterial culture or multiplex PCR tests nor eye discharge, aqueous humor, nor vitreous. After vitrectomy, we prescribed steroid eye drops (betamethasone sodium phosphate) and antibiotic eye drops (moxifloxacin hydrochloride) six times daily to his left eye.

After vitrectomy, the fibrin and opacity improved; however, the corneal ulcer gradually enlarged from the day after surgery. Despite eye drops, the mild ocular discharge also did not improve at all (Fig. 2B). We suspected LDAK and performed a lacrimal syringe test 7 days after the vitrectomy. An abundance of discharge and concretion refluxed and failed to pass through the nasal cavity during the lacrimal syringe tests. The bacterial culture from the concretions detected *Actinomycetes*. A dacryocystorhinostomy was performed, and approximately 10 mm of bacterial concretion from the lacrimal sac was removed (Fig. 3A and B).

After the dacryocystorhinostomy (DCR) operation, the superficial stromal opacity of the cornea persisted and the peripheral corneal ulcer and conjunctival hyperemia improved, the eye discharge disappeared, and no recurrence of the corneal ulcer was observed for 3 months (Fig. 3C and D).

The patient provided written consent for the publication of this report, including record details and photographs.

3. Discussion

Here, we reported a patient with LDAK and endophthalmitis. In the present case, fibrin was abundant in the anterior chamber. In contrast,

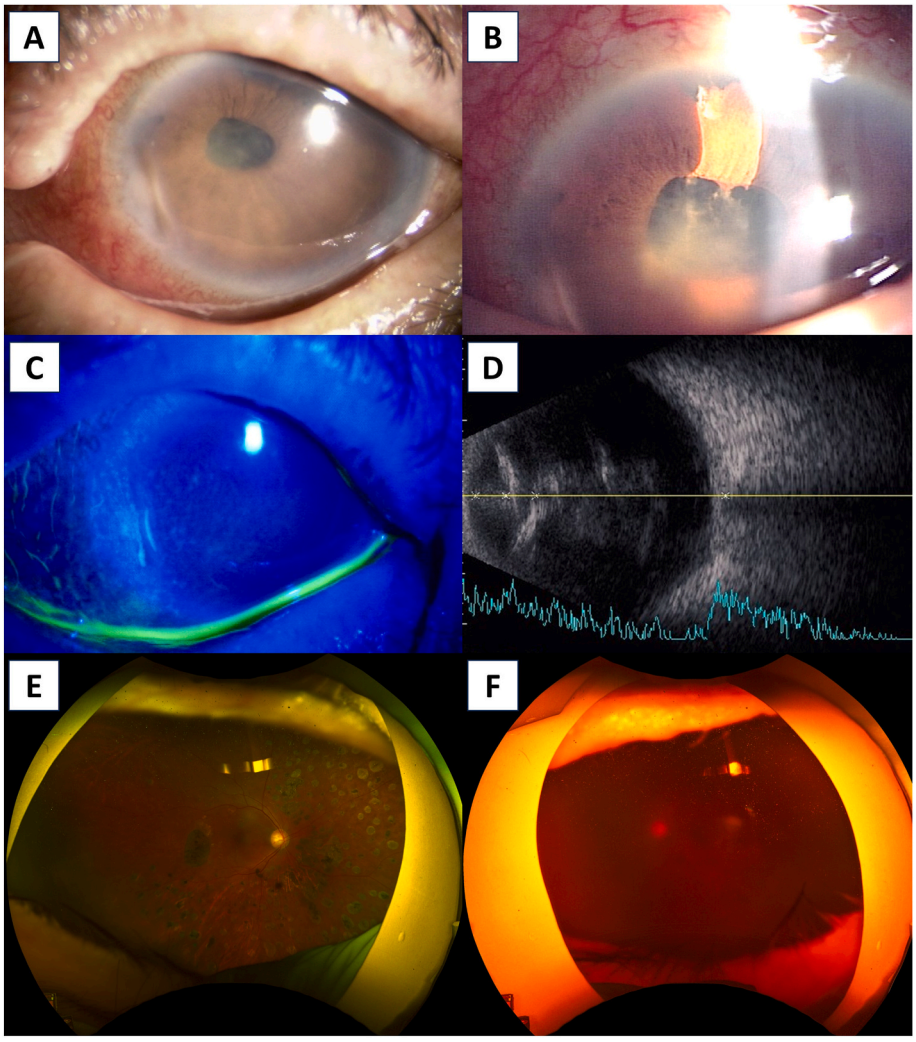

Fig. 1. Slit lamp photographs of the left cornea and conjunctiva on the first day. (A, C) The corneal ulcer was observed on the nasal side of the peripheral cornea. Diffuse hyperemia was observed at the conjunctiva. Fluorescein staining revealed punctate staining in the conjunctiva surrounding the corneal ulcer. (B) A lot of fibrin and iris synechia were observed in the anterior chamber. (D) B-mode echo reveals the opacity of the vitreous. (E,F) Fundoscopic examination of the right eye revealed scars from panretinal photocoagulation, while in the left eye, visualization was poor, with only a blurred view of the optic disc being discernible.

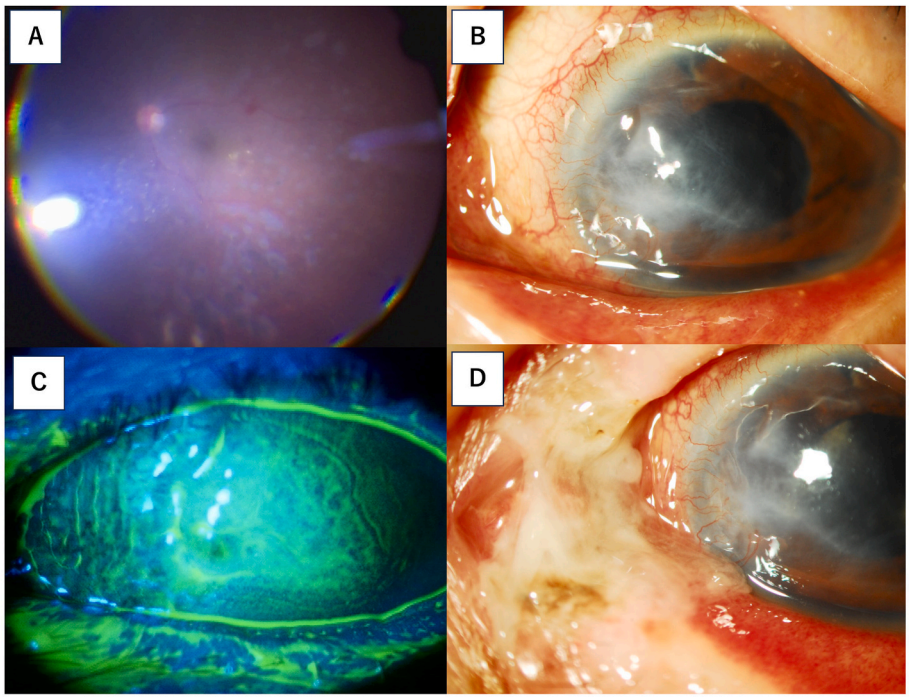

Fig. 2. Photographs during par plana vitrectomy (PPV) surgery and 7 days after.
(A) Vitreous opacities were primarily located in the anterior vitreous. Hard exudate and retinal hemorrhage due to diabetic retinopathy were seen. The retinal vessel was not occluded. (B, C) Peripheral corneal ulcer was extended after PPV. Fibrin of the anterior chamber was improved. (D) After the lachrymal syringing test, massive eye discharge was reflexed from the lacrimal pathway.

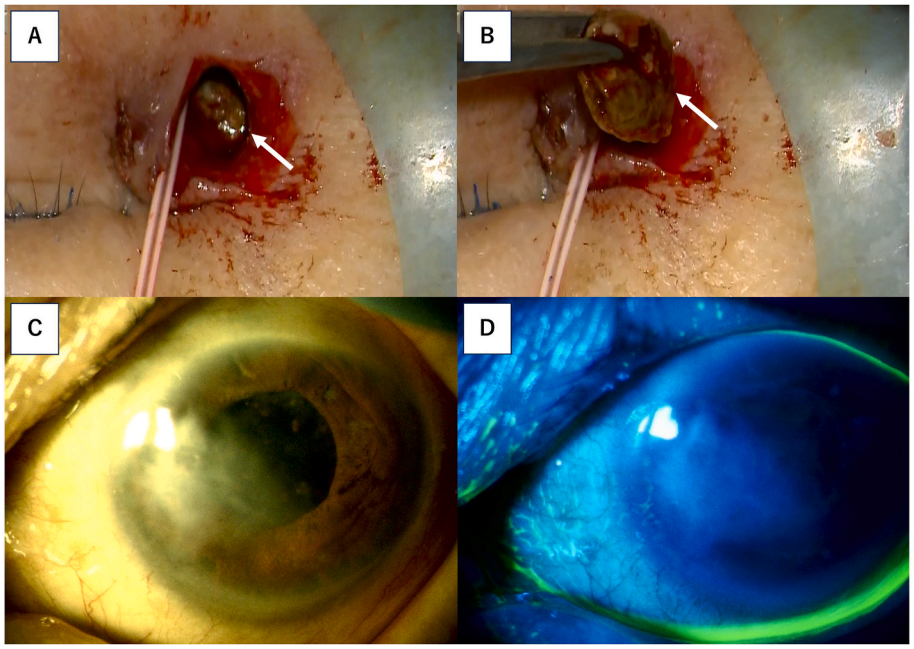

Fig. 3. Photographs of the dacryocystorhinostomy (DCR) surgery and 28 days after the DCR surgery.
(A, B) Bacterial concretion (arrows) was seen in the lacrymal sac. The size of the concretion was about 10mm. (C, D) After the DCR surgery, the superficial stromal opacity of the cornea persisted and the peripheral corneal ulcer and conjunctival hyperemia improved.

neutrophils and lymphocytes were observed in the anterior chamber and vitreous, leading to intraocular inflammation. Since the bacterial culture and PCR tests were negative for aqueous humor and vitreous humor, we speculated that intraocular inflammation was likely non-infectious in nature and that the bleb eye may have facilitated the spread of inflammation from the ocular surface to the inside of the eye.

We considered four possible causes of inflammation in the aqueous and vitreous humors. Firstly, inflammation can be derived from lacrimal drainage infection, and patients with lacrimal drainage pathway disease have been reported to show elevated levels of various inflammatory cytokines, such as interleukins and matrix metalloproteinases in the tear fluid.[8,9] In this case, we detected *Actinomyces* spp. In the bacterial concretion. *Actinomyces* spp. are commonly detected in LDAK cases.[1,4] *Actinomycetes* produce elastase, a protease, which may play a role in

melting the corneal stroma.[10] Some reports suggest that LDAK is possibly induced by toxins from the bacteria, leading to lacrimal drainage pathway disease.[2,11] We previously reported that among the 16 patients with non-infectious corneal perforation, 13 (81 %) had lacrimal drainage disease, but only three (19 %) had lacrimal puncta, as revealed by slit-lamp examinations.[4] Infection in the lacrimal pathway is often missed due to a lack of findings on slit-lamp examination, which may lead to sustained infection and elevated inflammatory cytokines. Inoue et al. reported that LDAK demonstrated limited cellular infiltrations of the ulcerated area.[1] In this case report, the patient had a history of glaucoma filtering surgery, and we speculate that inflammation may have spilled over into the eye through the bleb.

Secondly, the inflammatory changes could have been derived from uveitis, classified as infectious, non-infectious, or neoplastic. In this case, we tested the eye discharge, aqueous humor, and vitreous humor for infection by bacterial culture and multiplex PCR test (strip PCR)[7] that detected 24 common ocular infectious disease pathogens simultaneously (herpes simplex virus 1–8, syphilis, tuberculosis, toxoplasma, chlamydia, acne bacillus, Toxocara, Bartonella, Candida, Fusarium, Aspergillus, Cryptococcus, Acanthamoeba, HTLV1, adenovirus, bacterial 16S rRNA, and fungus 28S rRNA). In this case, no pathogens were detected in the bacterial culture or multiplex PCR test of the aqueous humor, vitreous humor, and eye discharge. This patient did not meet the diagnostic criteria for sarcoidosis and Bechet syndrome; however, the possibility of diabetic iritis could not be ruled out. Glyceraldehyde-derived advanced glycation end-products are highly toxic and play an essential role in the pathogenesis of chronic inflammatory diseases.[12] Although it is possible that the reduction of inflammatory cytokines and inflammatory mediators by surgery and subsequent steroid treatment improved intraocular inflammation, the corneal lesion worsened and developed an enlarged periocular ulcer rather than a prolonged epithelial defect, which is an atypical outcome. The patient also exhibited relatively good glycemic control.

Third, the inflammation changes could have originated from a bleb-related infection. Bleb leakage is the leading risk factor for infection.[5] and diabetes has been reported to be a risk factor for late endophthalmitis.[13] Risk factors for bleb leakage, general conjunctival thinning, reduced cellularity, and avascular blebs have been reported,[13] but were not observed in our patient. No pathogen was detected in the bacterial culture or multiplex PCR test from the aqueous and vitreous humors; therefore, we considered the possibility of bleb-related infection low.

Fourth, lacrimal pathway infection was occurred after vitrectomy. Post-vitrectomy, an *Actinomyces* infection occurred in the lacrimal sac, and it was possible that the steroid eye drops administered after the vitrectomy exacerbated the infection. However, the size of the bacterial concretion exceeded 2 cm, making it unlikely that it grew to this extent within one week after vitrectomy. It has been reported that bacterial concretion cultures mostly contained less pathogenic *Actinomycete species*.[14] Since the corneal ulcer showed no signs of improvement and progressively worsened after the vitrectomy, we speculate that the bacterial concretion had formed in the lacrimal sac prior to the vitrectomy, and that the postoperative steroid eye drops may have enhanced the activity of the *Actinomyces*.

For complete removal of concretions, canalicular debridement in the form of canaliculotomy is the mainstay of treatment and is more effective than medical therapy.[15] In this case, bacterial concretion was about 10 mm, so extracting from the lacrimal puncta was difficult. We opted for DCR for the extracted bacterial concrete and treated the nasolacrimal obstruction. Another treatment option for bacterial removal is lacrimal endoscopy with curettage.[15,16]

4. Conclusions

LDAK can cause not only corneal ulcers and perforations but also intraocular inflammation. Herein, we report a case of LDAK with endophthalmitis-like characteristics. Therefore, if atypical corneal ulcer or intraocular inflammation is observed, a lacrimal syringe test should be performed even if there are no findings of tear ducts on slit-lamp examination.

CRediT authorship contribution statement

Sho Ishikawa: Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Takafumi Maruyama:** Resources, Data curation. **Kei Shinoda:** Writing – review & editing, Validation, Supervision, Project administration, Formal analysis.

Patient consent

The patient's legal guardian provided written consent for the publication of the case.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

The authors have no conflict of interest.

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References

1. Inoue H, Toriyama K, Ikegawa W, et al. Clinical characteristics of lacrimal drainage pathway disease-associated keratopathy. *BMC Ophthalmol*. 2022;22(1):353. https://doi.org/10.1186/s12886-022-02580-y.
2. Cohn H, Mondino BJ, Brown SI, Hall GD. Marginal corneal ulcers with acute beta streptococcal conjunctivitis and chronic dacryocystitis. *Am J Ophthalmol*. 1979;87(4):541–543. https://doi.org/10.1016/0002-9394(79)90246-0.
3. Nitta K, Mukai R, Todokoro D, Akiyama H. Lacrimal duct obstruction and infection associated with non-traumatic corneal perforation: a case series. *Int Med Case Rep J*. 2022;15:313–322. https://doi.org/10.2147/IMCRJ.S363034.
4. Ishikawa S, Sasaki T, Maruyama T, Shinoda K. Proportion and characteristics of lacrimal drainage pathway disease and keratopathy in non-infectious corneal perforation using lacrimal syringing test. *Sci Rep*. 2023;13(1), 19734. https://doi.org/10.1038/s41598-023-47248-9.
5. Yamamoto T, Sawada A, Mayama C, et al. The 5-year incidence of bleb-related infection and its risk factors after filtering surgeries with adjunctive mitomycin C: collaborative bleb-related infection incidence and treatment study 2. *Ophthalmology*. 2014;121(5):1001–1006. https://doi.org/10.1016/j.ophtha.2013.11.025.
6. Mochizuki M, Sugita S, Kamoi K, Takase H. A new era of uveitis: impact of polymerase chain reaction in intraocular inflammatory diseases. *Jpn J Ophthalmol*. 2017;61(1):1–20. https://doi.org/10.1007/s10384-016-0474-9.
7. Nakano S, Tomaru Y, Kubota T, et al. Evaluation of a multiplex strip PCR test for infectious uveitis: a prospective multicenter study. *Am J Ophthalmol*. 2020;213:252–259. https://doi.org/10.1016/j.ajo.2019.10.031.
8. Lee JK, Kim TH. Changes in cytokines in tears after endoscopic endonasal dacryocystorhinostomy for primary acquired nasolacrimal duct obstruction. *Eye*. 2014;28(5):600–607. https://doi.org/10.1038/eye.2014.33.
9. Woo SE, Jang SY. Matrix metalloproteinase-9 point-of-care immunoassay after dacryocystorhinostomy in patients with nasolacrimal duct obstruction. *Semin Ophthalmol*. 2021;36(3):128–131. https://doi.org/10.1080/08820538.2021.1889619.

10. Ishikawa S, Kato N. A case with corneal perforation due to bacterial concretion derived from lacrimal canaliculitis. *Am J Ophthalmol Case Rep*. 2018;9:116–118. https://doi.org/10.1016/j.ajoc.2018.01.004.
11. Yokogawa H, Kobayashi A, Yamazaki N, Masaki T, Sugiyama K. Surgical therapies for corneal perforations: 10 years of cases in a tertiary referral hospital. *Clin Ophthalmol*. 2014;8:2165–2170. https://doi.org/10.2147/OPTH.S71102.
12. Dong Z, Iwata D, Kitaichi N, et al. Amelioration of experimental autoimmune uveoretinitis by inhibition of glyceraldehyde-derived advanced glycation end-product formation. *J Leukoc Biol*. 2014;96(6):1077–1085. https://doi.org/10.1189/jlb.3A0513-288RRR.
13. Lehmann OJ, Bunce C, Matheson MM, et al. Risk factors for development of post-trabeculectomy endophthalmitis. *Br J Ophthalmol*. 2000;84(12):1349–1353. https://doi.org/10.1136/bjo.84.12.1349.
14. Perry LJ, Jakobiec FA, Zakka FR. Bacterial and mucopeptide concretions of the lacrimal drainage system: an analysis of 30 cases. *Ophthalmic Plast Reconstr Surg*. 2012;28(2). https://doi.org/10.1097/IOP.0b013e31824c88a6, 126-123.
15. Pal SS, Alam MS. Lacrimal canaliculitis: a major review. *Semin Ophthalmol*. 2024: 1–9. https://doi.org/10.1080/08820538.2024.2354689.
16. Okajima Y, Suzuki T, Miyazaki C, et al. Metagenomic shotgun sequencing analysis of canalicular concretions in lacrimal canaliculitis cases. *Curr Issues Mol Biol*. 2021;43 (2):676–686. https://doi.org/10.3390/cimb43020049.