Investigation of the clinical features in filamentary keratitis in Hangzhou, east of China

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Abstract

Filamentary keratitis (FK) is a chronic and recurrent disorder of the cornea. FK is reportedly associated with various kinds of ocular surface diseases or conditions. Until now, there have been lacks of studies based on quantitative sample analysis concerning FK incidence regularity and inducement characteristics at different ages. This was a retrospective study of 147 patients (162 eyes) with FK who had been continuously and completely recorded from August 2012 to August 2015 at the Second Affiliated Hospital of Zhejiang University in Hangzhou, east of China. Our results suggest that the causative factors of FK varied at different ages and the distribution of filaments on the corneal surface was also diverse with different inducements.

By exploring the frequency and clinical features of FK, we believe that the findings from our research will be clinically significant and aid in the early prevention and treatment guidance of the disease.

Abbreviations: AQD = aqueous tear-deficient, FK = filamentary keratitis, GVHD = graft-versus-host disease, PKP = penetrating keratoplasty, RA = rheumatoid arthritis, SLE = systemic lupus erythematosus, SS = Sjogren syndrome, TFBUT = tear film breakup time.

Keywords: conjunctivitis, dry eye, filamentary keratitis, keratitis

1. Introduction

Filamentary keratitis (FK) is a chronic and recurrent disorder of the cornea and, rarely, the conjunctiva. Patients with FK generally experience a foreign body sensation, chronic pain, tearing, mucoid discharge, photophobia, and blepharospasm. To date, reported studies regarding filaments are limited to basic pathologic examinations. However, the exact pathogenesis of FK remains unknown. FK is reportedly associated with various kinds of ocular surface diseases or conditions such as dry eye, exposure keratitis, keratoconjunctivitis, brain stem injury, postcataract surgery, penetrating keratoplasty (PKP), recurrent erosion, prolonged eye patch use, prosis, and large-angle strabismus. Until now, there have been lacks of studies based on quantitative sample analysis concerning FK incidence regularity and inducement characteristics at different ages. In this study, we explored the causative factors and various distributions of FK in different groups.

2. Materials and methods

2.1. Objects

According to slit-lamp microscope examination, anterior segment photographs, and computer-based patient records, a retrospective study was conducted on patients with FK. These findings were evaluated in terms of sex, age, causative factor, treatment history, and the location and number of filaments. The patients had been continuously and completely recorded from August 2012 to August 2015 at the Ophthalmology Clinic of the Second Affiliated Hospital of Zhejiang University, which was a general research hospital in Hangzhou, east of China. The inclusion criteria were those eyes with excessive abnormal mucous debris and tenacious mucus strands or plaques, which were often several millimeters long and attached to the cornea. Observation indices included the quantity of the filaments and their distribution. The positions of the filaments on the corneal surface were divided into the interpalpebral zone, corneal limbus, corneal damage or suture site, and total cornea.

2.2. Methods

Each patient was examined with a slit-lamp microscope and photographed with an anterior segment camera. Corneal fluorescein staining and tear film breakup time (TFBUT) were also performed on each patient. The patients were divided into 3 age groups: 0 to 25 years (group A), 26 to 50 years (group B), and 51 to 81 years (group C).
The patients were also assigned into 3 different groups according to the cause of the FK (dry eye and exposure keratitis group, autoimmune diseases and ocular inflammation group, and surgery and chemical injury of the eye group). These latter groups were assigned in order to investigate the different locations of filaments distributed on the corneal surface.

2.3. Management

After a topical anesthetic was applied in the lower conjunctiva fornix of the eye, the filaments were removed using cotton swabs moistened with saline. The patients were also prescribed preservative-free artificial tears. In addition, we gave different treatments for various causative factors: patients with exposure keratitis were given tarsorrhaphy; patients with allergic conjunctivitis were prescribed topical antihistaminics; those with dry eyes were given topical nonsteroidal anti-inflammatory or topical low concentrations of steroids; patients with viral keratitis were given topical antiviral drugs; those who had ocular surgical procedures, chemical injury, or autoimmune disease were prescribed topical high concentrations of steroids and oral steroids; and patients with refractory or severe stimulating symptoms after surgery were given a bandage contact lens with topical and oral steroids. Dosage adjustments may have been needed based on the severity of the disease.

2.4. Statistical analysis

Data were presented as the mean and standard deviation or frequencies. The categorical data were analyzed by chi-square tests. P values of <0.05 were considered statistically significant.

3. Results

Patient details are summarized in Table 1. A total of 147 patients (162 eyes) were included in this study, ranging in age from 6 to 81 years old (mean: 43.54±18.58 years). All patients had symptoms of foreign bodies in the eyes. There were 28 eyes in group A, 74 eyes in group B, and 60 eyes in group C. FK was found to be involved in both eyes in 15 patients. Among these 15 patients, 11 cases were caused by autoimmune factors, 2 by allergic conjunctivitis, 1 by dry eye, and 1 case was caused by ocular surgery. The causative factors inducing FK included allergic conjunctivitis, nonautoimmune forms of dry eye, viral keratitis, exposure keratitis, ocular surgeries, chemical injury, and autoimmune diseases.

In group A, 15 eyes (53.57%) with FK were caused by allergic conjunctivitis. In groups B and C, FK caused by dry eye were found in 33 cases (44.59%) and 24 cases (40.00%), respectively. The detailed causative factors of FK included 16 eyes with allergic conjunctivitis, 62 with dry eye, 28 with viral keratitis, 3 with exposure keratitis, and 19 with ocular surgical procedures or chemical injuries. Other causative factors included 34 eyes with autoimmune diseases including graft-versus-host disease (GVHD) (9 eyes), Sjogren syndrome (SS) (19 eyes), rheumatoid arthritis (RA) (4 eyes), and systemic lupus erythematosus (SLE) (2 eyes).

FK induced by allergic conjunctivitis in group A was significantly higher than the other 2 groups (15/28 vs 1/74, 15/28 vs 0/60) (P < 0.001, P < 0.001). However, FK cases caused by dry eye and autoimmune disease among group A patients were much lower than the other 2 groups (5/28 vs 33/74, 5/28 vs 24/60 and 1/28 vs 19/74, 1/28 vs 14/60) (P = 0.013, P = 0.040 and P = 0.012, P = 0.046). FK caused by surgery and chemical injury in group C was significantly higher than the other 2 groups (14/60 vs 1/28, 14/60 vs 4/74) (P = 0.046, P = 0.002). The findings of FK due to viral keratitis were not significantly different among the 3 groups (P > 0.05).

The filament locations are summarized in Table 2. The filaments of 52 eyes (80.00%) were restricted to the exposed interpalpebral zone (Fig. 1) in the dry eye and exposure keratitis group. The filaments of 41 eyes (52.56%) were distributed in the corneal limbus (Fig. 2) in the autoimmune factors and ocular inflammation group. The filaments of 8 eyes (42.11%) were distributed in the corneal damage or suture site (Fig. 3) in the surgery and chemical injury of the eye group.

In most cases, filaments disappeared, and fluorescein staining of corneal epithelial shedding became negative within a month of treatment. The treatment effect in the cases due to exposure keratitis or ocular surgical procedures was good. However, the treatment effects in the cases due to severe dry eye or autoimmune diseases were not ideal because, while the filaments decreased, the disease course was long (6 months–3 years).

4. Discussion

FK was most often caused by dry eye, especially aqueous tear-deficient (AOD) dry eye. Both autoimmune and nonautoimmune forms of AQD dry eye can give rise to corneal filaments. Other conditions associated with FK include viral keratitis, ocular surgical procedures (cataract surgery, PKP, and large-angle strabismus), recurrent erosion, neurotrophic keratopathy, vernal keratoconjunctivitis, prolonged use of an eye patch, and ptosis, among others.[5]

The FK induced by allergic conjunctivitis in group A was significantly higher than the other 2 age groups. The members of group A were at their childhood and youth stages, thus, their immune systems might be much more vulnerable to the influence of the external environment. Due to more severe atmospheric pollution, the incidence of allergic conjunctivitis is getting higher among others.[6,7] According to the literature, allergic conjunctivitis is often accompanied by dry eye, with an incidence of 62.5% to 83.3%. Symptom overlap was demonstrated in many of the patients. Of all the patients with itchiness, 57.7% had clinically significant dryness. Another 45.3% of patients with dry eyes had

| Table 1 | Causative factors of filamentary keratitis among different age groups (eyes n [%]). |
|---------|---------------------------------------------------------------------------------|
| Age, y  | Eyes | Allergic conjunctivitis | Dry eye | Viral keratitis | Exposure keratitis | Ocular surgical or injury | Autoimmune diseases |
| 0–25    | 28   | 15 (53.57) | 5 (17.86) | 6 (21.43) | 0 (0) | 1 (3.57) | 3 (3.57) |
| 26–50   | 74   | 1 (1.35) | 33 (44.59) | 14 (18.92) | 3 (4.05) | 4 (5.41) | 19 (25.68) |
| 51–81   | 60   | 0 (0) | 24 (40.00) | 8 (13.33) | 0 (0) | 14 (23.33) | 14 (23.33) |
| Total   | 162  | 16 (9.88) | 62 (38.27) | 28 (17.28) | 3 (1.85) | 19 (11.73) | 34 (20.99) |
a clinically significant itch. Among the patients with apparent
redness, 61.9% had itchiness and 49.4% had dryness.[8–10]
Allergic conjunctivitis could cause tear film instability in eyes.
With the development of the disease and ocular surface damage, a
combination of all of these factors can cause an increased
instability of the tear film. Moreover, tear film instability will
exacerbate ocular surface damage, thus possibly resulting in a
vicious cycle.[11] As a result, the repair of the corneal epithelium
may be delayed and FK will eventually occur.
The FK caused by nonautoimmune forms of dry eye in group A
was much lower than the other 2 age groups. Patients in groups B
and C were more likely to develop dry eyes because of daily
activities including long-term contact lens wear, smoking, extended
visual tasks with computers or mobile phone use, television
watching, and prolonged reading. Furthermore, other
factors that exacerbate dry eyes include being in an indoor
environment and air pollution. These factors lead to excessive
tear evaporation[12], they destroy the balance of the tear film
components and affect the stability of the tear film. These
changes can cause decreases in anti-inflammatory cytokines[13]
and increases in proinflammatory cytokines,[14] thus promoting
ocular surface inflammation. Meanwhile, with aging, the glands
and cells that secrete tears gradually decrease and degenerate.
Thus, FK will ultimately occur because of the reduced tear
production and component changes. Also, the FK due to
autoimmune forms of dry eye in group A was much lower than
the other 2 groups. The major autoimmune disease that caused
FK was GVHD among group A. In addition to GVHD, the ocular
manifestations of other autoimmune diseases including SLE, RA,
and SLE would be gradually present with aging in the other
2 groups. Because of systemic immune dysfunctions, inflamma-
tion in the lacrimal functional unit causes dysfunction and even
death of the tear-secreting epithelium in the lacrimal gland and
conjunctiva that alters tear composition and stability.[15]
Eventually this can contribute to FK.

The FK caused by surgery and chemical injury of the eyes in
group C was significantly higher than the other 2 age groups.
With aging, tear production is reduced and the number of people
who undergo cataract or pterygium surgery gradually increases.
It takes a period of time to recover the composition and
production of the tear film and the healing of the corneal wound
because of the inflammation from surgical stimulation. For these
reasons, they are likely to lead to FK during this period.
In this study, the filaments of 52 eyes (80.00%) were restricted to
the exposed interpalpebral zone in the dry eye and exposure keratitis
because of the exposure keratitis group. The first part of the ocular surface involvement generally
occurs in the exposed interpalpebral zone, among the nonautoim-
mune forms of dry eye and exposure keratitis because tear secretion
and TFBUT decreases. It is also characterized histologically by
ocular surface inflammation, abnormal production of ocular surface
mucins, alterations of epithelial morphology, and premature corneal
epithelial exfoliation.[16] The fragile, inflamed, and poorly lubricated
ocular surface epithelia in these patients are more susceptible to the
shearing forces of the lid. Eventually, this makes filaments distribute
in the interpalpebral zone. The filaments of 41 eyes (52.56%) were
distributed in the corneal limbus in the autoimmune factors and
ocular inflammation group. The corneal limbal tissue is vulnerable
to the impact of the attacks caused by lymphocytes, antibodies, and
complements that reach the corneal limbus through the circulatory
system. Meanwhile, autoimmune diseases, which often involve the
lacrimal gland, conjunctival goblet cells, and other tissues, could
cause dry eyes that further reduce the speed of restoration of the
corneal epithelium in the corneal limbus. Ultimately, it makes
filaments distribute in the corneal limbus. The filaments of 8 eyes
(42.11%) were distributed in the corneal damage or suture site from
surgery and chemical injury of the eyes group. Ocular surgery and
injury can destroy the nerve plexus beneath the corneal epithelium,
which may decrease the sensitivity of the cornea and TFBUT.[17,18]
Moreover, mechanical injury from surgical instrumentation,
chemical injury, and postoperative suture irritation could cause

| Table 2 |
| Locations of filaments among different groups (eyes n [%]). |
| Causative factors | Eyes (n) | Exposed interpalpebral zone | Corneal limbus | Corneal damage or suture site | Entire cornea |
|-------------------|---------|-----------------------------|----------------|-----------------------------|--------------|
| Dry eye and exposure keratitis | 65 | 52 (80.00) | 3 (4.62) | 2 (3.08) | 8 (12.31) |
| Autoimmune factors and ocular inflammation | 78 | 7 (8.97) | 41 (52.56) | 10 (12.82) | 20 (25.64) |
| Ocular surgery and injury | 19 | 6 (31.58) | 2 (10.53) | 8 (42.11) | 3 (15.79) |

![Figure 1](image1.png)

**Figure 1.** Filaments were restricted in the exposed interpalpebral zone caused by nonautoimmune forms of dry eye.

![Figure 2](image2.png)

**Figure 2.** Filaments were distributed in the corneal limbus due to viral keratitis.
inflammation that releases inflammatory mediators.[19,20] All of these factors may contribute to corneal epithelial damage, resulting in slow epithelial healing, and ultimately, causing filaments to develop in the corneal damage or suture site. By exploring the frequency and clinical features of FK, we believe that the findings from our research will be clinically significant and aid in the early prevention and treatment guidance of the disease.

References
[1] Gumus K, Lee S, Yen MT, et al. Botulinum toxin injection for the management of refractory filamentary keratitis. Arch Ophthalmol 2012;130:446–50.
[2] Tanioka H, Yokoi N, Komuro A, et al. Investigation of the corneal filament in filamentary keratitis. Invest Ophthalmol Vis Sci 2009;50:3696–702.
[3] Lv H, Liu Z, Li X, et al. Effect of lacrimal plugs combined with deproteinized calf blood extract eye gel for filamentary keratitis. J Ocul Biol Dis Infor 2010;3:134–40.
[4] Actis AG, Rolle T. Ocular surface alterations and topical antiglaucoma therapy: a review. Open Ophthalmol J 2014;8:67–72.
[5] Albuza J, Sanfilippo P, Troutbeck R, et al. Management of filamentary keratitis associated with aqueous-deficient dry eye. Optom Vis Sci 2003;80:420–30.
[6] Celik T, Turkoğlu EB. Comparative evaluation of olopatadine 0.01% combined fluorometholone 0.01% treatment versus olopatadine 0.01% combined ketorolac 0.4% treatment in patients with acute seasonal allergic conjunctivitis. Curr Eye Res 2014;39:42–6.
[7] Kumah DB, Larrey SY, Yemany F, et al. Prevalence of allergic conjunctivitis among basic school children in the Kumasi Metropolis (Ghana): a community-based cross-sectional study. BMC Ophthalmol 2015;15:69.
[8] Hom MM, Nguyen AL, Bielory L. Allergic conjunctivitis and dry eye syndrome. Ann Allergy Asthma Immunol 2012;108:163–6.
[9] Kim TH, Moon NJ. Clinical correlations of dry eye syndrome and allergic conjunctivitis in Korean children. J Pediatr Ophthalmol Strabismus 2013;50:124–7.
[10] Dogru M, Nakagawa N, Tetsumoto K, et al. Ocular surface disease in atopic dermatitis. Jpn J Ophthalmol 1999;43:53–7.
[11] Li K, Liu X, Chen Z, et al. Quantification of tear proteins and sPLA2-IIa alteration in patients with allergic conjunctivitis. Mol Vis 2010;16:2084–91.
[12] Gayton JL. Etiology, prevalence, and treatment of dry eye disease. Clin Ophthalmol 2009;3:405–12.
[13] Narayanan S, Redfern RL, Miller WL, et al. Dry eye disease and microbial keratitis: is there a connection? Ocul Surf 2013;11:75–92.
[14] Grosskreutz CL, Hickey HU, Serra D, et al. Dry eye signs and symptoms persist during systemic neutralization of IL-1β by canakinumab or IL-17A by secukinumab. Cornea 2013;34:1551–6.
[15] Piluggleider SC. What causes dryness in Sjögren’s syndrome patients and how can it be targeted? Expert Rev Clin Immunol 2014;10:425–7.
[16] Ueda K, Matsumiya W, Otsuka K, et al. Effectiveness and relevant factors of 2 % rebamipide ophthalmic suspension treatment in dry eye. BMC Ophthalmol 2013;15:58.
[17] Cho YK, Kim MS. Dry eye after cataract surgery and associated intraoperative risk factors. Korean J Ophthalmol 2009;23:65–73.
[18] Belmonte C, Acosta MC, Gallar J. Neural basis of sensation in intact and injured corneas. Exp Eye Res 2004;78:513–25.
[19] Guo S, Li S, Liu L. Early changes in ocular surface and tear inflammatory mediators after small-incision lenticule extraction and femtosecond laser-assisted laser in situ keratomileusis. PLoS One 2014;9:e107370.
[20] Denoyer A, Landman E, Trinh L. Dry eye disease after refractive surgery: comparative outcomes of small incision lenticule extraction versus LASIK. Ophthalmology 2015;122:669–76.