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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 erythematous, 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.[1] To date, reported studies regarding filaments are limited to basic pathologic examinations. However, the exact pathogenesis of FK remains unknown.[2] 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, ptosis, and large-angle strabismus.[3] 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 examinations, 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).

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Study approval: This study was conducted according to the principles expressed in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of the 2nd Affiliated Hospital, School of Medicine, Zhejiang University in China. All participants provided written informed consent for the collection of samples and subsequent analyses.

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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 eyes 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 antiallergic agents; 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 combined 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 erythematous (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 eyes 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 (AQD) dry eye. Both autoimmune and nonautoimmune forms of AQD dry eye can give rise to corneal filaments.[4] 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 because the conjunctiva is in direct contact with air pollutants.[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)	1 (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)

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)

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 SS, RA, and SLE would be gradually present with aging in the other 2 groups. Because of systemic immune dysfunctions, inflammation 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 group. The first part of the ocular surface involvement generally occurs in the exposed interpalpebral zone among the nonautoimmune 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

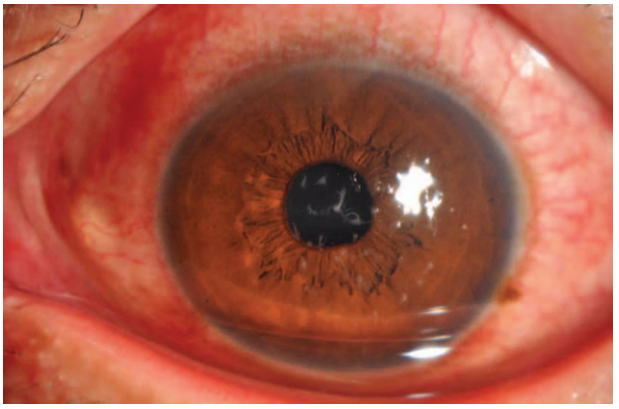

Figure 1. Filaments were restricted in the exposed interpalpebral zone caused by nonautoimmune forms of dry eye.

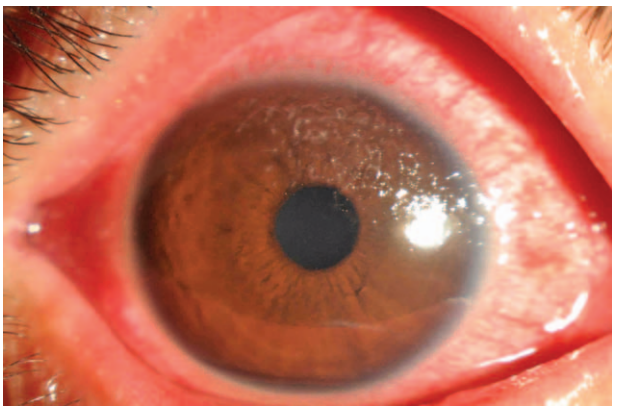

Figure 2. Filaments were distributed in the corneal limbus due to viral keratitis.

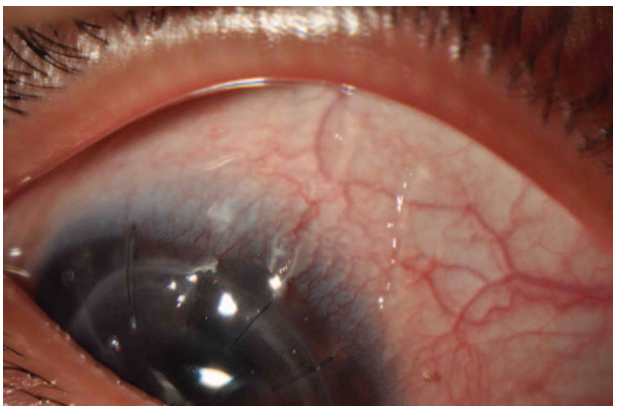

Figure 3. Filaments were distributed in the corneal suture site after penetrating keratoplasty.

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.

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