J Vet Clin 27(6) : 751-754 (2010)

Journal of Veterinary Clinics
www.ksvc.or.kr

A Case of Feline Proliferative Eosinophilic Keratitis Treated by Topical Cyclosporine and Corticosteroids

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(Accepted: December 08, 2010)

Abstract : A 6-year-old spayed female Persian cat presented with a 3-month history of recurrent ulcerative keratitis with noticeable opacification and vascularization of the right cornea. The lesion was nonresponsive to topical antibiotics and to nonsteroidal anti-inflammatory drugs. Ophthalmic examination showed signs of ocular discomfort, such as epiphora and blepharospasm, in the right eye. Biomicroscopic examination revealed an irregular, edematous, vascularized mass with pink to white tissue on the entire cornea and mild conjunctivitis. A tentative diagnosis of feline proliferative eosinophilic keratitis (FPEK) was made on the basis of clinical appearance. Cytologic examination of the cornea showed a mixture of numerous eosinophils and mast cells, which confirmed the original diagnosis of FPEK. The cat was treated with a topical antibiotic-corticosteroid combination, cyclosporine ointment, trifluridine eye drops, and oral L-lysine. The clinical signs improved remarkably 18 days after the cat was first examined. The short-term use of corticosteroids and long-term use of cyclosporine and an anti-viral agent resolved the lesion without recurrence of the disease for 1 year.

Key words **:** cat, corneal cytology, cyclosporine, feline proliferative eosinophilic keratitis.

Introduction

Feline proliferative eosinophilic keratitis (FPEK) is a slowly progressive keratopathy of unknown etiology (13). The lesion is often unilateral, but usually progresses to affect both eyes if not treated or if improperly treated. In most cases, early manifestations are shown in the dorsotemporal limbus (15). As the lesion progresses, an irregular-shaped and vascularized mass with white to pink corneal plaques is observed (10,13,15). The disease tends to appear more often in young to middle-aged castrated males. Clinical signs do not usually improve with topical antibiotic treatment only. A tentative diagnosis of FPEK is made based on the appearance of characteristic lesions, pattern of progression, and treatment history. Cytologic identification of non-keratinized squamous epithelial cells, eosinophils, mast cells, neutrophils, eosinophilic granules, and nuclear debris in the cornea typify FPEK (10,13,14). FPEK is thought to be caused by a chronic hypersensitive immune response to feline herpesvirus (FHV-1)-an antigen that plays an initial role in the pathogenesis of the disease (10,12,15).

The recommended primary treatment of FPEK is topical corticosteroids (10,13,14,15). The frequency of corticosteroid application to the lesion is tapered for several weeks on the basis of the therapeutic response (5,9). Recurrence of the manifestation is common after cessation of steroid treatment. Recent studies have shown that topical cyclosporine is effective against FPEK (5,15). Concurrent treatment of the underlying FHV-1 infection with antiviral and anti-inflammatory agents is strongly suggested on the basis of previous studies (5,11,15). This case report indicates that recurrent keratitis in cats should be diagnosed on the basis of both clinical appearance and corneal cytologic findings. In addition, concurrent treatment of FPEK with topical corticosteroids and cyclosporine is also useful.

Case

A 6-year-old spayed female Persian cat was referred to the Veterinary Medical Teaching Hospital of Seoul National University. The cat had a 3-month history of recurrent ulcerative keratitis in the right eye. The cat had previously been treated with topical antibiotics and nonsteroidal anti-inflammatory drugs (NSAIDs) at a local veterinary clinic, but no laboratory tests had been conducted. Despite this treatment, the lesion worsened.

Ophthalmic examination of the right eye indicated blepharospasm, epiphora, and absence of the menace response; the pupillary light reflex was not evaluated because of extensive infiltrated corneal plaques. Intraocular pressure was estimated with an applanation tonometer (Tono-Pen XL®; Medtronic Ophthalmics, FL, USA) to be 5 and 8 mmHg in the right and

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left eyes, respectively. After both eyes were stained with fluorescein sodium ophthalmic strips (Fluorescein Paper®; Haag-Streit AG, Köniz, Switzerland), the extent of staining was evaluated in a dark room with a direct ophthalmoscope using a cobalt blue filter. Only the cornea in the right eye retained the stain on its surface, but retention of the fluorescent dye on the corneal surface was probably due to the irregular shape of the cornea and not to a corneal ulcer.

The biomicroscopic examination revealed an irregular edematous vascularized mass with pink to white tissue on the entire cornea and mild conjunctivitis in the right eye (Fig 1A). Small proliferative foci of the dorsolateral perilimbal cornea were present in the left eye (Fig 1B). A tentative diagnosis of FPEK was made on the basis of the characteristic appearance of the corneal lesion. The right cornea was scraped with the edge of a scalpel blade for cytological evaluation. The cytologic findings showed a mixture of numerous eosinophils and eosinophil granules, which confirmed the tentative diagnosis of PFEK (Fig 2).

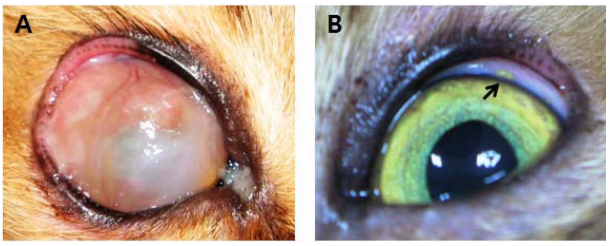

Fig 1. Clinical features of a 6-year-old spayed female Persian cat with feline proliferative eosinophilic keratitis (FPEK). Irregular and raised white to pink plaques are evident on the vascularized corneal surface of the right eye (A). Note the small foci (black arrow), which indicate early manifestation of FPEK in the dorsolateral perilimbal cornea of the left eye (B).

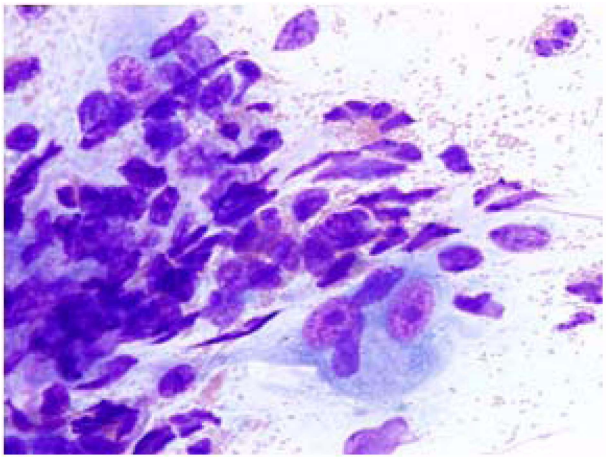

Fig 2. Photomicrograph of right corneal scrapings stained with Diff-Quik®. Numerous eosinophils and rod-shaped eosinophil granules are present.

Initial treatment of both the right and left eyes consisted of a topical combination of antibiotics and corticosteroid: Maxitrol® QID (Alcon-Couvreur NV, Belgium), the cyclosporine ointment Opticare® BID (Cipla, Mumdai, India), and trifluridine QID (Ocuflidine®; Samil, Seoul, Korea). Oral treatment with 250 mg/kg L-lysine BID (Viralys®; Buena, NJ, USA) was also initiated.

Seven days after treatment began, the lesion in the right cornea improved significantly (Fig 3A). Both the edema and the size of the plaques in the cornea decreased remarkably. As a result, menace response was present in the right eye. Because of these clinical improvements, trifluridine treatment was discontinued. However, fluorescein staining indicated the presence of corneal ulcerations in the right eye. Hence, the topical antibiotics-corticosteroid combination treatment was changed to a topical antibiotic (Ecolicin® QID; Tae Joon, Seoul, Korea) plus cyclosporine ointment. Treatment of the left eye was discontinued because of resolution of the lesion.

The cat was reexamined on day 18, at which time the clinical signs had improved markedly (Fig 3B). Both eyes were negative on fluorescein staining. After the lesion was considered to be in remission, the topical antibiotic treatment was decreased to TID for 2 weeks, and the cyclosporine ointment treatment was decreased to SID. On day 95, the lesion was completely resolved (Fig 3C) and all treatments were discontinued.

Discussion

FPEK is an infiltrative and progressive corneal disease in cats. Initially, the lesions typically present as single or multiple focal, raised pink plaque resembling granulation tissue in the peripheral area (2,3,5,9,10,13). In advanced cases, superficial vascularization and stromal infiltration are observed in

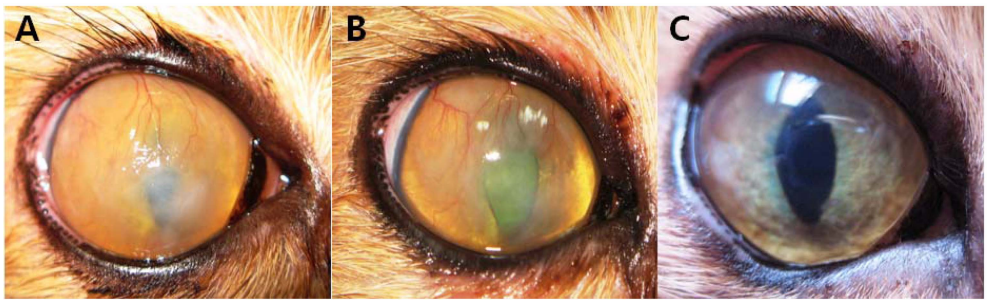

Fig 3. Healing process of right eye. A: Day 7. B: Day 18; the thick granulation tissue decreased significantly. C: Day 95; the lesions fully resolved without recurrence.

the entire cornea. Corneal ulceration is also possible in the affected eye, and conjunctival involvement is common.

FPEK is usually suspected when there is a history of no response to topical and/or systemic antibiotic treatment in combination with the characteristic appearance of lesions (6). According to one retrospective study, approximately 80% of FPEK cases are unilateral (10). Frequently, one eye is affected first and then the second eye shows signs several months later. Bilateral lesions usually occur when treatment of the initial lesion is ineffective (13).

FPEK in the current case was typical in several aspects. First, on the basis of the cat's medical history, the initial lesion occurred in the perilimbal region of the cornea of the right eye. Second, the lesion in the right eye did not respond to 3 months of treatment with topical antibiotics and NSAIDs. Finally, a lesion developed in the left eye that had typical initial manifestations of FPEK. All of these findings were completely consistent with previous reports (5,6,9,10,13,15) of the manifestation of FPEK.

Cytologic examination of corneal scrapings from whitish and raised lesions is a valuable tool for diagnosing FPEK (9,14). The presence of eosinophils, eosinophilic granules, and mast cells is considered to indicate a diagnosis of FPEK (10,13,14). In this case, corneal scrapings of the right eye showed numerous eosinophils and an elevated number of mast cells.

FPEK is characterized by a chronic lesion with an underlying hypersensitivity reaction to an unknown antigenic stimulus (8,14). Detection of FHV-1 with immunofluorescent antibody and polymerase chain reaction (PCR) suggests that the virus plays an initial role in the pathogenesis of the disease (10,12). FHV-1-DNA was detected by PCR in 76.3% of the corneal scrapings from cats with FPEK, but in only 5.9% of corneal scrapings from healthy cats (12). Hence, even though neither immunofluorescent antibody nor PCR was used in the current case, anti-viral drugs, topical trifluridine, and oral supplementation of L-lysine were used.

FPEK is usually treated initially with a topical corticosteroid, because of its efficacy as an immunosuppressive agent (8,10,12,14). The frequency of topical treatment with corticosteroids is tapered, depending on the symptoms (1,11,16). However, the treatment of FPEK with topical corticosteroids has three disadvantages. First, because the frequency of application decreases gradually, clinical signs can recur. Eosinophilic lesions have been reported to recur in 65.5% of cases (10). Second, lesions may not respond to corticosteroid therapy. In such cases, systemic administration of megestrol acetate can be considered (2,5,8,10,13). However, megestrol acetate should be used with caution because its use is associated with various complications, such as mammary hyperplasia, diabetes mellitus, and mammary neoplasia (4). Last, the long-term use of topical corticosteroids increases the risk of activation and latent infection of FHV-1 (11,15). Because of these disadvantages, cyclosporine A has been studied as an alternative treatment.

Cyclosporine A acts as an immunosuppressant with a selective inhibiting effect on T-helper and T-cytotoxic lymphocytes (15). Cyclosporine A is used in a number of immune-mediated ocular diseases in dogs, including keratoconjunctivitis sicca, chronic superficial keratitis (pannus), and plasmacytic conjunctivitis (7,15). A few reports on the treatment of eosinophilic keratitis with topical cyclosporine have been published. One study reported that 31 of 35 cats with a diagnosis of FPEK improved after treatment with topical cyclosporine (15). Because FHV-1 may be associated with eosinophilic keratitis (12), concurrent treatment with antivirals during the use of immunosuppressive agents, such as topical corticosteroids and cyclosporine, is strongly suggested (5,12,15).

In this case, initial treatment with a combination of topical antibiotics and a corticosteroid, cyclosporine ointment with trifluridine eye drops, and oral L-lysine supplementation dramatically diminished corneal stromal infiltration and vascularization. One week after initial treatment, the lesions showed sustained improvement with only topical cyclosporine and antibiotics, even though topical corticosteroid therapy was discontinued. The right corneal lesion completely resolved in 8 weeks (Fig 3C). The lesions were rechecked periodically by contacting and receiving photographs from the owner. The lesions have not recurred for 1 year.

Conclusion

A 6-year-old spayed female Persian cat presented with a 3-month history of recurrent ulcerative keratitis that was nonresponsive to topical antibiotics and NSAIDs. FPEK was confirmed by clinical signs and cytology of right corneal scrapings. After treatment with topical corticosteroids, cyclosporine ointment, and antiviral agents, the lesions improved remarkably. This case report indicates that recurrent keratitis in cats should be diagnosed on the basis of both clinical signs and corneal cytologic results. Early concurrent treatment with topical corticosteroids and cyclosporine is a useful therapy for FPEK.

Acknowledgements

This study was supported through the BK21 Program for Veterinary Science and the Research Institute for Veterinary Science, College of Veterinary Medicine, Seoul National University, Korea.

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고양이 증식성 호산구성 각막염에서 국소적인 사이클로스포린과 코르티코스테로이드 점안 1례

안정택 · 정만복 · 김세은 · 박영우 · 김태현 · 안재상 · 이소라 · 이창우 · 서강문[1]

서울대학교 수의과대학

요 약 : 6 년령 중성화 암컷 페르시안 고양이가 3개월동안 우안의 재발성 각막궤양, 각막혼탁, 각막 혈관화를 주증상으로 내원하였다. 병변은 그 기간동안 국소적인 항생제와 비스테로이드성 소염제 점안에 치료반응이 없었다. 우안에서 유루증, 안검경련과 같은 안구통증 증상이 확인되었다. 미세 틈새등 현미경 검사에서 우안의 각막 전체에 분홍색에서 흰색을 띄는 부종성의 불규칙한 덩어리와 미약한 결막염을 확인하였다. 임상증상을 통해 고양이 증식성 호산구성 각막염으로 잠정 진단하였다. 각막의 세포학적 검사결과에서 다수의 호산구와 비만세포가 관찰되어 잠정적으로 내렸던 진단을 확진하였다. 본 환자는 국소적인 항생-코르티코스테로이드 합제, 사이클로스포린 연고, 트리플루리딘 점안과 전신적인 L-lysine 의 경구투여로 치료하였다. 치료시작 18일 후 내원 시 병변은 눈에 띄게 호전되었다. 국소적인 코르티코스테로이드와 사이클로스포린의 병용치료는 고양이 증식성 호산구성 각막염에 유용한 치료법으로 생각된다.

주요어 : 고양이, 각막 세포학적 검사, 사이클로스포린, 고양이 증식성 호산구성 각막염