

Unusual Neutrophil Infiltration Under the Soft Contact Lens in a Patient with Behçet's Disease

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Background: Behçet's disease (BD) characterized by multisystemic disorders has many kinds of ocular involvement. We report one case of BD with unusual neutrophil infiltration under a soft contact lens (SCL).

Case: A 31-year-old woman diagnosed as having BD exhibited bilateral recurrent phlyctenular keratitis and finally developed corneal perforation in the cornea of her right eye.

Observations: A therapeutic SCL was immediately fitted on the right cornea as a bandage and another SCL on the left, as prophylaxis. White gelatinous membrane suddenly appeared between the bandage SCL and the cornea in the left eye. After peeling off this gelatinous membrane from the cornea, we examined it after hematoxylin-eosin staining. We also measured the levels of interleukin-8 (IL-8) both in the tears of the patient and on the surface of the SCL. A great amount of neutrophils had infiltrated into this gelatinous membrane. Laboratory data showed a marked increase of IL-8 levels both on the SCL and in the reflex tears (right SCL, 4980 pg/mL; left SCL, 6810 pg/mL. Reflex tears: right, 2080 pg/mL; left, 2170 pg/mL).

Conclusion: This case emphasizes the association between the IL-8 level and the disease activity in BD, and provides additional evidence that a BD attack can be induced on the ocular surface under certain conditions. **Jpn J Ophthalmol 2003;47:469–472** © 2003 Japanese Ophthalmological Society

Key Words: Behçet's disease, interleukin-8, neutrophil.

Introduction

Behçet's disease (BD) is a multisystemic disorder characterized by recurrent oral aphthae, skin lesions, eye lesions, and genital ulcerations. While the main ocular involvement lies in uveitis, a keratitis varying from superficial punctate keratitis to recurrent corneal ulcerations or circumscribed stromal opacities, that may become vascularized, may be occasionally found.¹ Corneal manifestations in BD usually have been treated with topical corticosteroids. Previous reports indicated that corneal ulceration in BD is uncommon and corneal perforation is most unusual.^{1,2} In this paper, we presented a case of BD in which phlyctenular keratitis developed into corneal perforation despite intensive therapy. In addition, we observed quite unusual neutrophil infiltrations between the

cornea and the soft contact lens (SCL) serving as a bandage.

Case Report

A 31-year-old Japanese woman with bilateral eye pains was referred to our clinic. She exhibited oral and genital ulcerations, erythema tuberculatum and panuveitis, and was diagnosed as having BD according to the international BD diagnosis criteria.³ On first admission in November 1999, her vision both OD and OS was 20/200. By slit-lamp examination we found white marginal infiltrations with vascularization on bilateral corneas and slight aqueous flare and cells (Figures 1A, 1B). Findings of the extensive microbiologic examinations of the ocular surface were negative. Though fundus examination in detail was difficult, slight optic atrophy and sheathed and attenuated vessels in both retinas could be observed. Systemic colchicine and cyclosporine along with topical antibiotics and betamethasone were applied for the treatment of keratitis and panuveitis. With this treatment the

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iritidocyclitis improved; however, keratitis with infiltrating ulcers developed and gradually spread onto the central corneas. Finally, corneal perforation occurred in the right eye in June 2000 (Figures 1C, 1D).

A therapeutic SCL was immediately placed on the right cornea to protect it during the blinking action of the lids. A bandage SCL was also placed on the left cornea

as prophylaxis because the left cornea also had become thinned in the central area and an epithelial defect was observed. Ten days later, a white gelatinous membrane suddenly appeared between the bandage SCL and the cornea in the left eye (Figures 1E, 1F). To the best of our knowledge, this phenomenon has not been reported elsewhere. After peeling off this gelatinous membrane

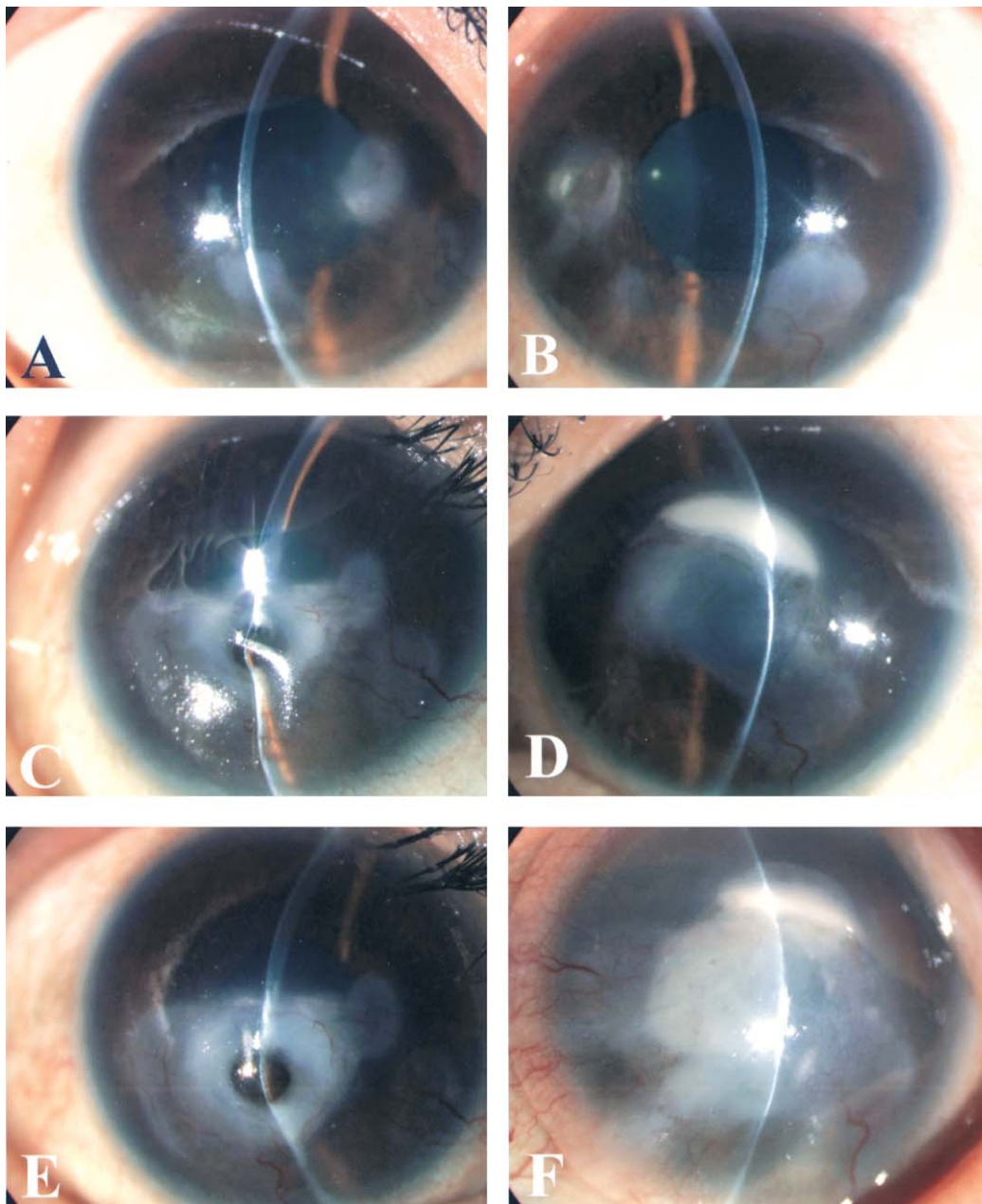


Figure 1. Slit-lamp photographs in eyes of Behcet's patient with recurrent bilateral phlyctenular keratitis. (A), (C), (E) : right cornea. (B), (D), (F) : left cornea. (A), (B) : At first examination, November 1999, white marginal infiltrations with vascularizations were found in both corneas. (C), (D) : Corneal perforation occurred in the right eye, June 2000. (E), (F) : Ten days later a white, gelatinous membrane appeared between the soft contact lens and the cornea in the left eye.

from the cornea, we examined it with ematoxylin-eosin staining and found a great amount of neutrophils there, just as seen in an hypopyon attack in BD (Figures 2A, 2B). We also measured the levels of interleukin-8 (IL-8), a neutrophil chemoattractant chemokine, both in tears of the patient and on the SCL. SCL samples were prepared by soaking the SCL and eluting the samples with 100 μ L saline. Reflex tear samples were obtained directly from the conjunctival sac. Laboratory data showed a marked increase of IL-8 levels both on the SCL and in the reflex tears (right SCL, 4980 pg/mL; left SCL, 6810 pg/mL. Reflex tears: right eye, 2080 pg/mL; left eye, 2170 pg/mL) when compared to a previous report.⁴ We also performed anterior fluorescein angiography to evaluate the vasculitis activity in the infiltrated neovascular vessels on the cornea, and we observed fluorescein dye leakage from the neovascular vessels (Figure 2C).

Bandage SCL on both corneas and topical and systemic medical treatment were continued. We did not observe the appearance of the white gelatinous membrane between the SCL and cornea thereafter. One month later, when keratitis became inactive, the IL-8 level in the sample from the SCL on the left cornea was 771 pg/mL (Figure 2D).

Discussion

As a hydrophilic SCL has the potential to accumulate proteins on the ocular surface, IL-8 on the SCL should be highly concentrated compared to that in the tears. Since it was technically difficult to evaluate the IL-8 level on the SCL, the data on the SCL IL-8 level might be underestimated. This concentrated IL-8 on the SCL seemed to attract a great amount of neutrophils from infiltrated neovascular vessels on the cornea. We speculate that the infiltrating neovascular vessels may be the suppliers of these neutrophils because we observed fluorescein dye leakage from these vessels at the central cornea.

Recently, Al-Dalaan et al reported that the elevated level of IL-8 in serum correlated with disease activity in BD.⁵ They indicated that the range of IL-8 level in active BD patients with ocular lesions was from 980 to 6,000 pg/mL and that the range in normal controls was below 100 pg/mL. Concerning tears, Nakamura et al reported that the IL-8 level of reflex tears in healthy controls was about 280 pg/mL.⁴ Although these previous data suggested that the IL-8 levels in tears may be higher than

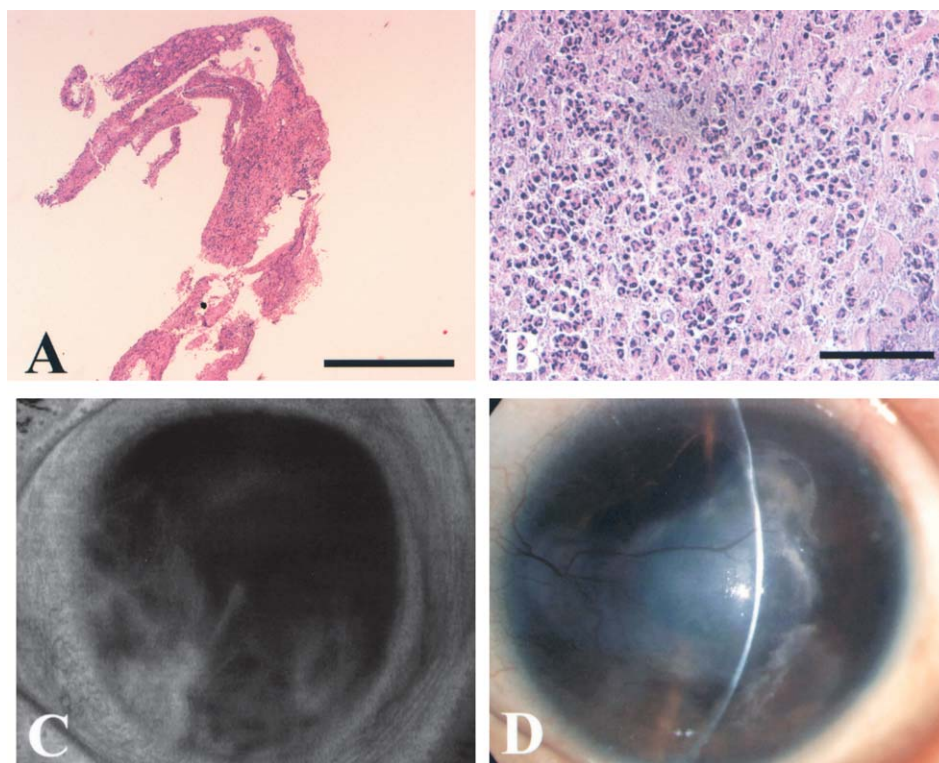


Figure 2. (A) : Histological examination of the membrane. A great amount of leukocyte infiltrations were observed. Hematoxylin and eosin (H&E) stain. Bar = 500 μ m. (B) : Infiltrated cells were found to be predominantly neutrophils in magnified vision. H&E stain. Bar = 50 μ m. (C) : Anterior fluorescein angiograph of the left cornea, 4 minutes, 20 seconds after dye injection, showing leakage from the neovascular vessels. (D) : slit lamp photograph of the left cornea one month later when keratitis had subsided.

that in serum, the tear IL-8 level in our case was obviously higher when keratitis was active and dramatically decreased when keratitis had subsided. This suggests that the IL-8 level in tears may also correlate with disease activity in BD, especially disease activity at the anterior segment of the eye.

The reason why this unusual neutrophil infiltration occurred only in the left cornea, not in the right, still remains unclear. One possibility is that the right cornea was perforated and, therefore, the SCL on the right cornea must have contained the aqueous humor, which has been reported to have immunosuppressive and modulatory factors,⁶ resulting in inhibition of the neutrophil infiltration.

While the hypopyon attack in BD is well known, this case indicates that the attack on the ocular surface can be induced under certain conditions: keratitis with neo-

vascularization, the use of SCL as bandage, and an elevated IL-8 level in the tears.

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