Clinical Case Report

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Unique circumferential peripheral keratitis in relapsing polychondritis

A case report

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Abstract

Rationale: Relapsing polychondritis (RP) is a rare collagen disease characterized by inflammation and destruction of cartilage throughout the body. The paper details the clinical course of a case of RP with unique circumferential peripheral keratitis.

Patient concerns: A 54-year-old Japanese woman was referred to the hospital presenting with auricular and ocular pain.

Diagnoses: Based on the auricle biopsy results and the three presenting symptoms (bilateral auricular chondritis, inflammatory arthritis and ocular inflammation), her condition was diagnosed as RP.

Interventions: The three presenting symptoms gradually improved with prednisolone (PSL), methylprednisolone and cyclophosphamide combination therapy, followed by PSL, methotrexate and infliximab combination therapy. However, one month after the initial visit, despite ongoing treatment, a unique circumferential peripheral keratitis suddenly occurred, in which the corneal infiltration gradually clumped together and shrank at the peripheral area. The eye and ear pain showed exacerbations and remissions on reducing the dosage of steroid drugs. The general condition was improved on altering systemic therapy to PSL, methotrexate and tocilizumab.

Outcomes: Keratitis gradually disappeared within 10 months of the initial visit.

Lessons: This is the first report of a case of RP causing unique circumferential peripheral keratitis. This keratitis occurred despite use of focal and systemic steroids and showed improvement with general recovery. This may indicate that stabilization of general condition is important for recovery from keratitis in RP.

Abbreviations: ANCA = anti-neutrophil cytoplasmic antibody, CRP = C-reactive protein, NSAIDs = nonsteroidal anti-inflammatory drugs, PSL = prednisolone, RP = relapsing polychondritis, WBC = white blood cells.

Keywords: peripheral keratitis, relapsing polychondritis, tocilizumab

1. Introduction

Relapsing polychondritis (RP) is a rare collagen disease characterized by inflammation and destruction of cartilage throughout the body. While the etiology of RP is not fully understood, immunologic mechanism is thought to play an important role in pathogenesis.[1,2] Autoantibodies to collagen type II, IX, and XI contained in sclera, cornea, and cartilage and the cartilage-specific protein matrilin-1 have been reported to correlate with disease activity.[3] McAdam et al[4] first set out clinical criteria for RP in a prospective study of 23 cases and a review of 136 reported cases. These criteria require the presence of pathological identifiers and 3 or more of the following 6 clinical features: bilateral auricular chondritis, nonerosive seronegative inflammatory arthritis, nasal chondritis, audio vestibular damage, respiratory tract chondritis, and ocular inflammation.[4]

Ocular complications, proptosis, lid edema, episcleritis/scleritis, iridocyclitis, retinopathy, optic neuritis, and keratitis have been reported to occur in about 50% of patients with RP.[5–7] However, little is known about the clinical manifestation of keratitis, and to our best knowledge, circumferential peripheral keratitis has not been reported in RP. The present paper details a case of RP with unique circumferential peripheral keratitis, which showed improvement with recovery in general condition.

2. Methods

We report the observational case report. The committee waived the requirement for approved the study for this single case study with medical records. Informed consent was given.

3. Case report

A 54-year-old Japanese woman was referred to the hospital, presenting with auricular and ocular pain. Before coming to the hospital, she had reported a 2-week history of auricular pain,

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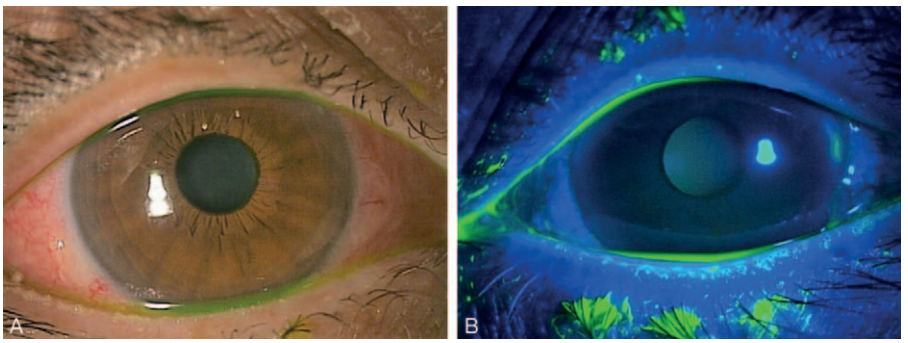

Figure 1. Slit-lamp photographs of the cornea (A) with fluorescein stain (B), showing dilation of conjunctiva and scleral vessel with no keratitis and no cells in the anterior chamber.

swelling, and redness in her right ear and was prescribed nonsteroidal anti-inflammatory drugs (NSAIDs) and varacyclovil medication at the otolaryngology clinic. She then developed conjunctivitis in the right eye, and the ophthalmology clinic started her on gatifloxacin and bromfenac eye drops. However, the auricular pain, swelling, and redness in her right ear remained and had spread to her left ear. Suspecting systemic disease, the otolaryngology clinic referred her to the hospital. She had no significant prior ear or ocular disease.

On her first hospital visit, she showed auricular pain, swelling, and redness in both ears, sore throat, lower left rib pain, edema of the eyelids, and ocular pain in both eyes. Ocular pain was spontaneous and increased with eye movement. Her best corrected visual acuity was 20/12 in the right eye and 20/16 in the left eye. Intraocular pressure was 11 mmHg in both eyes. Slit-lamp examination revealed dilation of the conjunctiva and scleral vessel (Fig. 1A, B). There was no keratitis and no cells in the anterior chamber. Fundus examination showed normal macula, peripheral retina, disk, and vessels in both eyes. Blood examination showed elevated C-reactive protein (CRP: 9.66 mg/dL) and white blood cells (WBC: 14900 cells/μL). Blood examination revealed no evidence of anti-neutrophil cytoplasmic antibody (ANCA)-related vasculitis, syphilis or tuberculosis.

Following hospitalization, hoarseness appeared, and auricle biopsy was immediately initiated. The pathology report showed degenerated cartilage, with eosinophilic staining of marginal cartilage tissue. Based on the auricle biopsy results, the patient was diagnosed as RP with 3 presenting symptoms: bilateral auricular chondritis, inflammatory arthritis, ocular inflammation.

Systemic symptoms improved gradually on commencing therapy with prednisolone (PSL), methylprednisolone, cyclophosphamide, methotrexate, and infliximab. Topical betamethasone and gatifloxacin was administered, and the ocular pain showed a little improvement. However, dilation of the conjunctival, episcleral, and scleral vessels persisted.

One month after the initial visit, unique multiple peripheral corneal infiltrates began to emerge in the corneal stroma (Fig. 2A, B). With fluorescein staining, those areas with multiple peripheral corneal infiltrates showed slight staining. At that time, there was no meibomian gland dysfunction in either eye, and bacteriologic cultures by corneal scraping at this time revealed only Corynebacterium but not *Staphylococcus aureus* or methicillin-resistant *S aureus*. Bromfenac eye drop was added to stabilize the corneal keratitis.

In outpatient follow up, systemic symptoms were generally stable, and PSL was reduced by 5 to 10 mg at intervals of 1 week or more. The multiple peripheral corneal infiltrates had concentrated and diminished (Fig. 3A, B), but the scleritis persisted. Four months after the initial visit, ear and ocular pain and redness were found to have suddenly worsened, and a small increase of PSL achieved no significant improvement in these systemic symptoms. The patient was again hospitalized at 6 months to increase PSL, and methylprednisolone, methotrexate, and tocilizumab combination therapy commenced. The conjunctival, episcleral, and scleral vessels improved a little, but multiple peripheral corneal infiltrates remained during this period. Under the combination therapy, the declining trend in ear and ocular pain and redness also stopped. Seven months after initial visit, the patient was discharged from hospital. Ear and ocular symptoms

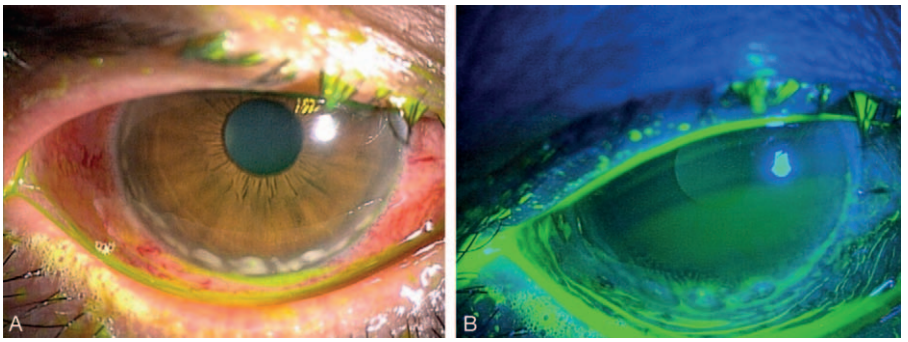

Figure 2. Slit-lamp photographs of the cornea (A) with fluorescein stain (B), showing multiple peripheral corneal infiltrates in corneal stroma.

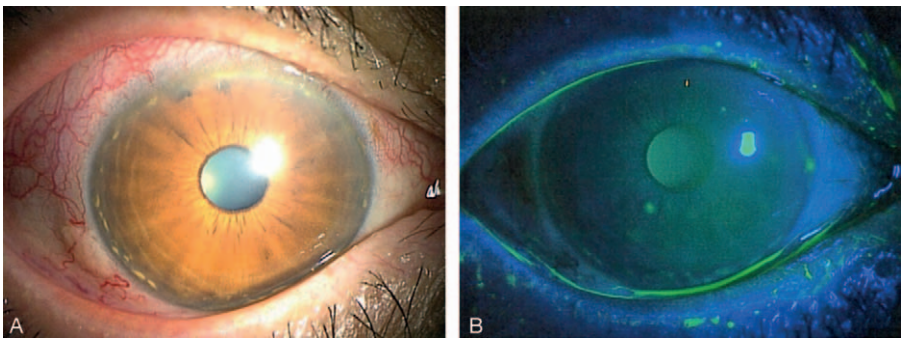

Figure 3. Slit-lamp photographs of the cornea (A) with fluorescein stain (B), showing peripheral corneal infiltrates to be concentrated and diminished.

gradually improved under PSL, methotrexate and tocilizumab combination therapy, and ear symptoms disappeared at 10 months. Dilation of the conjunctival, episcleral, and scleral vessels and the multiple peripheral corneal infiltrates gradually disappeared around the same time (Fig. 4A, B), and the patient showed no recurrence of keratitis for 6 months.

4. Discussion

We reported for the first time a case of RP with unique multiple circumferential peripheral keratitis as an ocular manifestation. The multiple peripheral corneal infiltrates appeared suddenly 1 month after initial treatment despite use of focal and systemic steroids. These infiltrates clumped and concentrated over a short period and gradually decreased over 10 months with general condition recovery.

Corneal infiltration in the peripheral area is observed in various diseases such as catarrhal keratitis and collagen disease. To distinguish catarrhal keratitis or collagen disease, corneal scraping is useful. In the reported case, bacteriologic cultures by corneal scraping revealed only Corynebacterium but not *S aureus* or methicillin-resistant *S aureus*, and no Meibomian gland inflammation was found. These findings suggest that unique corneal infiltrates were associated with RP pathogenesis.

The mechanism of peripheral keratitis was indicated by its morphology and immunology characteristics. The peripheral cornea is close to the annular vessel and the lymph duct, and immune-related substances such as complement exist at a higher concentration than at the center of the cornea.[8,9] Immune complexes deposited at the peripheral cornea activate the complement and trigger the leukocyte infiltrate into the cornea, leading to epithelial defect.[8,9]

In a review of 112 RP patients, Isaak et al[5] reported a level of about 3.6% of peripheral corneal infiltrates. Generally, corneal inflates with RP appears as arcuate shape in peripheral cornea. However, little is known about clinical manifestation and clinical histology. We found the unique multiple peripheral corneal infiltrates in the corneal stroma. To our best knowledge, such an entire circumferential peripheral keratitis has not previously been reported in cases of RP.

We added topical NSAIDs, reported to be associated with corneal toxicity,[10] when improvement of the symptoms is not recognized with steroid instillation alone. Combined use of topical NSAIDs and steroid was reported more useful for the therapy of ocular inflammation than each drug alone.[11] Superficial punctate keratitis, corneal infiltrates, and epithelial defect were reported to associate with NSAIDs.[10,12–14] Fortunately we found no side effects on corneal surface. However, it may be necessary to be careful in the use of NSAIDs in such cases.

Multiple peripheral corneal infiltrates in RP patients show improvement with general condition recovery. It has previously been reported that ocular topical therapy offers limited relief, and that systemic therapy is useful for peripheral ulcerative keratitis in collagen vascular diseases.[15] Messmer and Foster[16] also reported that systemic treatment reduces inflammation in cases of ocular disease. In the present case too, there was a limited response to topical therapy, with gradual improvement following combined systemic therapy and topical therapy. In particular, improvement of general condition was observed after changing to tocilizumab,[17] and peripheral keratitis gradually improved.

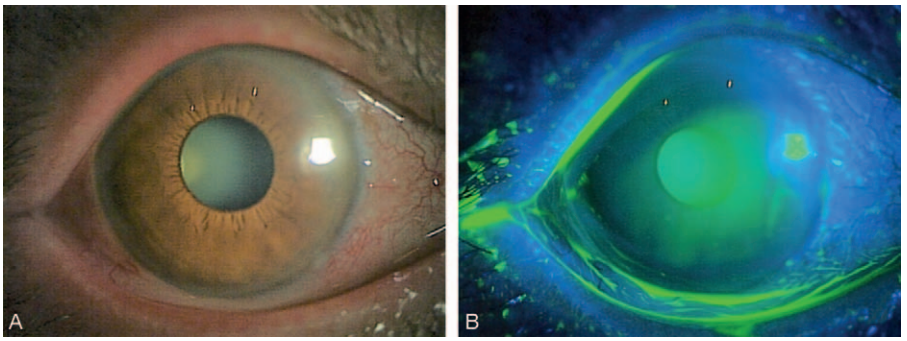

Figure 4. Slit-lamp photographs of the cornea (A) with fluorescein stain (B), showing peripheral corneal infiltrates to have completely disappeared.

In conclusion, the reported case of RP with unique circumferential peripheral corneal infiltrates as ocular manifestations of RP showed that systemic control of RP-associated inflammation is essential for treatment of local ocular complications.

References

[1] Foidart JM, Abe S, Martin GR, et al. Antibodies to type II collagen in relapsing polychondritis. N Engl J Med 1978;299:1203–7.

[2] Hundeiker M, Brehm K, Go M. [Infiltration and cartilage decomposition in Polychondritis. (Histochemical and immunofluorescence histological findings)]. Z Haut Geschlechtskr 1970;45:437–43.

[3] Emmungil H, Aydın SZ. Relapsing polychondritis. Eur J Rheumatol 2015;2:155–9.

[4] McAdam LP, O'Hanlan MA, Bluestone R, et al. Relapsing polychondritis: prospective study of 23 patients and a review of the literature. Medicine (Baltimore) 1976;55:193–215.

[5] Isaak BL, Liesegang TJ, Michet CJJr. Ocular and systemic findings in relapsing polychondritis. Ophthalmology 1986;93:681–9.

[6] Zeuner M, Straub RH, Rauh G, et al. Relapsing polychondritis. clinical and immunogenetic analysis of 62 patients. J Rheumatol 1997;24:96–101.

[7] Yoo JH, Chodosh J, Dana R. Relapsing polychondritis. systemic and ocular manifestations, differential diagnosis, management, and prognosis. Semin Ophthalmol 2011;26:261–9.

[8] Seal D, Ficker L. Immunology and therapy of marginal ulceration as a complication of chronic blepharitis due to S. aureus. In: Lass JH, the editor. Advances in Corneal Research Springer, Boston, MA:1997;19–25.

[9] Albers FW, Majoor MH, Van der Gaag R. Corneal autoimmunity in a patient with relapsing polychondritis. Eur Arch Otorhinolaryngol 1992;249:296–9.

[10] Kim SJ, Flach AJ, Jampol LM. Nonsteroidal anti-inflammatory drugs in ophthalmology. Surv Ophthalmol 2010;55:108–33.

[11] Ogawa T, Ohara K, Shimizu H, et al. Effects of a combined use of steroidal and nonsteroidal anti-inflammatory drugs on E. coli endotoxin-induced uveitis in pigmented rabbits. Jpn J Ophthalmol 1995;39:353–9.

[12] Gills JP. Voltaren associated with medication keratitis. J Cataract Refract Surg 1994;20:110.

[13] Sher NA, Krueger RR, Teal P, et al. Role of topical corticosteroids and nonsteroidal antiinflammatory drugs in the etiology of stromal infiltrates after excimer photorefractive keratectomy. J Refract Corneal Surg 1994;10:587–8.

[14] Shimazaki J, Saito H, Yang HY, et al. Persistent epithelial defect following penetrating keratoplasty: an adverse effect of diclofenac eyedrops. Cornea 1995;14:623–7.

[15] Gregory JK, Foster CS. Peripheral ulcerative keratitis in the collagen vascular diseases. Int Ophthalmol Clin 1996;36:21–30.

[16] Messmer EM, Foster CS. Vasculitic peripheral ulcerative keratitis. Surv Ophthalmol 1999;43:379–96.

[17] Stael R, Smith V, Wittoek R, et al. Sustained response to tocilizumab in a patient with relapsing polychondritis with aortic involvement: a case based review. Clin Rheumatol 2015;34:189–93.