Annals of Clinical Case Reports

Case Report
Published: 11 Oct, 2023

Acute Bilateral Sterile Paracentral Corneal Perforation in a Steroid-Resistant Rheumatoid Arthritis Patient Treated with Penetrating Keratoplasty

*Tao T and Sha X**

Department of Ophthalmology, The Second Affiliated Hospital of Guangzhou Medical University, China

Abstract

Objective: To present a case of central ulcerative keratitis that progressed from unilateral corneal perforation to bilateral perforation.

Methods: A retrospective case report was conducted.

Result: A 37-year-old female with Rheumatoid Arthritis (RA) presented with a one-month history of blurred vision in both eyes. After receiving inpatient care for paracentral corneal perforation and two corneal ulcers in her left eye, she was diagnosed with severe dry eyes. During the course of treatment involving systemic steroids and topical artificial tears, spontaneous perforation of interpalpebral ulcers occurred in her left eye. Three months after undergoing penetrating keratoplasty on both eyes, a corneal ulcer was observed in the right eye. Following treatment with immunosuppressants, topical autologous serum drops, and preservative-free artificial tears, significant recovery was noted along with improved vision.

Conclusion: Long-lasting RA may result in ulcerative keratitis, which can be a significant contributor to corneal perforation. Therefore, it is crucial to conduct regular and thorough ocular examinations for RA patients before the onset of blurred vision.

Keywords: Rheumatoid arthritis; Paracentral Corneal Perforation; Blurred vision; Penetrating Keratoplasty; immunosuppressants

OPEN ACCESS

Correspondence:
Xiangyin Sha, Department of Ophthalmology, The Second Affiliated Hospital of Guangzhou Medical University, 250# Changgang Road East, Haizhu District, Guangzhou 510260, Guangdong Province, China, Tel: 86-20-34153028

Received Date: *19 Sep 2023*
Accepted Date: *06 Oct 2023*
Published Date: *11 Oct 2023*

Citation:
Tao T, Sha X. Acute Bilateral Sterile Paracentral Corneal Perforation in a Steroid-Resistant Rheumatoid Arthritis Patient Treated with Penetrating Keratoplasty. Ann Clin Case Rep. 2023; 8: 2494.

ISSN: 2474-1655.

Abbreviations

PKP: Penetrating Keratoplasty; UK: Ulcerative Keratitis; PUK: Peripheral Ulcerative Keratitis; CUK: Central Ulcerative Keratitis; BCVAs: Best-Corrected Visual Acuities; RA: Rheumatoid Arthritis; CRP: C-Reactive Protein; sSS: Sjögren's Syndrome Secondary; ANCAs: Antineutrophil Cytoplasmic Antibodies; anti-CCP: anticyclic Citrullinated Peptide Antibodies

Introduction

Based on the location of the lesion, Ulcerative Keratitis (UK) can be categorized into two groups, Peripheral UK (PUK) and Central UK (CUK). The majority of reported studies have primarily focused on PUK [1]. There is limited information available in the literature regarding the symptoms, treatment and prognosis of CUK. In contrast to PUK, CUK can be caused by dry eye conditions with or without Sjögren's syndrome [2]. Herein, we present a case involving acute sterile corneal perforation in a steroid-resistant patient with rheumatoid arthritis who had undiagnosed dry eye syndrome. We also describe her subsequent treatment using penetrating keratoplasty and immunosuppressants.

Case Presentation

A 37-year-old female presented with symptoms of blurred vision in both eyes lasting for over a month, bilateral foreign body sensation, diplopia, asthenopia, xerostomia, and a six-day history of excessive tearing in her right eye. Her Best-Corrected Visual Acuities (BCVAs) were 0.1 and Fc/30 cm in the right and left eye, respectively. The patient's upper eyelids partially covered the upper part of the pupil. Slit-lamp examination revealed ciliary congestion in both eyes. Notably, there was a paracentral corneal perforation with iris plugging causing the disappearance of the peripheral anterior chamber in the right eye. Additionally, two ulcers on the left cornea. One eye exhibited a rounded paracentral deficiency of the epithelium, covered by the upper eyelid at 12 o'clock, while

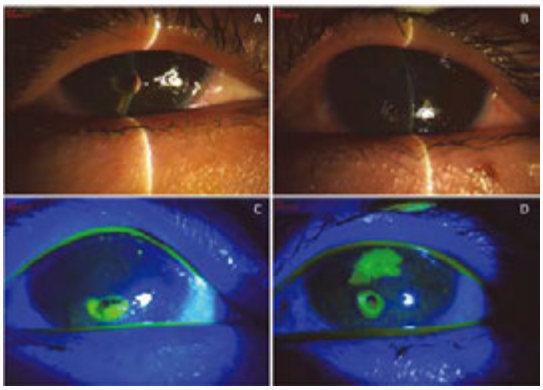

Figure 1: Slit-lamp photographs of both eyes on the first visit. A) Prolapse of the iris and corneal perforation in the right eye; B) Thinning of the underlying stroma at 12 o'clock and rounded deficiency of the epithelium and anterior stroma at 7 o'clock in the left eye; C, D) The corneal fluorescein staining showing the positions of the corneal lesions.

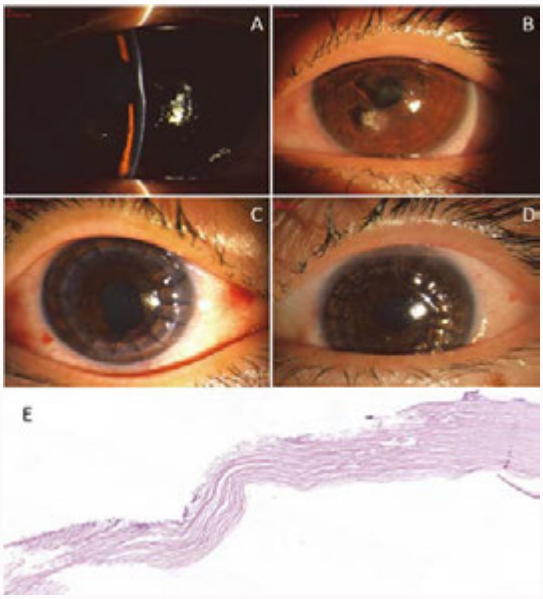

Figure 2: Before and after PKP in both eyes. A, B) The stroma of the left eye became thinner and the lower ulcer was suspected to have been perforated within the shallowed anterior chamber; C) PKP of the left eye; D) PKP of the right eye. E) Biopsy of the right cornea showing a perforation and thinning stroma with a few infiltrated lymphocytes.

the other eye displayed an anterior stromal abnormality at 7 o'clock (Figures 1A-1D). The intraocular pressure in the right eye was high at 24.1 mmHg, whereas it remained within normal range in the left eye. Both corneal reflex and conjunctival sensation were markedly diminished.

The patient had a prior diagnosis of rheumatoid arthritis 13 years ago and was currently receiving treatment with Prednisolone (5 mg PO QD), Celecoxib (0.2 g PO BID), and Leflunomide (20 mg PO QD). However, the disease was not effectively managed as evidenced by progression of the patient's joint-related symptoms in addition to intermittent episodes of joint pain. A series of tests were conducted to determine the underlying cause of the patient's ocular condition.

A Schirmer's I test revealed tear production less than 1 mm of moisture on the filter paper after 5-min interval for both eyes was.

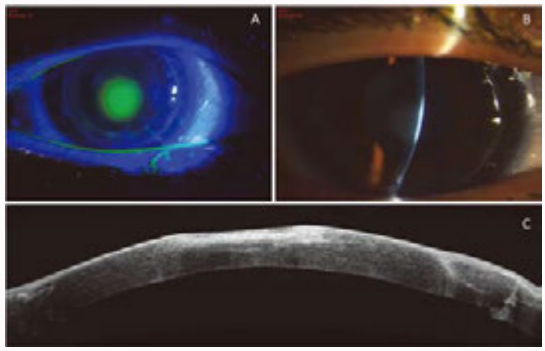

Figure 3: The corneal ulcer recurred three months after the PKP on the right eye. Slit-lamp photographs (A, B) and optical coherence tomography (C) of the right eye showing rounded deficiency of the epithelium.

Sialography examination indicated a decline in the functionality of the left submandibular and parotid glands. The diagnosis Sjögren's syndrome was inconclusive due to insufficient salivary gland tissue samples. Nevertheless, both Anti-Sjogren's Syndrome A (SSA) and Anti-Sjogren's Syndrome B (SSB) tests yielded negative results. Cultures obtained from the bilateral ulcers were negative for all tested infectious organisms, including hepatitis B and C, tuberculosis, syphilis, and HIV. Routine blood analysis revealed mild anemia while C-Reactive Protein (CRP) was absent in the patient's serum sample. The serum rheumatoid factor titer demonstrated a significantly elevated level of 62.7 IU/mL (normal range 0-20 IU/mL), accompanied by strong positive results for Antineutrophil Cytoplasmic Antibodies (ANCAs). Furthermore, the concentration of anti-Cyclic Citrullinated Peptide antibodies (anti-CCP) exceeded 300 U/mL (normal range 0-15 U/mL). The Electrocardiograph (ECG) and chest X-ray findings were within normal limits.

The patient initially presented with a diagnosis of rheumatoid ulcerative keratitis and severe dry eyes. To alleviate the local inflammation, dexamethasone (10 mg, IV) was administered. Autologous serum and sodium hyaluronate eye-drops were utilized to improve the ocular desiccation. During the one-week preparatory period prior to Penetrating Keratoplasty (PKP) of the right eye, the thinning and perforation of the stroma in the lower ulcer of the left eye were observed, as evidenced by pupil deformation and shallow anterior chamber (Figure 2A, 2B). Due to successful stabilization of the plugged perforation in the right eye, PKP was performed on the left eye. Surgery on the right eye took place two weeks later (Figures 2C-2F). The patient's Best-Corrected Visual Acuity (BCVA) improved to 0.4 in the right eye and 0.7 in the left eye one month after each surgery.

Three months post PKP on the right eye, the patient presented with recurrent visual blurring in the same eye. Slit lamp revealed a superficial ulcer located at the central transplant cornea graft site. The therapeutic approach included frequent administration of Tacrolimus (three times daily), topical application of autologous serum drops (four times daily), and regular instillation of preservative-free artificial tears every two hours. Encouragingly, positive response to this treatment regimen was observed as evidenced by significant healing of the ulcer within five days. Subsequent follow-up visits demonstrated improved Best-Corrected Visual Acuity (BCVA) measurements, reaching 0.5 in the affected right eye and 0.8 in the unaffected left eye until her most recent visit in January 2020 (Figure 3).

Discussion

Rheumatoid Arthritis (RA) is the most prevalent autoimmune disorder associated with dry eye syndrome and is also the primary cause of vision-threatening ocular diseases such as Peripheral Ulcerative Keratitis (PUK) and necrotizing scleritis, etc. [3]. Some RA patients with PUK have been reported to present with impending corneal perforations [4]. The prevalence of UK in patients with RA is approximately 1.4%, and around 25% of these individuals develop secondary Sjögren's Syndrome (sSS) [2]. Bilateral corneal ulcers are uncommon in the patient population. The exact pathogenesis underlying ulcerative keratitis associated with RA remains incompletely understood. In the present case, the described patient experienced corneal ulceration followed by unilateral and then bilateral noninfectious central corneal perforations, despite only complaining of blurred vision. We have deduced that chronic keratoconjunctivitis sicca and prolonged usage of Non-Steroid Inflammatory Drugs (NSAIDs) elevate the pain threshold, resulting in diminished sensitivity toward the ocular symptoms. Consequently, we have concluded that delayed treatment combined with immune system dysfunction can cause lead to acute corneal perforation in Rheumatoid Arthritis (RA). This effect is particularly pronounced in individuals undergoing aerodyne treatment or experiencing dry eyes. Although PUK often manifests without symptoms in RA patients, CUK is associated with conditions such as blurred vision, diplopia, and asthenopia. In this particular patient's case, augmented secretions were only observed subsequent to the occurrence of corneal perforation.

Bilateral, noninfectious corneal perforation is rarely reported, especially in patients with RA [5]. In this case report, we present the first documented instance of a patient with RA exhibited progressive perforated ulcers in the non-interpalpebral zone. Furthermore, these ulcers differ from the typical dry eye ulcer commonly observed as large fused epithelial defects in the palpebral fissure area. The development of such perforated ulcers in the present case can primarily be attributed to the patient's immune disorder, where abnormal antibodies have caused damage to the cornea and reduced tear production has further exacerbated this process. Although accurately distinguishing specific therapeutic effects during actual treatment procedures poses challenges, there may exist a correlation between immune disorders and severe dry eyes. Therefore, combination treatment could potentially yield greater benefits for similar cases.

Most hospital patients with ulcerative keratitis in hospitals are promptly administered treatments such as high-dose steroids, immunosuppressants, cyanoacrylate glue, amnion membrane coverage, and bandage contact lenses [6,7]. Although corneal ulceration is a rare complication in RA, it can potentially result in ocular perforation if timely and effective treatment is not provided [8].

Given the potential grave consequences associated with dry eye syndrome, frequent administration of artificial tears alongside intravenous steroids was employed for this patient. Regrettably, due to corneal perforation in the left eye, this approach demonstrated limited effectiveness. Nevertheless, a therapeutic strategy incorporating immunosuppressants along with preservative-free artificial tears and blood-derived eye drops exhibited significant benefits by successfully addressing relapse symptoms observed in the right eye. Analysis of the patient's medical history indicated joint dysfunction characterized by intermittent swelling and pain despite low levels of C-Reactive Protein (CRP). These findings suggest that her ongoing rheumatic treatment regimen for her autoimmune condition might not have provided sufficient efficacy and could potentially be linked to steroid resistance. Disease-Modifying Antirheumatic Drugs (DMARDs), including systemic immunosuppressants, are considered as the cornerstone of RA treatment. RA treatment with DMARDs is associated with a reduced risk of extra-articular diseases and fewer comorbidities. This further suggests that systemic and topical immunosuppressants are efficacious in treating ulcerative keratitis in steroid-resistant RA patients with severe dry eyes.

Serious ocular morbidity and high mortality are associated with corneal perforation in patients diagnosed with PUK and RA, despite receiving treatment [6]. The mortality rates can significantly increase with the development of bilateral corneal ulcers, serving as a crucial indicator of an impending serious medical condition. Despite the patient's stable systemic condition at the time of her perforation, it is imperative to consider the possibility of an underlying severe ailment. Ocular symptoms such as keratoconjunctivitis sicca, episcleritis, and scleritis may suggest potential extra-articular diseases [4,9]. Therefore, ophthalmic laboratory tests and joint radiography are recommended for assessing RA activity in cases involving corneal ulcer or perforation, particularly they are bilateral perforation or associated with secondary Sjögren's Syndrome (sSS). Furthermore, inflammatory joint involvement is linked with severe dry eyes and could also be valuable for diagnosing Sjögren's syndrome.

Furthermore, it is widely recognized that non-classic TH1 cells exhibit a greater propensity to transition towards a TH17 phenotype, potentially contributing to the prevalence of TH17 cells in the peripheral blood of patients diagnosed with RA [10]. These specific subsets of T cells demonstrate enhanced resistance to both inhaled and systemic steroids [11]. Consequently, meticulous monitor of changes in T-cell subtypes during patient follow-up becomes imperative, even if the treatment proves efficacious.

Conclusion

For ocular symptoms, such as severe dry eyes, blurred vision, foreign body sensation, photophobia, and increased eye secretions, it is recommended to include ophthalmic follow-up in the management guidelines for RA, particularly for patients on long-term oral NSAIDs. This would facilitate timely screening for corneal ulcers or perforations and enable prompt diagnosis and treatment. Once a diagnosis of dry eye condition is established, it is crucial to implement more frequent follow-up care in order to prevent vision loss resulting from serious ocular complications and monitor the emergence of other potentially life-threatening rheumatic conditions such as Sjögren's syndrome and rheumatoid vasculitis. Immunosuppressants play a pivotal role in halting the progression of diseases. Furthermore, it is crucial to consider steroid resistance in RA patients who experience joint deformity and swelling accompanied by pain. Timely adjustment of systemic medications is also imperative for delaying the onset of extra-articular complications. Additionally, stringent monitoring should be implemented for RA patient with severe dry eyes experiencing persistent corneal epithelial defects and ulcer recurrence, so that immunosuppressants and topical cornea protection drugs can be promptly utilized to prevent serious and potentially life-threatening complications.

Funding

This work was supported by Guangzhou Science & Technology

Developing Project (No. 202102010045) and the Natural Science Foundation of Guangdong Province (No. 2015A030313479).

References

1. Morgan-Warren PJ, Dulku S, Ravindran J, Smith G. Peripheral ulcerative keratitis as the presenting feature of systemic rheumatoid vasculitis without joint involvement. Int Ophthalmol. 2014;34(4):933-5.
2. Watanabe R, Ishii T, Yoshida M, Takada N, Yokokura S, Shirota Y, et al. Ulcerative keratitis in patients with rheumatoid arthritis in the modern biologic era: A series of eight cases and literature review. Int J Rheum Dis. 2017;20(2):225-30.
3. Tong L, Thumboo J, Tan YK, Wong TY, Albani S. The eye: A window of opportunity in rheumatoid arthritis? Nat Rev Rheumatol. 2014;10(9):552-60.
4. Artifoni M, Rothschild PR, Brezin A, Guillevin L, Puéchal X. Ocular inflammatory diseases associated with rheumatoid arthritis. Nat Rev Rheumatol. 2014;10(2):108-16.
5. Knox Cartwright NE, Tole DM, Georgoudis P, Cook SD. Peripheral ulcerative keratitis and corneal melt: a 10-year single center review with historical comparison. Cornea. 2014;33(1):27-31.
6. Timlin HM, Hall HN, Foot B, Koay P. Corneal perforation from peripheral ulcerative keratopathy in patients with rheumatoid arthritis: Epidemiological findings of the British Ophthalmological Surveillance Unit. Br J Ophthalmol. 2018;102(9):1298-302.
7. Deswal J, Arya SK, Raj A, Bhatti A. A case of bilateral corneal perforation in a patient with severe dry eye. J Clin Diagn Res. 2017;11(4):ND01-ND02.
8. Elasri F, Souhail H, Reda K, Iferkhass S, Massoudi R, Idrissi A, et al. [The value of corticosteroids in the treatment of sterile ulcer in rheumatoid arthritis: A case report]. J Fr Ophtalmol. 2011;34(10):739.e1-3.
9. Hajiabbasi A, Shenavar Masooleh I, Alizadeh Y, Sadredin Banikarimi A, Ghavidel Parsa P. Secondary Sjögren's syndrome in 83 patients with rheumatoid arthritis. Acta Med Iran. 2016;54(7):448-53.
10. Leipe J, Pirronello F, Klose A, Schulze-Koops H, Skapenko A. Increased plasticity of non-classic Th1 cells toward the Th17 phenotype. Mod Rheumatol. 2020;30(5):930-6.
11. Chen R, Zhang Q, Chen S, Tang H, Huang P, Wei S, et al. IL-17F, rather than IL-17A, underlies airway inflammation in a steroid-insensitive toluene diisocyanate-induced asthma model. Eur Respir J. 2019;53(4):pii:1801510.