American Journal of Ophthalmology Case Reports 29 (2023) 101796

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

A case of lattice corneal dystrophy type 1 with bilateral Mooren's ulcer

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ARTICLE INFO

Keywords:
Lattice corneal dystrophy
Mooren's ulcer
Bilateral
Cyclosporine

ABSTRACT

Purpose: To report a rare case of lattice corneal dystrophy type 1 (LCD1) with bilateral Mooren's ulcer.
Observations: This case involved a 62-year-old male patient with LCD1 who presented with the primary complaint of experiencing pain and photophobia in both eyes for 2 months prior to his initial visit. Upon examination, a peripheral corneal ulcer was observed in both eyes covering more than 3 of the 4 quadrants, accompanied with ciliary injection and severe corneal infiltration. He was diagnosed with Mooren's ulcer, and treatment with 0.1% betamethasone and 0.5% levofloxacin eye drops and systemic cyclosporine and betamethasone was initiated. At 1-month post treatment initiation, a remaining ulceration ridge was observed on the corneal surface in his left eye, which was subsequently resected. Complete epithelialization was achieved at 1-month postoperative in the left eye and after 6-months of conservative topical treatment in the right eye. At 8–9 years post onset of Mooren's ulcer, the patient underwent penetrating keratoplasty in both eyes while undergoing treatment with oral cyclosporine administration for severe corneal opacity due to progression of lattice dystrophy. Post treatment, there has been no recurrence of ulcerations, even though more that 10 years has passed since the onset of Mooren's ulcer.
Conclusions and importance: To the best of our knowledge, this is the first reported case of LCD1 with bilateral Mooren's ulcer, and in this rare case, the patient was successfully treated with a combination of steroid, cyclosporine, and peripheral superficial keratectomy, and a good visual outcome was achieved after penetrating keratoplasty (PK) under the use of systemic cyclosporine.

1. Introduction

First described by Mooren in 1867,[1] Mooren's ulcer is an idiopathic progressive ulceration of the peripheral corneal that is characterized by severe pain and conjunctival injection. Although the etiology of Mooren's ulcer remains unclear, it is thought to be an autoimmune reaction to corneal antigens, such as calgranulin C, the zinc-binding protein S100A12,[2] and previous studies have reported that cataract surgery, corneal transplantation, trauma, infection, and being a carrier of the hepatitis C virus are risk factors for the disease.[3] For treatment, topical and systemic corticosteroid and immunosuppressive agents such as cyclosporine A are commonly used,[4] however, in severe cases that cannot be controlled by such conservative therapy, surgical treatments such as conjunctival excision and keratoepithelioplasty are reportedly sometimes effective.[5,6]

Lattice corneal dystrophy type 1 (LCD1) is an autosomal dominant disease characterized by diffuse thin branching refractive lattice lines that was first described by the Swiss ophthalmologist Hugo Biber in 1890.[7] As described in a 1997 report by Munier et al.,[8] R124C mutation in the human transforming growth factor-β-induced *(TGFBI)* gene is the primary cause of LCD1. Patients with LCD1 tend to develop recurrent corneal epithelial erosions that result in ocular pain and a gradual worsening of subepithelial corneal opacity.

The purpose of this study was to report a rare case of LCD1 in which bilateral Mooren's ulcer suddenly developed during the routine follow-up examination period, and to the best of our knowledge, this is the first report of bilateral Mooren's ulcer being observed in a case of LCD1. The patient presented in this study was successfully treated with a combined application of steroid, cyclosporine, and peripheral superficial keratectomy, and a good visual outcome was achieved after penetrating keratoplasty (PK) was performed under the use of systemic cyclosporine.

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https://doi.org/10.1016/j.ajoc.2023.101796
Received 24 July 2022; Received in revised form 24 December 2022; Accepted 9 January 2023
Available online 12 January 2023

2. Case report

A 62-year-old male who had previously been diagnosed with LCD1 and bilateral cortical cataracts presented to the Kyoto Prefectural University of Medicine Hospital, Kyoto, Japan with the primary complaint of slow, yet progressive, loss of vision over the past 20 years. Upon initial examination, his visual acuity (VA) was 20/600 in both eyes, and slit-lamp examination revealed subepithelial corneal opacity at the central region and thin branching opacities at the mid-peripheral corneal stroma. There was a familial history of corneal opacity (i.e., the patient's father, son, and nephew), and genetic analysis revealed that he had an R124C variant in *TGFBI* as a heterozygous band, thus resulting in the diagnosis of LCD1.

At 5 years after his initial visit, the patient presented with the primary complaint of pain and photophobia in both eyes. Examination revealed a peripheral corneal ulcer covering more than 3 of the 4 quadrants accompanied by ciliary injection and severe corneal infiltration. The ulcer was found to have spread from the 9- to 6-o'clock region in his right eye, and from the 8- to 6-o'clock region in his left eye (Fig. 1). His VA was 20/2000 in both eyes. Blood test findings were negative for antinuclear antibodies and rheumatoid factor, thus resulting in a clinical diagnosis of Mooren's ulcer.

For treatment, 0.1% betamethasone eye drops and 0.5% levofloxacin eye drops were administered once daily, and betamethasone ointment was administered twice daily. We started with low dose topical steroids in an effort to prevent the development of infectious keratitis associated with corneal epithelial erosion. In addition, the patient was administered oral cyclosporine (2mg/kg per day) and betamethasone (1mg per day), with the oral cyclosporine being gradually tapered down to 0.5mg/kg per day at 2 weeks after the start of treatment. Oral betamethasone was continued at a dose of 1mg per day for the first 2 months of treatment. The corneal infiltration gradually decreased and the size of the corneal ulcer was reduced. After 1 month of immunosuppressive treatment, a ridge of the corneal ulcer remained on the corneal surface of the patient's left eye, so the ridge was surgically resected. Following the resection, the corneal ulcer markedly diminished, with complete epithelialization being achieved at 1-month postoperative. In the patient's right eye, the conservative therapy resulted in complete epithelialization being achieved after 6 months. Oral cyclosporine was continued for one year while blood levels were checked.

Subsequently, the corneal opacity due to LCD1 and cataract formation progressively worsened, so cataract surgery was performed 3 years later on his right eye and 5 years later on his left eye, and PK was performed at 8 years post onset on his right eye and at 9 years post onset on his left eye. Oral cyclosporine was added with a routine postoperative course of management consisting of a three-times-daily administration of 0.1% betamethasone and 0.3% gatifloxacin eye drops to suppress the recurrence of Mooren's ulcer, which was ultimately successful. A 2mg/kg daily administration of oral cyclosporine was started at 1 week prior to PK being performed, which was subsequently tapered down to 0.5mg/kg per day at 1-month postoperative, then gradually tapered off over the following 2 years. The patient's VA in both eyes improved to 20/30, and there has been no recurrence of the ulcerations for more than 5-years postoperative (Fig. 2) (see Fig. 3).

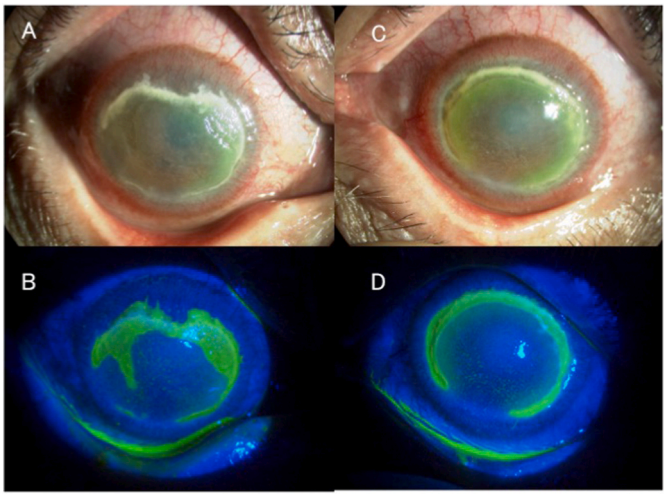

Fig. 1. Slit-lamp photographs of the eyes of a 62-year-old male patient with Mooren's ulcer obtained at disease onset. Right eye: (A, B). Left eye: (C, D). As can be seen in the images, there is a peripheral corneal ulcer covering more than 3 of the 4 quadrants accompanied by ciliary injection and severe infiltration in both eyes.

3. Discussion

To the best of our knowledge, and although bilateral Mooren's ulcer has previously been reported, this is the first report of bilateral Mooren's ulcer occurring in a case of LCD1. The disease is characterized by plasma inflammatory cell infiltration of the conjunctiva, and is thought to be an autoimmune reaction to a corneal antigen.[2] In a previous study by Shinomiya et al.,[9] the authors reported finding helper T lymphocytes and macrophages in the submucosa of the conjunctival tissues adjacent to the corneal ulceration. Interestingly, the case in this present study had no apparent history of the risk factors for Mooren's ulcer (i.e., cataract surgery, corneal transplantation, trauma, infection, or being a carrier of the hepatitis C virus[3]).

It is unclear whether the two diseases were only incidentally combined or related in some way. If there is any causal relationship between the two diseases, it can be speculated that repeated episodes of recurrent corneal epithelial erosion due to LCD1 induces an autoimmune reaction to corneal antigens and contributes to the pathophysiological mechanism of Mooren's ulcer. However, and to the best of our knowledge, there have been no previous reports of Mooren's ulcer caused by corneal epithelial erosion, such as seen in cases of lattice corneal dystrophy and map-dot-fingerprint dystrophy, also known as epithelial basement membrane dystrophy. Therefore, this case alone does not tell us whether or not there is an association between the two diseases.

In patients afflicted with Mooren's ulcer, proper treatment commonly includes the administration of topical steroids as a 'first line' therapy, followed by conjunctival resection in cases that are unresponsive to topical steroid therapy. Usually, treatment with systemic immunosuppressive agents is initiated only when patients do not respond to topical steroids and conjunctival resection. However, in

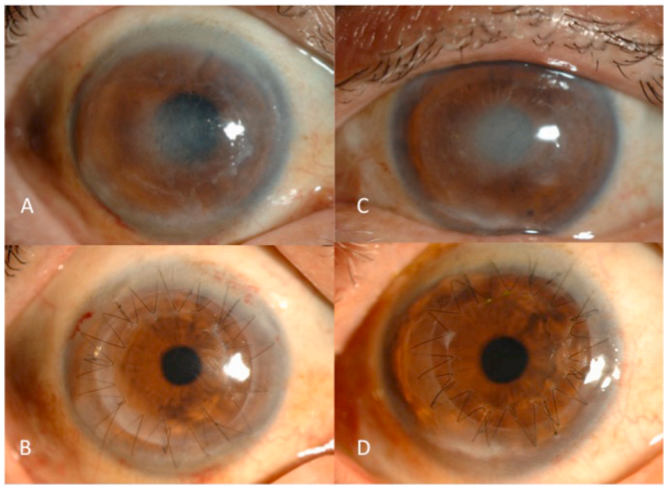

Fig. 2. Slit-lamp photographs obtained pre and post penetrating keratoplasty. Right eye: (A, B). Left eye: (C, D).

Fig. 3. Slit-lamp photograph obtained prior to surgery revealing thin branching opacities at the mid-peripheral corneal stroma.

recently years, it has been found that aggressive use of immunosuppressive agents such as cyclosporine enables a reasonable control of Mooren's ulcer.[10]

In conclusion, it should be noted that in this present case, although the patient underwent both cataract surgery and PK, there has been no recurrence of Mooren's ulcer for more than 10 years since disease onset, which is important, as surgical procedures are a risk factor for the recurrence of Mooren's ulcer.[11] Thus, the findings in this case indicate that it is possible to perform aggressive surgical treatments such as cataract surgery and PK in cases of Mooren's ulcer when the disease is under appropriate management with systemic cyclosporine.

Patient consent

Consent to publish this case was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Funding

No funding or grant support.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Acknowledgments and Disclosures

None.

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