

Recurrent and refractory corneal perforation secondary to rheumatoid arthritis treated with infliximab

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Abstract:

Rheumatoid arthritis (RA) can affect many organs including the eyes. Corneal perforation in the form of peripheral ulcerative keratopathy can be debilitating and difficult to manage. A 48-year-old female with known RA presented with sudden loss of vision in her left eye, she was diagnosed with left corneal perforation secondary to severe dry eye. Penetrating keratoplasty (PKP) and punctum occlusion were done. Amniotic membrane transplant (AMT) was done 1 month later due to nonhealing epithelial defect. Her RA was clinically inactive, and no changes in her current medications were made. However, 4 months later, she presented with a second corneal perforation with melting. She had another PKP and AMT with permanent tarsorrhaphy. Cyclosporine 100 mg P. O. twice daily was added, but after 5 months, she presented again with a third left corneal perforation with melting. Again, PKP and AMT with tarsorrhaphy were done, and she was started on infliximab. Since then, she had a stable graft with no further corneal perforations. In summary, patients with RA can have corneal perforations even if other signs of RA are absent. If the systemic treatment that is used to treat RA fails, one should consider using other classes of drugs, such as monoclonal antibodies (e.g., rituximab), tumor necrosis factor alpha blockers (such as infliximab or adalimumab), interleukin (IL)-1 receptor antagonists (e.g., anakinra), or IL-6 receptor antagonist (e.g., tocilizumab).

Keywords:

Corneal perforation, Rheumatoid arthritis, Infliximab

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic disease that can have many manifestations affecting other organs including the eyes. Peripheral ulcerative keratopathy (PUK) causing corneal perforation is a well-known complication,^[1] and this usually happens when the rheumatoid is active in other areas of the body in addition to the eye. However, RA can also cause dry eyes and keratolysis, which can be difficult to manage. We describe a case in which the patient had three recurrent corneal perforations with no other signs of active RA. We consulted with her rheumatologist and elected to use infliximab, which was very effective in stabilizing the graft and stopping the recurrence of perforations

CASE REPORT

A 48-year-old female known to have seropositive RA with a history of dry eyes and hypertension, presented to the emergency department complaining

of sudden loss of vision in the left eye. Her visual acuity was 20/30 in the right eye and hand motion in the left. The pupil was reactive to light in the right eye with no clear detail to the left pupil, but there was no reverse relative afferent pupillary defect. The extraocular motilities were normal. The patient had diffuse superficial punctate keratitis in the right eye. She also had central corneal perforation with surrounded corneal melting and edema in the left eye. In the right eye, the Schirmer's test was positive with < 2 mm wetting during testing for 5 min without anesthesia.

She was diagnosed with a left corneal perforation secondary to the severe dry eye. Penetrating keratoplasty (PKP) and punctum occlusion were done. Amniotic membrane transplant (AMT) was done 1 month later due to nonhealing epithelial defect. Rheumatology was consulted regarding this, but their thought was that the rheumatoid was inactive. She was labeled as being stable, and there was no need to adjust her medications. Her current rheumatoid medications included methotrexate

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20 mg P. O. once weekly, prednisone 5 mg every other day, and hydroxychloroquine 200 mg P. O. daily with diclofenac 100 mg P. O. as needed. She was also on cyclosporine ophthalmic emulsion, artificial tears, lubricant eye ointment, and topical steroid.

Four months later, the patient presented with a second corneal perforation with melting in the same eye. She had another PKP and AMT with permanent temporal tarsorrhaphy. Her rheumatologist added cyclosporine 100 mg P. O. twice daily for only a short time. After 5 months of the second perforation, she presented again with a third left corneal perforation with melting. Again, PKP and AMT with tarsorrhaphy were done. After discussion with the rheumatologist this time, the decision was made to start this patient on infliximab. It was given as an induction dose of 3 mg/kg intravenously for 3 doses (weeks 1, 2, and 6), followed by a maintenance dose of 3 mg/kg every 8 weeks. After starting the infliximab, the patient had a stable graft with less frequent epithelial defects. She remains, until now, stable (around 8 years after starting the infliximab) with no further corneal perforations.

DISCUSSION

RA can have many ophthalmic manifestations, including dry eye, PUK, uveitis, and scleritis. Most cases reported in the literature describe PUK as the cause of corneal perforations.^[1-6] PUK causes local vasculitis and thinning of the cornea that can lead to perforation, which can be debilitating and recurrent.^[2] However, the pathophysiology is not very well understood. The effect of T-cells and antibodies from the RA could play a significant role^[7] by immune complex deposition in the cornea and the release of cytokines. T-helper cells produce tumor necrosis factor α (TNF- α), which is involved in the pathophysiology of RA, causing cartilage destruction. Angiogenesis in the limbus can increase the rate of the immune complex deposition in the periphery of the cornea, which leads to the accumulation of inflammatory cells, producing more cytokines and stimulating the keratocytes to produce metalloproteinases that degrades the extracellular matrix.^[3] Dry eyes are also a manifestation of RA that can cause melting of the cornea and perforation.

Presenting with recurrent corneal perforation with a stable RA is rare. Antao *et al.*^[2] reported a case in which a patient had had a nonactive RA with recurrent corneal perforations, that prompted the use of infliximab with excellent response and no more perforations. Jifi-Bahloul *et al.*^[4] described three cases of PUK in which the RA was quiescent. Thomas *et al.*^[5] also reported on three patients, who had RA associated keratolysis that was not responding to conventional RA systemic therapy. Clinical improvement was noted in all patients after starting the infliximab, and it prevented further ulcerations in the cornea. Infliximab was also used to treat a necrotizing scleritis in a 60-year-old male with known RA, who did not have active synovitis during the attack.^[6] It was refractory to steroids and cyclophosphamide, but responded to infliximab. Hata *et al.*^[8] describe a case in which a patient presented with atypical continuous keratitis that was associated with RA that needed Infliximab. In our case, the patient had a

total of three corneal perforations and she did not have any other signs of active RA. Having PUK (without signs of active RA) could be in fact a sign of active RA that requires intervention. Ophthalmologists should be aware about this phenomenon and earlier intervention with a biologic might be needed if corneal perforation recurs, despite the RA being under control.

Infliximab, one of the biologics, inhibit TNF- α and is used in severe cases of RA to control the disease. This was effective in preventing further corneal perforations in our case and in others.^[2,5] It is thought that it can lead to a reduction in the metalloproteinases, resulting in the reduction of the destruction of the cornea.^[3] Another agent that has an activity against TNF- α is etanercept, which has been used to treat keratitis and scleritis. Newer TNF- α blockers (e.g., adalimumab) are also likely to be effective. Other biologics that are used to treat RA such as interleukin (IL)-1 receptor antagonists (e.g., anakinra) and IL-6 receptor antagonist (e.g., tocilizumab) will likely also be beneficial.

In summary, patients with RA can have corneal perforations even if the RA is inactive. Our patient had three corneal perforations, until the infliximab was used then, no more corneal perforation occurred. If the systemic treatment that is used to treat RA fails, one should consider using newer agents such as biologics.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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