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CASE REPORT

Conjunctival resection in the management of peripheral ulcerative keratitis

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Abstract

Purpose: The purpose of the study was to present a case with refractory peripheral ulcerative keratitis (PUK) that was managed with conjunctival resection surgery in addition to medical treatment.

Methods: A 78-year-old female patient was admitted with sudden decrease in vision, redness, and pain in the right eye. Her medical history was unremarkable except for early stage diabetes and hypertension. In the first examination, her visual acuities were counting fingers from 1 m in the right eye and 1.0 in Snellen lines in the left eye. Biomicroscopy revealed crescent-shaped stromal ulceration with accompanying epithelial defect, stromal thinning, and limbal inflammation in the temporal cornea consistent with PUK. Immediate management included bandage contact lens application, topical preservative-free dexamethasone, moxifloxacin, cyclosporine 0.05%, polyvinyl alcohol/povidone artificial tear eye drops, as well as I.V. pulse methylprednisolone. Rheumatology consultation revealed no underlying autoimmune disease. During her follow-up with oral maintenance dose steroids and topical medication, the ulcer progressed to perforation with protrusion of the iris. Therefore, surgical correction including conjunctival resection and amniotic membrane transplantation had to be performed.

Results: In follow-up, healing in stromal ulceration was observed with dramatic improvement in ocular surface inflammation. Visual acuity improved to 0.2 in the 3rd month. Her cornea was transparent, anterior chamber was quiet, and PUK area was healed with no epithelial defect. The patient was followed up under topical cyclosporine and carboxymethylcellulose maintenance therapy.

Conclusion: In PUK cases refractory to I.V. pulse steroid or immunosuppressive therapy, "conjunctival resection" surgery may be a useful tool in the armamentarium of cornea specialists, to remove perilimbal immune complexes, suppress inflammation, and accelerate surface healing.

Keywords: Conjunctival; cornea; keratitis; management; peripheral; peripheral ulcerative keratitis; resection; ulcerative.

Peripheral ulcerative keratitis (PUK) is an autoimmune disorder believed to involve activation of the complement system through immune complexes in the peripheral cornea. Most cases of PUK are of immunological origin and more than half are associated with autoimmune diseases, although infections were also accused of its pathogenesis. The peripheral corneal localization of this condition is explained by the immunological differences between periph-

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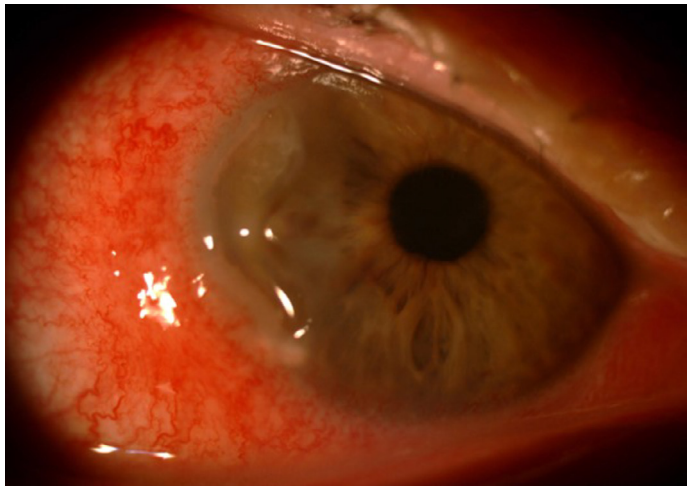

Fig. 1. Acute peripheral ulcerative keratitis and adjacent limbal, conjunctival and episcleral inflammation.

eral and central parts of the cornea.[1] Peripheral cornea is closer to the conjunctival and limbal vasculature, as well as lymphatic circulation, which eases the occurrence of autoimmune reactions by the release of various mediators.[2] Particularly, neutrophils and macrophages destroy corneal stroma by releasing collagenase and other proteases that cause enzymatic destruction of the local cellular structure. This leads to a localized inflammatory response.[3]

Clinical findings of PUK include eye irritation, redness, pain, photophobia, and decreased vision with severe irregular astigmatism. There is usually conjunctival, episcleral, and scleral inflammation.[4,5] The characteristic lesion is a crescent-shaped stromal inflammation of the juxtalimbal cornea. Spontaneous or traumatic corneal perforation and vision loss may occur in patients with PUK. A multidisciplinary approach is needed for PUK cases. In addition to systemic and topical immunomodulatory treatments and surgical interventions to preserve tectonic integrity of the globe, perilimbal conjunctival resection has also been recommended to remove precipitated immune complexes, reduce the formation of collagenase and proteinases, and thereby suppress inflammation.[6]

In this case report, we aim to present the clinical result obtained by conjunctival resection with amniotic membrane transplantation (AMT), in a treatment refractory PUK patient who progressed to perforation, and to summarize the synergistic mechanism of this approach.

Case Report

A 78-year-old female patient was admitted with sudden decrease in vision, redness, and pain in the right eye. Her medical history was unremarkable except for early stage diabetes and hypertension. In the first examination, her visual acuities were counting fingers from 1 m in the right eye and 1.0 in Snellen lines in the left eye. Biomicroscopy revealed crescent-shaped stromal ulceration with accompanying epithelial defect, stromal thinning, and limbal inflammation in the temporal cornea consistent with PUK (Fig. 1). No infectious infiltration of the cornea or scleral involvement of the melt was noted.

Immediate management included bandage contact lens application, topical preservative-free dexamethasone q2hr, moxifloxacin qid, cyclosporine 0.05% qid, polyvinyl alcohol/povidone artificial tear eye drops qhr, as well as I.V. pulse methylprednisolone at a dose of 1000 mg for 3 days and then 1 mg/kg orally. There were no infiltration indicating any infectious etiology and that would necessitate scrape and culture of the ulcer area. However, to cover any possible herpetic etiology for a marginal ulcer, valacyclovir 3 × 500 mg per oral was also commenced along with

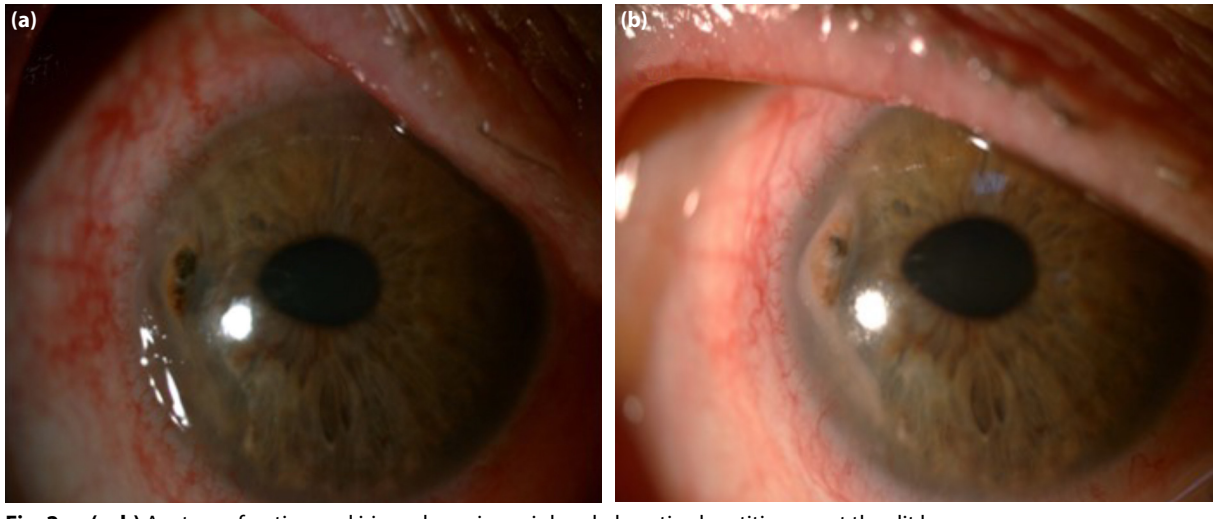

Fig. 2. **(a, b)** Acute perforation and iris prolapse in peripheral ulcerative keratitis area, at the slit lamp.

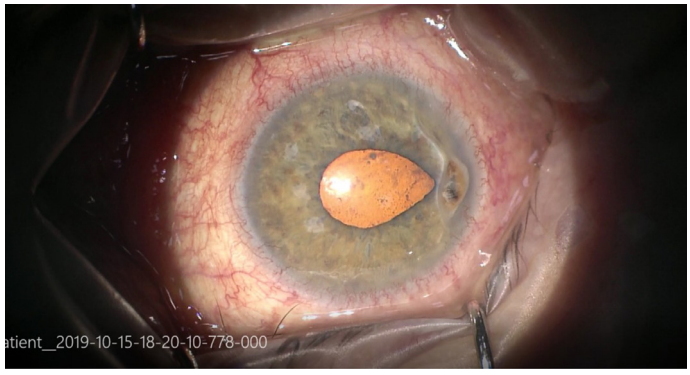

Fig. 3. Acute perforation and iris prolapse in peripheral ulcerative keratitis area, under the operation microscope.

systemic steroids. Systemic workup including FTA-ABS for syphilis did not reveal any infectious underlying disease, as well. Rheumatology consultation revealed no underlying autoimmune disease diagnosis including rheumatoid arthritis or polyangiitis granulomatosis, despite ANA positivity and mild elevation of C-reactive protein in the serum. During her follow-up with oral maintenance dose steroids and topical medication, the ulcer progressed to perforation with protrusion of the iris. Therefore, surgical correction including conjunctival resection and AMT had to be performed (Fig. 2a and b).

Amniotic tissue was obtained from a donor seronegative for human immunodeficiency virus, hepatitis B surface antigen, hepatitis C virus, and syphilis under sterile conditions after elective cesarean section. Membranes (amnion and chorion) were detached from the placenta cleaned and preserved after processing with gentamicin. The patient was operated under local anesthesia with topical proparacaine (Alcaine®, Alcon, USA) (Fig. 3). Inflamed conjunctival tissue adjacent to PUK area extending from 7 to 10 o'clock orientation was removed by Vannas scissors, with a width of approximately 3 mm. On entrance of the right eye anterior chamber at 11 o'clock position with a stiletto knife, viscoelastic material was injected to push back the iris tissue protruded from the perforation area. The iris was removed from the perforation area with the aid of a manipulator. Then, the amniotic membrane monolayer was fixed with to the denuded episcleral area with the basement membrane side facing away from the corneal surface and stromal surface facing the globe, using fibrin sealant (Tisseel, Baxter, USA) and sutured to the cornea by 10/0 nylon and to the conjunctiva with 8/0 Vicryl sutures (Fig. 4a-d). Corneal perforation area was also sutured by separate 10/0 monofilament sutures. The operation was terminated by applying a bandage contact lens. Postoperatively, cyclopentolate tid was added to the topical treatment regimen. Topical and oral steroid therapies were tapered and discontinued, on healing of the ulcer and dissolution of the amniotic membrane.

At the post-operative 3rd month, visual acuity was 0.2, cornea was transparent, anterior chamber was quiet, and PUK

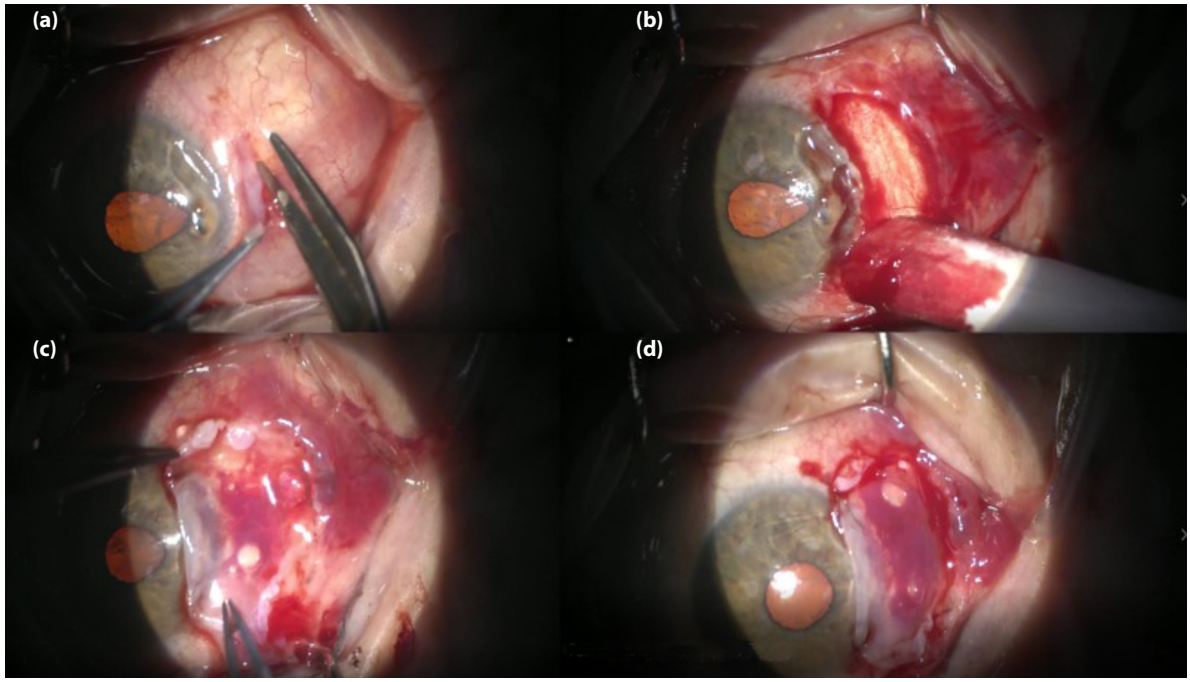

Fig. 4. **(a-d)** Surgical repair of the ulcer area and conjunctival resection. **(a)** Conjunctival resection, **(b)** Healthy appearance of the sclera with no signs of melt, **(c)** Application of the amniotic membrane with fibrin sealant, **(d)** Saturation of the amniotic membrane to adjacent cornea and conjunctiva.

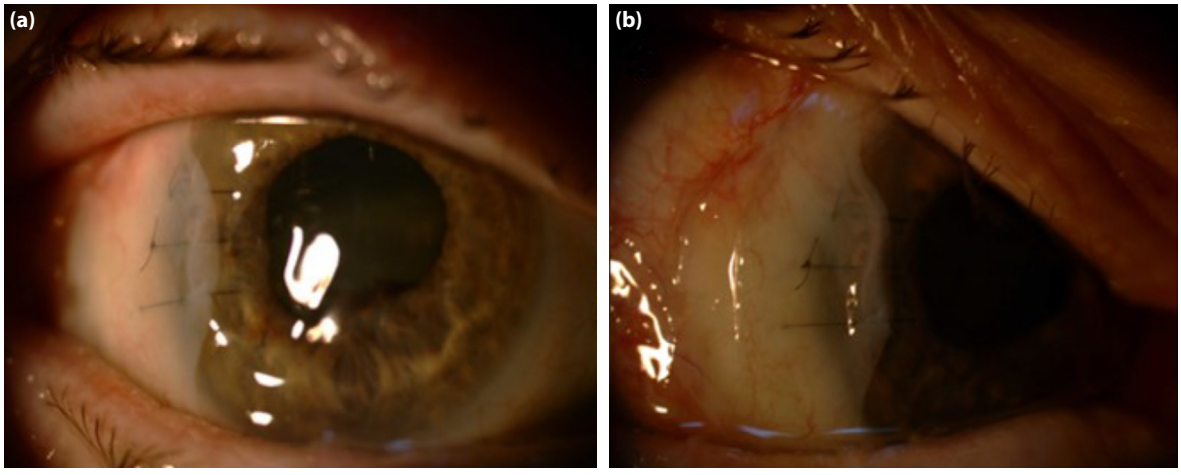

Fig. 5. **(a, b)** Postoperatively, peripheral ulcerative keratitis area and conjunctival resection area were seen covered with the amniotic membrane graft, under the bandage contact lens. Corneal and adjacent limbal inflammation has had subsided and the anterior chamber was quiet.

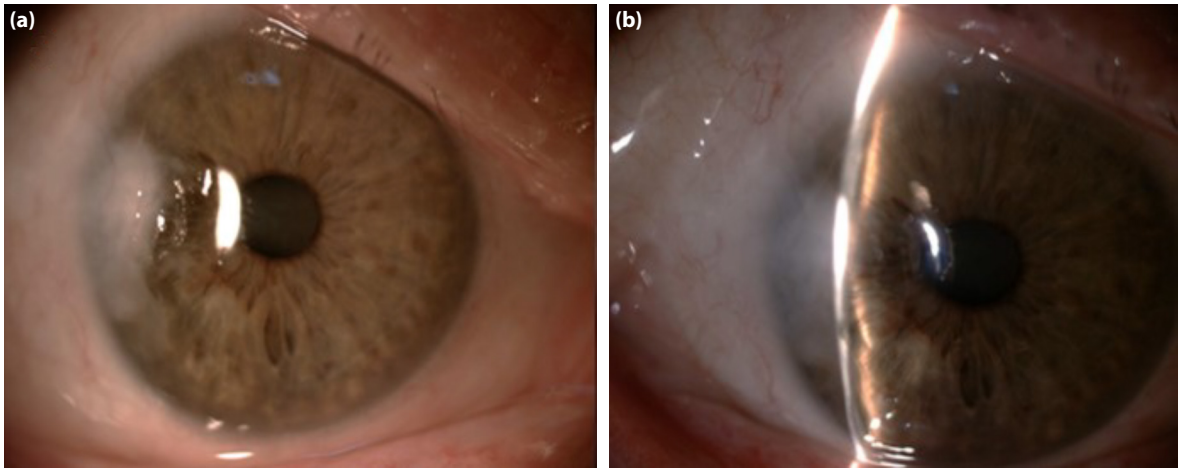

Fig. 6. **(a, b)** At the 6th month, peripheral ulcerative keratitis area had been healed with scar formation and quiet conjunctiva.

area was already epithelialized (Fig. 5a and b). The visual acuity improved to 0.3 at the post-operative 6th month (Fig. 6a and b). The globe was normotonous at all visits, but 3+ nuclear cataracts restricted further visual gain. She is still under follow-up under 0.05% cyclosporine bid and carboxymethylcellulose qid maintenance therapy.

Discussion

PUK is a corneal disease of mostly autoimmune origin, which manifests by ulceration and thinning in the peripheral cornea and can cause perforation with rapidly progressive necrosis. Corneal inflammation is associated with inflammation at the adjacent conjunctiva, episclera, and sclera. It is often initially manifested by localized conjunctivitis or episcleritis followed by adjacent scleritis and development of peripheral corneal infiltrates. Corneal ulcer begins with epithelial demolition and progresses by circumferentially and centrally advancing stromal destruction. The depth of peripheral corneal thinning is variable. In severe cases, tissue loss may progress to non-traumatic perforation.[3]

The relationship of PUK with autoimmune diseases is well established; with ~4/10th of the cases associated with rheumatoid arthritis. PUK may also be associated with other autoimmune diseases such as lupus, Wegener granulomatosis, polyarteritis nodosa, ulcerative colitis, sarcoidosis, and Sweet's syndrome.[5] Although very rare, cases of Behçet's disease have also been reported.[7] Ocular infections, palpebral malformation, lagophthalmos, and neurotrophic factors may also cause PUK with non-autoimmune origin.[3] On the other hand, laboratory work-up and investigation for an underlying autoimmune association may not yield positive results at all times, as were in our case. Even in cases of no accurate diagnosis of an autoimmune disease, PUK cases should be treated as an autoimmune condition, although the pathogenesis of PUK has not been clearly explained, as of today.

The main symptoms of the disease are ocular redness, photophobia, and, in advanced cases, induced astigmatism and reduced vision. Pain is characteristically present but may vary in severity. The physician needs to make differential diagnosis with non-ulcerative forms of peripheral stromal thinning, such as Terrien's marginal degeneration. Although epithelial defect and subepithelial inflammation are seen together in PUK, the corneal epithelium will be preserved in the thinning area in non-ulcerative form.[8] However, it should also be kept in mind that non-ulcerative form can rapidly progress into PUK, if autoimmunity plays a role in the process. Therefore, patients should be followed up carefully.

PUK treatment depends on the severity of the findings in the cornea and the extent of the extraocular disease. The goals of medical therapy are to reduce inflammation, promote epithelial healing, and minimize stromal loss. Despite advances in new immunomodulators and biological agents, the outcome of PUK primarily depends on timely diagnosis and treatment of the accompanying disease. Systemic immunomodulatory treatment is essential in acute PUK. For this purpose, corticosteroids are used in the first line of treatment. However, when used alone, it usually cannot prevent the progression of the disease.[2] The normal starting dose of P.O. treatment is 1 mg/kg/day (maximum 60 mg/day). In patients with risk of vision loss, oral therapy can be initiated after 1 g/day pulse I.V. steroid for 3 consecutive days.[9] Immunosuppressive drugs or biological agents can be used in cases refractory to glucocorticoids and when steroid-associated side effects such as osteoporosis, hypertension, exacerbation of diabetes, electrolytic imbalance, and gastrointestinal bleeding develop. Antimetabolites, alkylating agents, T-cell inhibitors, or biological agents can be used as steroid-sparing immunosuppressive drugs.[10]

Intense lubrication with preservative-free artificial tears and local immunomodulatory cyclosporine drops, as well as topical prophylactic antibiotics, may be help rapid epithelization to take place. Topical agents are also useful for the removal and dilution of harmful inflammatory proteins and mediators on the ocular surface. Oral tetracycline derivatives may provide additional benefit in preventing progressive stromal loss by reducing protease activity.[11] Perforation smaller than 2 mm may require tissue adhesives or bandage contact lenses. Larger perforations might require AMT to accelerate surface healing and suppress inflammation, as well as graft surgery.

Although the use of conjunctival resection in the treatment of rheumatoid stromal ulcers has been reported previously, the mechanism of action is unclear.[12,13] The effectiveness of conjunctival resection may include removal of the source of collagenase production. Polymorphonuclear leukocytes appear to play an active role in ulceration of the cornea. These inflammatory cells gain access to the area of ulceration through perilimbal blood vessels or conjunctival secretions. If immune complex accumulation occurs in the limbal conjunctiva, excision of this tissue would theoretically interrupt the sequence of events leading to inflammatory cell invasion. Conjunctival resection can be considered as a minor surgery that can be performed under topical anesthesia, but care must be taken in the very thin ulcer area. This procedure can eliminate the need for bandage lenses, tissue glue, and AMT; or can be performed concurrently.[14–16] The amniotic membrane supports healing of the corneal ulcer with many antiangiogenic factors, anti-inflammatory factors, growth factors, and protease inhibitors.[16] Amniotic membrane graft of equal size to the ulcer area, together with conjunctival resection, seems to provide a healthy substrate, rapid epithelization, and reduce inflammation significantly. The graft also acts a useful tectonic barrier to prevent corneal melting and possible perforation.[17] If the ulceration recurs, the procedure can be repeated.

Conclusion

"Conjunctival resection" surgery should be present in a cornea specialist's armamentarium, to remove perilimbal immune complexes and suppress inflammation in PUK cases that are refractory to intense immunosuppressive therapy.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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Authorship Contributions: Concept: C.A.U.; Design: C.A.U., U.G.; Supervision: C.A.U., U.G.; Resource: F.G., C.A.U.; Materials: F.G., C.A.U.; Data Collection and/or Processing: F.G., C.A.U.; Analysis and/or Interpretation: F.G., C.A.U., U.G.; Literature Search: F.G.; Writing: F.G.; Critical Reviews: C.A.U., U.G.

Conflict of Interest: None declared.

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References

1. Acikalin B, Akova Y, Akkaya S, Garli M, Yamic M. Clinical findings, pathogenesis, and treatment in non-infectious peripheral ulcerative keratitis. Beyoglu Eye J 2018;3(2):43–51. [CrossRef]
2. Pelit A, Akova Y, Dursun D. Peripheral ulcerative keratitis. Turk J Ophthalmol 2004;33:84–91.
3. Yagci A. Update on peripheral ulcerative keratitis. Clin Oph-

thalmol 2012;6:747–54. [CrossRef]
4. Murray PI, Rauz S. The eye and inflammatory rheumatic diseases: The eye and rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis. Best Prac Res Clin Rheumatol 2016;30:802–25. [CrossRef]
5. Silva BL, Cardozo JB, Marback P, Machado FC, Galvao V, Santi-ago MB. Peripheral ulcerative keratitis: A serious complication of rheumatoid arthritis. Rheumatol Int 2010;30:1267–8.
6. Galor A, Thorne JE. Scleritis and peripheral ulcerative keratitis. Rheum Dis Clin N Am 2007;33:835–54. [CrossRef]
7. Ayar O, Yazgan S, Akdemir M. An uncommon ocular finding in Behçet's disease: Peripheral ulcerative keratitis. Turk J Ophthalmol 2014;44:484–5. [CrossRef]
8. Shiuey Y, Foster CS. Peripheral ulcerative keratitis and collagen vascular disease. Int Ophthalmol Clin Winter 1998;38(1):21–32. [CrossRef]
9. Foster CS, Forstot SL, Wilson LA. Mortality rate in rheumatoid arthritis patients developing necrotizing scleritis or peripheral ulcerative keratitis: Effects of systemic immune suppression. Ophthalmology 1984;91:1253–63. [CrossRef]
10. Messmer EM, Foster CS. Vasculitic peripheral ulcerative keratitis. Surv Ophthalmol 1999;43:379–96. [CrossRef]
11. Perry HD, Golub LM. Systemic tetracyclines in the treatment of non-infected corneal ulcers: A case report and proposed new mechanism of action. Ann Ophthalmol 1985;17:742–4.
12. Brown SI. Mooren's ulcer; treatrnent by conjunctival excision. Br J Ophthalmol 1975;59:675-82.
13. Eiferrnan RA, Carothers OJ, Yankeelov JA Jr. Peripheral rheumatoid ulceration and evidence for conjunctival collagenase production. Arn J Ophthalmol 1979;87:703–9. [CrossRef]
14. Feder RS, Krachmer JH. Conjonctival resection for treatment of the rheumatoid corneal ulceration. Ophthalmology 1984;91:111–5. [CrossRef]
15. Berman M. Regulation of collagenase; therapeutic considerations. Trans Ophthalmol Soc UK 1978;98:397–405.
16. Kenyon KR, Berman M, Rose J, Gage J. Prevention of stromal ulceration in the alkali-burned rabbit comea by glued-on contact lens. Evidence for the role of polymorphonuclear leukocytes in collagen degradation. Invest Ophthalmol Vis Sci 1979;18:570-87.
17. Dua HS, Gomes JA, King AJ, Maharajan VS. The amniotic membrane in ophthalmology. Surv Ophthalmol 2004;49:51–77.