

Case Report

Transformation of neglected corneal ulcer

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ABSTRACT

A corneal ulcer is a sight-threatening condition that can be found in an outpatient clinic. Managing the corneal ulcer precisely and rapidly can minimize its symptoms and improve the vision for a better quality of life. In our case, a 52-year-old man came to the eye clinic with chief complaints of redness, tearing, blurring, and pain in his right eye three weeks ago. The other complaints were photophobia, hard to open his eye, and accompanied by yellowish secretion. He never got any medical treatment for his eye. From the examination, his visual acuity was hand movement; we found blepharospasm and lagophthalmos, conjunctiva hyperemia with chemosis, 6 mm central corneal ulcer with perilimbal neovascularization, and without hypopyon. The patient was admitted for hospitalization for intensive monitoring and treatment. The symptoms were lessened at first, but sadly there was no significant change in the vision and corneal condition. The eye condition was stable for the first week after he went home. However, the next week, the hypopyon and decemetocoele show up as new manifestations and due to the patient's delay, his condition even got worse. In consequence, patient awareness and compliance play an essential role in promoting the healing of the cornea.

Keyword: Corneal ulcer, Hypopyon, Descemetocoele, Corneal neovascularization

INTRODUCTION

The cornea is an eye protector located on 1/6 anterior of the eyeball. Besides, it also has an important function as a medium of refraction. Its transparency plays an essential role in our vision. However, in Indonesia, according to basic health research by the Indonesian ministry of health in 2013, blindness caused by corneal problems is still second place to cataracts.¹ One of the causes is due to corneal scars. Infection, vitamin A deficiency, trauma, autoimmunity are some of the most common reasons that can cause corneal scars.³ Infection of the cornea can be caused by various pathogens, which if the infection hits the deeper layers of the cornea, it can be called a corneal ulcer. Symptoms of a corneal ulcer include red eyes, pain, photophobia, tearing, a sensation of foreign bodies, decreased vision, and pus that can form in the anterior chambers of the eye. In this paper, we would like to

report a case of transformation of neglected corneal ulcer and its manifestation.

CASE REPORT

A 52-year-old man came to the eye clinic with chief complaints of redness, tearing, blurring, and pain in his right eye for three weeks ago. It started when he felt an object accidentally entered his eye while working, but he did not look for treatment immediately because of his reason. Since then, he just used an eye drop that he brought freely at the drugstore without consulting the doctor. His complaint had been getting worse for three days ago, and now he only could see a blurred image in the near distance. He also complained about photophobia, hard to open his eye, and accompanied by yellowish secretion. He never had any trauma or eye surgery before and used contact lens/ glasses. History of well-controlled diabetic and smoking around 15 years are approved.

As the result of the examinations, there were found that VA in the right eye was 1/300 (hand movement) and the left eye was 5/7.5. From the slit-lamp investigation in the right eye, there were found slight edema, blepharospasm, lagophthalmos at the palpebral; conjunctival and perilimbal injection accompanied by chemosis especially at the inferior; Hazy cornea with neovascularization at perilimbal and a white, undefined border ulcer with ± 6 mm diameter at the center of the cornea; and no hypopyon in the anterior chamber was found (Figure 1). The iris, pupil, and lens were difficult to evaluate, so we performed B-scan ultrasonography to ensure the posterior segments. The vitreous body and retina were still in good condition (Figure 2). The intraocular pressure at the right eye was 18.7 mmHg measured by non-contact tonometry. There was no abnormality in the left eye. Both eyes were able to move in all directions.



Figure 1: The first day, 6 mm central corneal ulcer with chemosis.



Figure 2: B-scan ultrasonography, no abnormality within the vitreous body and retina.

The patient was diagnosed with a corneal ulcer with chemosis for his right eye. He was prepared for hospitalization because it required further monitoring and needed an intravenous antibiotic. The patient was also scheduled for corneal scrapping for cultures and

antibiotic sensitivity testing. While waiting for the results, the patient was given systemic, subconjunctival, and topical antibiotics; artificial tears; cycloplegic drops; analgesic; vitamin C; doxycycline; and a non-selective beta-blocker. The examination results were gram-positive +2 bacteria, KOH/fungi culture was negative.

After five days of hospitalization, the symptoms improved, but the vision came with no progression, the ulcer border became more defined. Outpatient was educated for control every three days and all the topical and oral medication should be continued. We also added a low potential steroid eye drop (Figure 3). After the first week, the condition had good improvement. Still, the following week suddenly, he came with 1/8 hypopyon on his right eye, and the inferior infiltrate got smaller but thinner (Figure 4). The intraocular pressure was 14.7 mmHg measured by non-contact tonometry. We advised the patient to be referred to the sub-specialist external eye disease division to get further management and therapy. Sadly, the patient postponed the appointment, and then he came back around one week with the worsened condition. Decemetocoele was formed, and the hypopyon was multiplied (Figure 5). We explained the condition and the worst possibility to him, and he accepted and took all the responsibility on him then he agreed to be referred.



Figure 3: The fifth day, the ulcer border became more define and smaller.



Figure 4: The second week, 1/8 hypopyon was present with inferior corneal thinning.

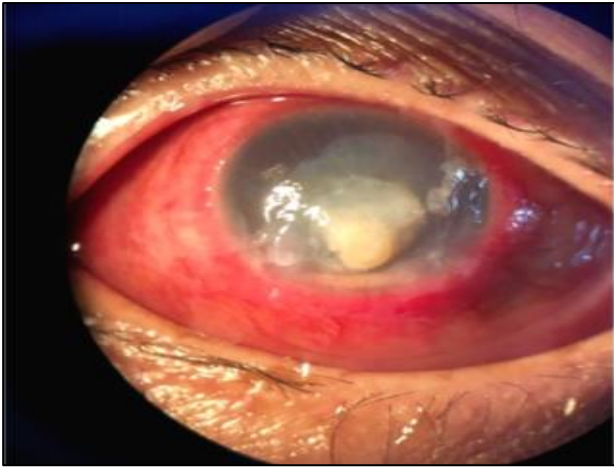


Figure 5: The third week, descemetocoele was present and the hypopyon was multiplied.

DISCUSSION

In this case, the diagnosis of the corneal ulcer was made based on the patient's symptoms and the clinical signs found in his right eye. The causes of corneal ulcers are divided into two, namely infectious and non-infectious. In this case, it tends to be more infectious corneal ulcers, preceded by trauma.

Corneal ulcers are one of the ocular emergencies that can cause ocular morbidity. It can be a worrying problem because it can cause blindness, especially in developing countries.² The cornea consists of five layers starting from the outermost, namely the epithelium; bowman's membrane; stroma; Descemet's membrane; and endothelium. The corneal layer capable of regeneration is only the epithelium and Descemet's membrane. Meanwhile, those that play an important role in maintaining corneal transparency are the endothelium layer because it functions as a metabolic pump spread across the cornea's surface to enter nutrients and remove excess fluid from the stroma so that its relative dehydration is maintained.³ Corneal ulcers can also originate from keratitis because the cause of the infection is the same; what distinguishes them is the corneal layers involved. In keratitis, the involved layer only reaches the epithelium layer, whereas corneal ulcers can reach deeper layers. So that in the corneal ulcer, there is a saucer-like appearance.^{4,5} A complication of corneal layer defect, especially when the stromal layer is involved, can lead to herniation or anterior bulging of an intact Descemet membrane through the locus minoris, which is called descemetocoele. Therefore, it has a greater tendency to become impending perforation.⁶

Corneal transparency and avascular are the main requirements for visualization. Factors that threaten its conditions are inflammatory reactions, neovascularization, and limbal deficiency. Inflammatory reactions, corneal ulcers, for example, will eventually end up with corneal healing. This healing is a complex

process involving cell death, migration, proliferation, differentiation, and remodeling of the extracellular matrix. The important segments of the healing process are located in the epithelial, stroma, and endothelium. Healing in the epithelial layer is highly dependent on limbal stem cells and the basement membrane remodeling. Meanwhile, the stromal layer transforms cells from keratocytes to fibroblasts and myofibroblasts, resulting in the build-up of extracellular matrixes that cause scar formation. The last, in the endothelial layer, involves cell migration and spreading accompanied by enlargement of endothelial cell size and fibroblastic transformation.⁷ The exosome is a bioactive molecule derived from corneal epithelial cells that mediate intercellular signaling and communication between epithelial cells and stromal cells during the corneal healing process. When this process occurs, the immune response, epithelial cells, and the immune signaling pathway (inflammasome pathway) must be modulated and limited because the increase in inflammatory cells causes scar formation, destruction of the limbal zone, and stimulates the formation of proangiogenic factors.^{8,9} Damage in the deeper layer of the epithelium will cause the formation of fibrotic tissue involving the disruption of basement membrane regeneration both in the anterior (epithelium basement membrane) and posterior (Descemet's basement membrane). It is the response of the cornea to maintain its function by replacing the lost tissue or structure.^{7,8} In a study by Step et al., they stated that if the wound size is more significant than 2 mm, it can cause morphological changes in the epithelial cells in the cornea, the presence of goblet cells in the cornea which caused by repeated erosions. Wounds located close to the limbus produce a more incredible immune response due to more leukocyte involvement in the cornea.¹⁰

Complete history taking and risk factors such as trauma; use of contact lenses; history of surgery and previous eye diseases; prolonged use of topical eye medications; as well as a record of systemic illness or immunosuppression and supported by clinical examination with slit-lamp biomicroscopy is a vital role for diagnosing corneal ulcer. The causes of infection also vary; bacteria, viruses, fungi are closely related to contact trauma with plants, parasites (acanthamoeba) which often occurs when using contaminated contact lenses. The presence of epithelial layer damage with infiltrate involvement in the stroma should be considered as the infection caused until proven otherwise. If there is an inflammatory reaction in the anterior chamber and hypopyon, it is a sign of how aggressive the infection has been.^{4,11,12}

In general, corneal ulcers should be evaluated by smear and or culture. While waiting for the results completed, antimicrobial therapy should be given to overcome all kinds of infection causes. Antifungal and topical anti-acanthamoeba should only be given if the result is supported. Because most of the infection causes are bacteria (64%), broad-spectrum antibiotics should be

given as the first choice. The antibiotics which usually used are the fluoroquinolone group. If the culture result has come out and there is no clinical improvement, consider switching the antibiotic based on the sensitivity test result.^{13,14} For additional therapy, cycloplegic, analgesics, artificial tears can be given to reduce the symptoms. An aqueous suppressant can be considered if there is corneal thinning, which tends to be perforated.^{4,13}

In this case, because the corneal ulcer had been neglected for three weeks, we gave the antibiotic aggressively. We gave fluoroquinolone intravenous twice a day, fluoroquinolone eye drops six times a day, and aminoglycoside as the subconjunctival injection once daily for five days in a row. We also give artificial tear drops for lubricating the corneal surface and help to the re-epithelialization; cycloplegic eye drops twice a day for comfort by reducing iris spasm and prevent synechiae formation; aqueous suppressant, non-selective beta blocker eye drops, twice a day to lower the intraocular pressure to avoid impending perforation. Anti-collagenase inhibitor, doxycycline was given twice a day orally, act as matrix metalloproteinase inhibitor that can potentiate further collagen breakdown and retard corneal healing. To stimulate collagen production, vitamin C was given twice a day orally.^{2,15}

Corneal neovascularization can arise from a variety of risk factors, including hypoxia as well as inflammation of the ocular surface caused by mechanical and chemical trauma, infection, and autoimmune disease.¹⁶ The pathology of angiogenesis that occurs in the proliferation phase during corneal healing can interfere with corneal transparency due to lipid deposits and scar formation. Neo-vascularization is closely related to the angiogenic signaling pathway, which is initiated by the presence of a large number of corneal infiltrations of neutrophils and macrophages.⁸ One proangiogenic factor that plays a role is the vascular endothelial growth factor (VEGF). Several drugs function to block VEGF, one of which is corticosteroids. Apart from being anti-inflammatory, other functions of corticosteroids also play a role in reducing the density of scars by reducing the immune-mediated tissue damage response. However, it has side effects such as slowing corneal reepithelization and is contraindicated for use in infections caused by fungi and *Nocardia* sp.^{5,17}

We were not giving the steroid as initial therapy to avoid the unwanted side effect in our patient. The patient had a history of diabetes; however, as a replacement for the anti-inflammatory agent, we were giving the non-steroid anti-inflammatory drug intravenously. After five days on an antibiotic, we added the low potential steroid eye drop to reduce the inflammation and neovascularization.

CONCLUSION

The corneal ulcer is still a challenge for ophthalmologists because delays in handling can significantly impact the

patient's sight. Accuracy in treatment is the primary key, but patient awareness and compliance also play an important role. It is crucial to do corneal scraping for smear and culture to determine the causative pathogens and adjust the antimicrobial selection. Because most etiologies are bacteria, broad spectrum antibiotic is always the first choice. Because the earlier the treatment is given, the better it will reduce the inflammatory process and the better corneal healing. In the treatment, we are racing against time to maximize the patient's sight still. In this case, because of the patient's delay and non-compliance was hard to control the infection even with the aggressive antibiotic. Another treatment such as surgical should be considered to prevent the infection spread away outside the eyeball and maintain the eyeball structure.

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