eISSN (Online): 2598-0580

Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Challenges in Managing Corneal Ulcer with Hypopyon in an Uncontrolled Diabetes Mellitus Patient: A Case Report

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ARTICLE INFO

Keywords:
Corneal ulcer
Diabetes mellitus
Diabetic keratopathy
Hypopyon

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v9i3.1217

A B S T R A C T

Background: Corneal ulcer is an ophthalmological emergency that can cause blindness. The risk of increasing this complication occurs mainly in patients with systemic diseases such as diabetes mellitus. **Case presentation:** a 50-year-old male patient was treated with OS corneal ulcer cum hypopyon with a history of diabetes mellitus. On the first visit, the visual acuity examination was found to be 6/7.5 in both eyes, and the results of the corneal erosion examination were in the left eye. However, on further evaluation, the left eye's visual acuity worsened to 6/45. Anterior segment examination of the left eye showed infiltration and hypopyon formation on the next visit evaluation. The patient's condition did not improve with conventional therapy, so surgical intervention was performed in the form of amniotic membrane transplantation, hypopyon aspiration, and intracameral antibiotic injection. Corneal and hypopyon scraping culture results did not show bacterial and fungal growth. Corneal condition improved after blood sugar was controlled with insulin. **Conclusion:** Corneal ulcers with hypopyon in patients with diabetes and diabetic keratopathy require a comprehensive approach to address infection, inflammation, and impaired healing. Multidisciplinary collaboration, especially blood sugar control, is important to improve long-term prognosis.

1. Introduction

Diabetes mellitus (DM) has emerged as a global health crisis, with its prevalence steadily increasing worldwide. In 2021, an estimated 536.6 million adults aged 20-79 years were affected by this metabolic disorder, and projections indicate a further surge to 783.2 million by 2045. This alarming trend poses significant public health challenges due to the substantial impact of DM on both morbidity and mortality. Among the myriad complications associated with DM, ocular manifestations are particularly concerning. These complications are a leading cause of blindness globally, constituting a major public health issue. While diabetic retinopathy is widely recognized as a serious ocular complication, DM can also lead to another sight-threatening condition: corneal ulceration.[1,2]

A corneal ulcer is characterized by an infiltration and subsequent defect in the corneal tissue, potentially progressing from the superficial epithelial layer to the deeper stroma. This condition can be accompanied by hypopyon, an accumulation of inflammatory cells in the anterior chamber of the eye resulting from increased permeability of the blood-aqueous barrier. In recent decades, there has been a notable rise in bacterial corneal ulcers. Several risk factors contribute to their development, including contact lens use, history of systemic diseases like DM, ocular trauma, and pre-existing ocular surface diseases. In cases presenting with hypopyon, the most frequently implicated bacteria are *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Pseudomonas*

aeruginosa. The presence of hypopyon in corneal ulcers can be attributed to various factors, such as antibiotic resistance, local or systemic immunosuppression, and predisposing conditions like diabetic keratopathy that impede the healing process.[3-5]

Diabetic keratopathy is a prevalent degenerative corneal disease among individuals with DM. It is characterized by a constellation of corneal abnormalities, including delayed wound healing, reduced corneal sensitivity, neurotrophic ulcers, corneal edema, and epithelial defects. These manifestations primarily stem from the hyperglycemic state associated with DM, leading to basement membrane abnormalities, oxidative stress, and nerve damage. The disruption of the corneal healing process or re-epithelialization can ultimately heighten the risk of infection and corneal opacity. The prognosis of diabetic keratopathy is often unfavorable, with the potential for complications like hypopyon formation. The incidence of diabetic keratopathy in DM patients ranges from 46-64% throughout the course of the disease. Notably, DM increases the risk of corneal ulcers by 1.31 times. Diabetic patients frequently experience dry eye syndrome (DES) and corneal epitheliopathy, which are attributed to hyperglycemia, peripheral neuropathy, and reduced tear secretion. These complications can lead to persistent epithelial defects, chronic erosions, and neurotrophic keratopathy. Corneal nerve damage disrupts the feedback mechanism regulating tear secretion, exacerbating the severity of diabetic DES.[6-8]

Furthermore, DM impairs epithelial healing by disrupting the aldose reductase pathway and causing the accumulation of secondary polyols in epithelial and endothelial cells. This cellular dysfunction and loss of epithelial adhesion to the basement membrane contribute to the poor response of corneal ulcers to standard treatment and increase the risk of recurrent corneal erosion. Managing corneal ulcers with hypopyon in patients with DM presents a formidable challenge due to the complex interplay of bacterial etiology and predisposing factors like diabetic keratopathy. These cases necessitate a comprehensive approach that addresses both the infection and the underlying systemic condition.[9-11] This case report aims to delve into the diagnostic and therapeutic challenges encountered in managing a corneal ulcer with hypopyon in a patient with multiple risk factors, namely DM and cranial nerve disorders. These factors significantly influence the disease course and response to therapy.

2. Case Presentation

A 50-year-old male patient came to the eye clinic with a primary complaint of pain in the left eye that had been felt since one day before after a foreign object hit the patient's eye in the yard. The pain was felt continuously and worsened when the patient rubbed his eyes. Blurred vision, watery eyes, and photophobia accompanied complaints. There was no use of medication to relieve the complaint. It is known that the patient has had a history of diabetes mellitus (DM) for 10 years that is not controlled with medication. The patient is also known to have a history of trauma to the left side of the face and clavicle bone, which resulted in a lesion on the VII cranial nerve. Complaints due to the lesion include weakness of the left side of the facial muscles, incomplete eye closure, and difficulty speaking due to facial muscle asymmetry.

On physical examination, visual acuity of both eyes was 6/7.5, and intraocular pressure (IOP) was 16 mmHg and 11 mmHg, respectively. On examination of the anterior segment of the right eye, normal eyelids, calm conjunctiva, clear cornea, deep anterior chamber (AFC), round and regular iris, and cloudy lens were found. Examination of the anterior segment of the left eye showed eyelid spasm, as well as conjunctival and pericorneal injection. There was corneal erosion in the paracentral area. Deep AFC, round and regular iris, cloudy lens. Fundus examination of the right and left eyes showed clear papillae, cup-to-disc ratio (CDR) 0.3, arterial/venous ratio (AA/VV) 2/3, and normal retina with positive macular reflex.

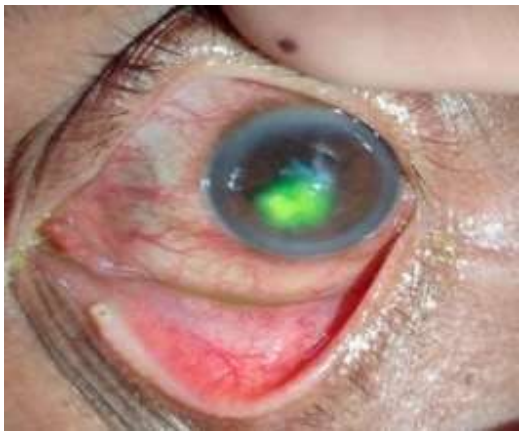

Figure 1. Paracentral corneal infiltrate at 1 week follow-up.

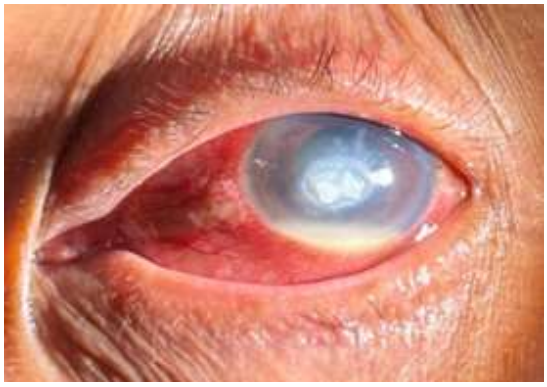

Figure 2. Hypopyon in the anterior chamber of the left eye.

Initial management of the patient's left eye included administering Levofloxacin eye drops six times a day, lubricating eye drops six times a day, vitamin C 500 mg twice a day orally, and diclofenac sodium 50 mg twice daily. The patient was then consulted by the internal medicine department for DM management and was advised to start insulin therapy, but the patient refused.

On control 8 days later, the left eye vision decreased to 6/21 and IOP 10 mmHg. The left cornea showed a 3x2 mm infiltrate with surrounding edema (Figure 1). Corneal sensibility examination showed a decrease in the left eye, while the right eye was within normal limits. TBUT (Tear Break-Up Time) examination of both eyes showed a time of 8 seconds in the right eye and 5 seconds in the left eye. Management continued using the previous therapy regimen.

Evaluation 2 weeks later found a decrease in left eye vision to 6/45, with findings of expansion of the infiltrate size and corneal epithelial defect measuring 4x3 mm. Corneal scraping examination was performed with gram staining, and KOH found leukocyte cells 10-15/lpk and epithelium 1-3/lpk without any findings of fungi or bacteria. Fasting blood sugar examination showed 203 mg/dL results and HbA1c levels of 8.5%. The patient was currently using oral antidiabetic therapy in the form of metformin tablets 500 mg twice a day and glimepiride tablets 1 mg once a day. The patient was given additional oral antibiotics, Cefixime 200 mg twice daily.

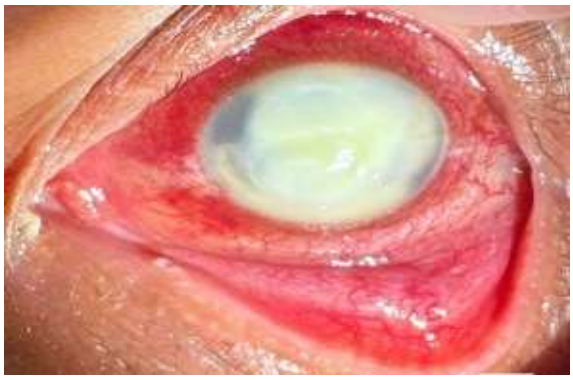

Figure 3. Post-amniotic membrane transplant corneal suture removal procedure.

On examination 1 month later, hypopyon was found in the anterior chamber of the left eye (2 mm high) with infiltration and corneal epithelial defects that remained (Figure 2). USG examination showed an ODS echo-lucent vitreous cavity, low mobility, low reflectivity, and intact RKS that was impressively within normal limits. Complete blood count and kidney function tests were within normal limits. Random blood sugar tests showed hyperglycemia at 246 mg/dL. Management consisted of administering Levofloxacin eye drops every hour to the left eye and Levofloxacin 500 mg orally daily. Tropine eye drops three times a day, Gentamycin eye ointment once daily, Glaucon once daily, and KSR once daily. During therapy, corneal stromal infiltrate and edema appeared to expand to 6x5 mm.

In the sixth week, the patient underwent amniotic membrane transplantation, hypopyon aspiration, and intracameral cefazoline injection, as well as bandage contact lens (BCL) placement. The therapy given was Levofloxacin eye drops every hour in the left eye, Glaucon once a day orally, and potassium supplementation (KSR) once daily. Pre-operative supporting examinations included complete blood count, liver function, kidney function, and coagulation function, with the impression within normal limits. Random blood sugar levels were 196 mg/dL.

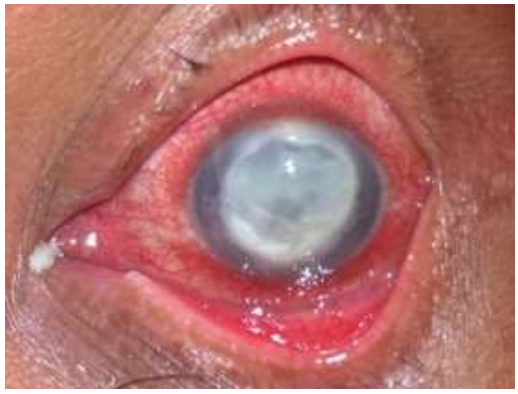

Figure 4. Post-surgery on both left eyes.

The results of TPHA and VDRL examinations showed negative results. The chest X-ray showed a picture within normal limits, good lung patterns, no consolidation or infiltrates, the diaphragm appeared normal, and no signs of pleural effusion or cardiac enlargement.

On the first day of the postoperative visit, the patient still complained of pain with BCL installed, and hypopyon was found again. A random blood sugar examination showed hyperglycemia at 290 mg/dL

with therapy from an internist in Metformin 500 mg three times a day orally and Glimepiride 2 mg once daily. From the results of the microbiological culture test of corneal scrapings and hypopyon, the results were leukocyte cells 2-3/lpk, epithelial cells 6-8/lpk, gram-negative rods 1-2/lpi and gram-positive cocci 2-4/lpi. The treatment plan includes the administration of Cefixime 200 mg twice a day orally for three days, Diclofenac sodium 50 mg three times a day orally; Moxifloxacin eye drops 6 times a day in the left eye, Tropin eye drops three times a day; lubricant eye drops six times a day in the left eye, and blood sugar control under the supervision of an internist. Glycemic control therapy was Ezelin once 6 IU, Metformin 500 mg three times a day orally, and Glimepiride 2 mg once a day orally. One week after the first procedure (seventh week), corneal suture removal, irrigation, and aspiration of hypopyon were performed, and an intracameral Levofloxacin injection was performed.

At the post-affective visit, corneal aspiration irrigation of hypopyon was done with intracameral cravit injection, corneal ulcer, and bacteria. The pain complaint was felt to have decreased; vision was 1/300, and hypopyon did not re-form, but there was still plaque on the corneal endothelium, cloudy corneal stroma, and neovascularization was found in the corneal stroma. USG supporting examination showed conditions within normal limits.

The treatment given was cefixime 200 mg twice daily orally, methylprednisolone 16 mg twice daily orally, and tapering off. Diclofenac sodium 50 mg orally thrice daily, cravit eye drop every 2 hours in the left eye, lubricant eye drop 6 times daily, and one drop in the left eye. Follow-up two weeks later (ninth week): The patient no longer felt pain, left eye vision remained 1/300, and the corneal condition began to move towards scarring. The patient's blood sugar examination results were 208 mg/dL. At this visit, the patient was not given insulin treatment.

3. Discussion

This case report presents a complex and challenging scenario of a 50-year-old male patient who developed a corneal ulcer in his left eye, complicated by hypopyon and bacterial infection. The presence of diabetic keratopathy, stemming from his 10-year history of poorly controlled diabetes mellitus, further compounded the complexity of this case. This report serves as a stark reminder of the devastating ocular complications that can arise from uncontrolled diabetes and underscores the urgent need for effective diabetes management to prevent vision-threatening conditions. Diabetes mellitus, a chronic metabolic disorder characterized by hyperglycemia, has reached pandemic proportions, affecting millions worldwide. Its impact extends far beyond elevated blood sugar levels, encompassing a wide array of microvascular and macrovascular complications that significantly impair quality of life and contribute to increased morbidity and mortality. Among these complications, diabetic eye disease stands out as a leading cause of vision loss and blindness, particularly among working-age adults. This demographic reality translates to substantial socioeconomic consequences, impacting individual productivity, healthcare systems, and national economies. Our patient's case exemplifies the detrimental effects of uncontrolled diabetes on ocular health. The development of a corneal ulcer, a sight-threatening condition, in the context of long-standing poorly managed diabetes highlights the complex interplay between systemic disease and ocular vulnerability.[12,13]

Persistent hyperglycemia, a defining characteristic of diabetes, disrupts the delicate metabolic balance within the body, triggering a series of pathophysiological events that ultimately lead to microvascular and macrovascular complications. In the context of ocular health, hyperglycemia wreaks havoc on the intricate network of blood vessels and tissues within the eye, paving the way for a range of vision-threatening conditions such as diabetic retinopathy, diabetic macular edema, and cataracts. One of the key mechanisms underlying the ocular complications of diabetes is the excessive expression of pro-inflammatory factors. These inflammatory mediators, including tumor necrosis factor-alpha

(TNF-α), interleukin-1β (IL-1β), and vascular endothelial growth factor (VEGF), play a pivotal role in orchestrating the inflammatory response, disrupting the delicate balance within the ocular microenvironment. TNF-α, a potent pro-inflammatory cytokine, is produced by various cells, including macrophages, monocytes, and T lymphocytes, in response to hyperglycemia and other stressors. In the eye, TNF-α exerts its detrimental effects by promoting vascular permeability, leukocyte adhesion, and the production of other inflammatory mediators. This increased vascular permeability allows fluid to leak into the surrounding tissues, contributing to macular edema, a condition characterized by the accumulation of fluid in the macula, the central part of the retina responsible for sharp, central vision. IL-1β, another key player in the inflammatory cascade, is also produced by a variety of cells, including macrophages and endothelial cells. IL-1β amplifies the inflammatory response by inducing the expression of adhesion molecules on endothelial cells, facilitating the adhesion and migration of leukocytes into the tissues. This influx of leukocytes further exacerbates inflammation and contributes to tissue damage. VEGF, a potent angiogenic factor, is also upregulated in response to hyperglycemia. VEGF promotes the formation of new blood vessels, a process known as angiogenesis. While angiogenesis is essential for normal tissue growth and repair, excessive or dysregulated angiogenesis can have detrimental consequences in the eye. In diabetic retinopathy, VEGF-induced neovascularization can lead to the formation of fragile, leaky blood vessels that are prone to bleeding and contribute to the development of macular edema and retinal detachment. The excessive expression of these pro-inflammatory factors disrupts the delicate balance within the ocular microenvironment, creating a chronic inflammatory state that promotes vascular permeability, leukocyte adhesion, and tissue damage. This chronic inflammation underlies the development and progression of diabetic ocular complications. In the case of our patient, the presence of macular edema and proliferative diabetic retinopathy underscores the detrimental effects of chronic inflammation on the ocular structures. The reduced visual acuity experienced by the patient can be attributed to the disruption of the normal retinal architecture caused by macular edema and the formation of abnormal blood vessels in proliferative diabetic retinopathy.[14-16]

This case report highlights the intricate interplay of factors contributing to corneal ulceration in a patient with diabetes, emphasizing the multifaceted nature of diabetic keratopathy (DK). DK encompasses a spectrum of corneal abnormalities, with corneal neuropathy, delayed wound healing, and tear film dysfunction playing pivotal roles in increasing the risk of ulceration. Diabetic neuropathy, a well-recognized microvascular complication of diabetes, affects not only the peripheral nerves but also the corneal nerves. These nerves are vital for maintaining corneal health by providing sensory innervation, promoting epithelial integrity, and regulating tear film stability. In diabetes, hyperglycemia induces a cascade of metabolic and vascular changes that lead to nerve fiber loss and dysfunction. This results in decreased corneal sensitivity, often leaving patients unaware of minor corneal injuries or foreign bodies. Consequently, these seemingly trivial insults can progress to sight-threatening ulcers, as exemplified in our patient. Studies using corneal confocal microscopy have demonstrated a significant reduction in corneal nerve fiber density and morphology in individuals with diabetes, even in the absence of overt clinical signs. These subclinical changes in corneal nerves can precede the development of clinically detectable corneal complications. Therefore, early detection of corneal neuropathy through corneal sensitivity testing and confocal microscopy is crucial for identifying patients at risk and implementing preventive measures. Hyperglycemia not only damages the corneal nerves but also impairs the function of corneal cells, particularly the epithelial cells and keratocytes. These cells are essential for maintaining corneal transparency and facilitating wound healing. High glucose levels disrupt various cellular processes,

including cell proliferation, migration, and adhesion, leading to delayed wound closure. This prolonged healing process creates an opportune environment for bacterial colonization and invasion, ultimately culminating in ulcer formation. Furthermore, hyperglycemia can alter the composition and function of the extracellular matrix, the scaffolding that supports corneal cells. This disruption further compromises the structural integrity of the cornea and hinders the healing process. In our patient, the sluggish healing of the corneal abrasion despite appropriate treatment underscores the impact of diabetes on corneal wound repair.[17-19]

The tear film, a complex mixture of lipids, proteins, and mucins, forms a protective barrier over the ocular surface. It provides lubrication, nourishes the cornea, and plays a crucial role in innate immunity by containing antimicrobial components. Diabetes can disrupt the tear film, leading to dry eye, a condition characterized by insufficient tear production or excessive tear evaporation. Dry eye disrupts the delicate balance of the ocular surface ecosystem, making the cornea more susceptible to damage and infection. The lack of adequate lubrication increases friction between the eyelids and the cornea, leading to epithelial erosion and micro-abrasions. Moreover, the compromised tear film reduces the delivery of nutrients and oxygen to the cornea, further hindering its ability to repair itself. In our patient, the presence of dry eye likely exacerbated the corneal damage and contributed to the development of the ulcer. Diabetes can also compromise the immune system, making individuals more susceptible to infections. Hyperglycemia impairs the function of various immune cells, including neutrophils, macrophages, and lymphocytes, which are crucial for fighting off invading pathogens. This weakened immune response makes it harder for the body to clear bacterial infections in the cornea, increasing the risk of ulcer development and progression. Moreover, diabetes can promote chronic inflammation, a state of persistent immune activation that can paradoxically contribute to tissue damage. In the cornea, chronic inflammation can disrupt the normal healing process and exacerbate the effects of infection. This case report underscores the importance of a comprehensive approach to managing patients with diabetes and corneal complications. Regular eye examinations, including corneal sensitivity testing, tear film assessment, and detailed corneal evaluation, are crucial for early detection and intervention. Aggressive glycemic control is paramount in preventing and managing DK, as it can mitigate the detrimental effects of hyperglycemia on corneal nerves, wound healing, and immune function.[20-22]

Bacterial keratitis, as observed in our patient, is a serious ocular infection that can lead to vision loss if not promptly and effectively treated. The cornea, the eye's outermost transparent layer, is crucial for clear vision. When bacteria invade and disrupt the corneal epithelium, it triggers an inflammatory cascade, leading to the classic signs and symptoms of keratitis: pain, redness, photophobia, tearing, and decreased visual acuity. In individuals with diabetes, the risk of bacterial keratitis is further elevated due to a complex interplay of factors. Diabetes can impair the ocular surface's defense mechanisms. Elevated blood glucose levels can alter tear film composition, reducing its antibacterial properties and making the cornea more susceptible to infection. Diabetic neuropathy can also affect corneal sensation, diminishing the protective blink reflex and delaying the recognition of corneal irritation, allowing infections to take hold more easily. Diabetes can compromise the body's immune response. Hyperglycemia can impair the function of neutrophils, key immune cells responsible for fighting bacterial infections. This impaired immune response allows bacteria to proliferate and invade deeper into the corneal tissue, potentially leading to severe complications like corneal ulceration and perforation. The presence of hypopyon, as seen in our patient, is a concerning clinical sign. Hypopyon refers to a collection of white blood cells in the anterior chamber of the eye, indicating a severe inflammatory response to the infection. This accumulation of inflammatory cells can further compromise vision and increase the

risk of complications such as secondary glaucoma and synechiae formation (adhesions between the iris and the lens or cornea).[23,24]

Several bacteria can cause corneal ulcers, with the most common culprits being *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Streptococcus pneumoniae*. Identifying the specific causative organism is crucial for guiding appropriate antibiotic therapy. *Staphylococcus aureus*, a gram-positive bacterium, is a frequent cause of bacterial keratitis, particularly in cases associated with contact lens wear. It produces various virulence factors, including enzymes and toxins, that can contribute to corneal tissue damage. *Pseudomonas aeruginosa*, a gram-negative bacterium, is another common cause of bacterial keratitis, especially in individuals with compromised immune systems or those who have sustained corneal trauma. *P. aeruginosa* is notorious for its ability to rapidly invade and destroy corneal tissue, leading to severe and sight-threatening infections. *Streptococcus pneumoniae*, a gram-positive bacterium, is also implicated in bacterial keratitis, although less frequently than the other two. It can cause a more indolent infection, but it can still lead to significant corneal damage if left untreated. Culture and sensitivity testing of corneal scrapings is the gold standard for identifying the causative organism and determining the most effective treatment. This involves collecting a sample of the infected corneal tissue and culturing it in a laboratory setting to identify the bacteria present. Sensitivity testing then determines which antibiotics are most effective against the isolated strain. Empirical antibiotic therapy, often with broad-spectrum antibiotics, is usually initiated before the culture results are available. This initial treatment aims to control the infection and prevent further corneal damage while awaiting the specific sensitivities. Once the culture and sensitivity results are available, the antibiotic regimen can be tailored to target the specific pathogen, ensuring optimal treatment efficacy. Topical corticosteroids can help reduce inflammation and prevent scarring, but they should be used cautiously and only under the close supervision of an ophthalmologist, as they can also suppress the immune response and potentially worsen the infection. Cycloplegic agents dilate the pupil and help relieve pain and photophobia. In severe cases with impending corneal perforation or uncontrolled infection, surgical intervention may be necessary. This may involve procedures such as corneal transplantation or therapeutic keratoplasty. The case of our patient highlights the challenges in managing bacterial keratitis in individuals with diabetes. The presence of diabetes necessitates a more vigilant approach, as the infection can progress rapidly and lead to severe complications. Early diagnosis, prompt initiation of appropriate antibiotic therapy, and close monitoring are essential for optimizing treatment outcomes and preserving vision.[25,26]

The cornea, a remarkable structure renowned for its transparency and avascularity, serves as the eye's primary refractive element. Its intricate architecture and unique physiological properties are essential for maintaining optimal visual acuity. The cornea's transparency, crucial for the unimpeded passage of light to the retina, is attributed to its highly ordered arrangement of collagen fibrils within the stroma, its avascular nature, and the meticulous maintenance of its hydration state. However, the very attribute that grants the cornea its clarity, its avascularity, also renders it susceptible to injury and infection. The cornea's metabolic needs and immune defense mechanisms rely heavily on the tear film and the aqueous humor. The tear film, a dynamic layer composed of water, lipids, and proteins, bathes the corneal surface, providing lubrication, nourishment, and protection against pathogens. The aqueous humor, produced by the ciliary body, circulates within the anterior chamber, supplying nutrients and removing metabolic waste products. The corneal epithelium, the outermost layer of the cornea, acts as the first line of defense against external insults. Its integrity is maintained by tight junctions between epithelial cells, forming a formidable barrier against pathogen entry. However, any disruption in this epithelial barrier, as observed in our patient's case,

compromises the cornea's defense mechanisms and predisposes it to infection. In the case presented, the patient's history of corneal abrasion, a common ocular injury resulting from mechanical trauma to the corneal surface, led to a breach in the epithelial integrity. This disruption in the epithelial barrier allowed for the opportunistic invasion of pathogens, leading to the development of microbial keratitis. Microbial keratitis, an inflammatory condition of the cornea caused by microbial infection, is a significant cause of visual impairment worldwide. The clinical presentation of microbial keratitis varies depending on the causative organism, the host's immune response, and the duration of infection. Common symptoms include pain, redness, photophobia, blurred vision, and the presence of a corneal infiltrate. The diagnosis of microbial keratitis is established through a comprehensive ophthalmological examination, including visual acuity assessment, slit-lamp biomicroscopy, and corneal scraping for microbiological analysis. Identifying the causative organism is crucial for guiding appropriate antimicrobial therapy.[26,27]

This case report vividly illustrates the complex interplay of factors that contribute to corneal ulcer development following a seemingly innocuous corneal injury. The initial insult, a foreign body abrasion, disrupted the corneal epithelium, the eye's first line of defense against external threats. This breach in the ocular surface integrity set the stage for a cascade of events culminating in a vision-threatening corneal ulcer. Upon injury, an intricate inflammatory cascade is triggered. Damaged epithelial cells release inflammatory mediators, such as cytokines and chemokines, which act as distress signals, attracting neutrophils and other immune cells to the site of injury. These cells, while essential for combating invading pathogens and initiating the healing process, also release enzymes and reactive oxygen species that can contribute to collateral tissue damage. This inflammatory response, if uncontrolled, can lead to further tissue breakdown, stromal involvement, and ultimately, ulcer formation. In this particular case, the presence of microbial contaminants, likely introduced at the time of injury or during the initial period of epithelial compromise, further complicated the clinical picture. The compromised epithelial barrier, coupled with the ongoing inflammatory response, facilitated the proliferation of these microorganisms. The development of a corneal ulcer signifies a deeper invasion of the cornea, with potential involvement of the stroma, the thickest layer of the cornea responsible for its transparency and refractive power. The presence of stromal inflammation, as evidenced by the clinical findings in this case – corneal edema, stromal infiltrate, and anterior chamber reaction – underscores the severity of the condition and the potential for vision-threatening complications. The cornea's avascularity, while crucial for maintaining its optical clarity, can also hinder the delivery of immune cells and therapeutic agents to the site of infection, potentially delaying the eradication of the invading microorganisms. The clinical course observed in this case highlights the importance of prompt and appropriate management of corneal injuries, even those that appear minor initially. Early intervention, aimed at restoring the epithelial barrier, controlling inflammation, and eradicating any microbial contamination, is critical for preventing complications and promoting optimal healing.[27,28]

The inflammatory response following corneal injury is a complex and dynamic process involving a multitude of cellular and molecular players. The initial insult triggers the release of damage-associated molecular patterns (DAMPs) from injured epithelial cells, keratocytes, and other resident corneal cells. These DAMPs, along with pathogen-associated molecular patterns (PAMPs) released by invading microorganisms, activate pattern recognition receptors (PRRs) on various immune cells, initiating a cascade of signaling events that culminate in the production of inflammatory mediators. These signaling molecules, such as interleukin-1 (IL-1), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ), orchestrate the immune response by attracting and activating immune cells, promoting

inflammation, and modulating tissue repair. These chemotactic cytokines, such as CXCL8 (IL-8) and CCL2 (MCP-1), guide the migration of neutrophils and other immune cells to the site of injury. Matrix metalloproteinases (MMPs) enzymes, produced by inflammatory cells and corneal cells, degrade the extracellular matrix, contributing to tissue breakdown and ulcer formation. Reactive oxygen species (ROS) highly reactive molecules, generated by neutrophils and other immune cells, can damage corneal cells and contribute to inflammation. The delicate balance between pro-inflammatory and anti-inflammatory mediators determines the outcome of the inflammatory response. In the context of corneal ulceration, an excessive or prolonged inflammatory response can lead to significant tissue damage and impair corneal healing.[24-26]

Microbial keratitis, the infection of the cornea by bacteria, fungi, or viruses, is a major cause of corneal ulceration and blindness worldwide. The compromised epithelial barrier following corneal injury provides an entry point for these microorganisms, allowing them to invade the corneal stroma and establish infection. The clinical presentation of microbial keratitis varies depending on the causative organism, the host's immune status, and the presence of predisposing factors. Bacterial keratitis, often caused by *Staphylococcus aureus*, *Pseudomonas aeruginosa*, or *Streptococcus pneumoniae*, typically presents with a rapidly progressive, suppurative infiltrate, often accompanied by hypopyon (accumulation of pus in the anterior chamber). Fungal keratitis, commonly caused by Aspergillus or Fusarium species, tends to be more indolent, with a feathery or filamentous infiltrate and a greater propensity for corneal perforation. Viral keratitis, most often caused by herpes simplex virus, typically presents with a dendritic or geographic ulcer, often associated with pain, photophobia, and reduced vision. The diagnosis of microbial keratitis relies on clinical findings, microbiological investigations (corneal scraping and cultures), and, in some cases, imaging studies. Prompt and appropriate antimicrobial therapy, tailored to the specific causative organism, is crucial for preventing complications and preserving vision. The involvement of the corneal stroma in the inflammatory process signifies a more severe form of corneal disease. The stroma, the thickest layer of the cornea, is composed primarily of collagen fibrils arranged in a highly organized lattice, which is essential for maintaining corneal transparency and refractive power. Stromal inflammation, characterized by edema, cellular infiltration, and collagen degradation, can disrupt this intricate architecture, leading to corneal scarring and vision impairment. Corneal scarring, the replacement of normal corneal tissue with disorganized collagen fibers, can result in a variety of visual disturbances. Scarring can scatter and distort light entering the eye, blurring the image formed on the retina. Scarring can alter the corneal curvature, leading to irregular astigmatism, which can further distort vision. Scarring can increase light scattering within the cornea, causing glare and halos around lights, particularly at night. In severe cases, corneal ulceration can lead to corneal perforation, a full-thickness defect in the cornea, which can result in endophthalmitis (infection of the intraocular contents), iris prolapse (protrusion of the iris through the corneal defect), and even loss of the eye.[23-25]

The cornea, the transparent front part of the eye, is a remarkable structure that plays a crucial role in vision. Its avascular nature and intricate layers of cells provide a unique defense against pathogens. However, breaches in this defense, often caused by trauma or contact lens wear, can lead to microbial invasion and the development of infectious keratitis. Bacterial keratitis remains a leading cause of corneal blindness worldwide. The most common culprits, as mentioned earlier, include *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Pseudomonas aeruginosa*. These bacteria possess an array of virulence factors that enable them to colonize the corneal surface, penetrate the epithelium, and induce inflammation. Bacterial adhesins facilitate attachment to the corneal epithelium, allowing the bacteria to establish a foothold. Once adhered, bacteria can invade the

corneal epithelium, gaining access to deeper layers of the cornea. Many bacteria produce enzymes, such as proteases and collagenases, that break down corneal tissue, leading to ulceration and tissue destruction. Some bacteria release toxins that contribute to inflammation and tissue damage. The clinical presentation of bacterial keratitis typically involves pain, redness, photophobia, decreased vision, and the presence of a corneal infiltrate or ulcer. The severity of the infection can range from mild, superficial involvement to severe, sight-threatening disease.[22-24]

The prompt initiation of appropriate antibiotic therapy is paramount in managing bacterial keratitis. Broad-spectrum antibiotics are often employed initially to cover a wide range of potential pathogens. The choice of antibiotics may be guided by factors such as the patient's history, clinical presentation, and local antibiotic resistance patterns. In cases where the causative organism is identified through corneal scraping and culture, antibiotic therapy can be tailored to target the specific pathogen. This approach helps to optimize treatment outcomes and minimize the risk of antibiotic resistance. While less prevalent than bacterial keratitis, fungal corneal ulcers pose a significant threat to vision, especially in individuals with a history of ocular trauma involving plant material. Filamentous fungi, such as Aspergillus and Fusarium species, are the most common causes of fungal keratitis. These fungi possess unique characteristics that enable them to invade and thrive in the corneal environment. Fungal hyphae can penetrate the cornea, reaching deeper layers and causing extensive tissue damage. Fungal infections often elicit a granulomatous inflammatory response, characterized by the formation of granulomas, which are collections of immune cells. This response can lead to significant corneal scarring and opacification. Fungal keratitis is often more challenging to treat than bacterial keratitis due to the limited number of effective antifungal agents and the ability of some fungi to develop resistance to these agents. The clinical presentation of fungal keratitis can be similar to that of bacterial keratitis, but it may also include features such as feathery borders of the corneal infiltrate, satellite lesions, and a slower response to treatment. In this particular case, the absence of a definitive microbiological diagnosis highlights the challenges that clinicians sometimes face in identifying the causative organism in infectious keratitis. The patient's use of topical antibiotics before presentation may have suppressed bacterial growth, making it difficult to isolate the causative organism. The success of corneal scraping and culture depends on proper technique and adequate sampling. In some cases, the causative organism may be present in low numbers or located in deeper layers of the cornea, making it difficult to obtain a positive culture. The ability of the laboratory to identify the causative organism depends on the availability of appropriate culture media and the expertise of the laboratory personnel. In the absence of a definitive microbiological diagnosis, clinical judgment plays a crucial role in guiding treatment decisions. The patient's clinical presentation, including the appearance of the corneal lesion, the presence of risk factors, and the response to initial therapy, can provide valuable clues to the likely etiology. In this case, the clinical presentation and the patient's positive response to broad-spectrum antibiotics strongly suggest a bacterial etiology. However, the possibility of a fungal infection cannot be completely ruled out, especially given the history of trauma. The timely initiation of appropriate therapy is essential to prevent complications and preserve vision in infectious keratitis. In cases where the causative organism is unknown, broad-spectrum antibiotics are often employed initially to cover a wide range of potential pathogens. If the patient fails to respond to initial therapy or if there is a high suspicion of fungal infection, antifungal agents may be added to the treatment regimen. In some cases, corneal biopsy may be necessary to obtain tissue for histopathological examination and culture, which can help to identify the causative organism and guide treatment decisions. The use of corticosteroids in infectious keratitis remains controversial. While corticosteroids can help

to reduce inflammation and improve symptoms, they can also suppress the immune response and potentially worsen the infection. In general, corticosteroids should be used with caution in infectious keratitis and only after the infection has been adequately controlled with antimicrobial therapy. Close monitoring is essential to ensure that the infection does not worsen with corticosteroid use.[27,28]

Hypopyon, the accumulation of pus in the anterior chamber, is a concerning clinical sign that indicates a severe inflammatory response. In the context of corneal ulcers, hypopyon often suggests bacterial infection, with pathogens such as *Staphylococcus aureus, Pseudomonas aeruginosa*, and *Streptococcus pneumoniae* triggering the inflammatory cascade.Bacterial invasion of the corneal stroma triggers a massive inflammatory response, causing neutrophil migration and the release of inflammatory mediators. The accumulation of inflammatory cells in the anterior chamber forms hypopyon, which can worsen the patient's prognosis. However, not all hypopyons are infectious. Sterile hypopyons, which arise from inflammatory mechanisms, do not contain microorganisms. Non-infectious conditions such as ocular Behçet's disease and HLA-B27-associated acute anterior uveitis are the leading causes of sterile hypopyon.[28,29]

In this patient, the presence of facial nerve palsy further complicated the clinical picture. Facial nerve palsy can cause dysfunction of the orbicularis oculi muscle, which plays a critical role in eyelid closure. The inability to close the eye completely (lagophthalmos) results in prolonged corneal exposure, leading to excessive evaporation of tears and loss of the protective layer on the corneal surface. This condition gives rise to exposure keratopathy, characterized by corneal epithelial damage, inflammation, and decreased corneal sensitivity. In advanced stages, non-healing corneal epithelial defects and chronic inflammation can trigger microbial invasion, leading to the development of corneal ulcers.[22]

The management of corneal ulcers, especially in the context of diabetes and facial nerve palsy, requires a multifaceted approach that addresses both the underlying systemic condition and the ocular complications. Early and appropriate antimicrobial therapy is essential in the management of corneal ulcers. Empirical treatment with broad-spectrum antibiotics is often initiated, with adjustments based on microbial culture results. Comprehensive management includes pharmacological and non-pharmacological aspects. Broad-spectrum topical antibiotics are the primary choice, considering adequate drug penetration into the corneal tissue. In this case, the patient received levofloxacin eye drops, eye fresh eye drops, vitamin C, and diclofenac sodium. Then, during the next check-up, the patient was given an additional oral antibiotic, Cefixime 200 mg. In this patient, initial management with topical antibiotics did not yield improvement. The patient's clinical condition did not improve and tended to worsen, with deteriorating left eye vision and the presence of hypopyon.The patient was decided to undergo surgical intervention, considering the lack of response to pharmacological therapy. The surgical intervention included amniotic membrane transplantation, intracameral cefazoline injection, hypopyon aspiration, and Bandage Contact Lens (BCL) placement. Amniotic Membrane Transplantation (AMT) effectively accelerates epithelialization, reduces inflammation, and suppresses fibrosis in corneal ulcers. AMT is particularly useful in managing persistent epithelial defects, severe corneal thinning, and perforation due to infectious keratitis. Cefazolin is a broad-spectrum antibiotic that is effective against various bacteria, making it suitable for treating bacterial keratitis. Intracameral injection ensures high local concentrations, directly targeting the site of infection. Hypopyon aspiration is performed to help reduce intraocular inflammation and prevent further damage to the corneal structure. BCL placement provides mechanical protection to the corneal surface, promotes re-epithelialization, and reduces pain.[27,29]

Post-surgical intervention, the patient received therapy with Cefixime, Diclofenac sodium, Moxifloxacin eye drops, Tropin eye drops, and lubricant eye drops. The use of fluoroquinolones, such as Moxifloxacin and Levofloxacin, is common in eye surgery care due to their broad-spectrum activity and good penetration into ocular tissues. In this case, the patient was initially treated with Moxifloxacin, a fourth-generation fluoroquinolone. However, due to a lack of improvement, Levofloxacin, a third-generation fluoroquinolone, was substituted. Levofloxacin has potent activity against various gram-positive, gram-negative, and anaerobic bacteria, and it has been shown to achieve higher concentrations in the aqueous humor compared to Moxifloxacin. Ultrasound (USG) can be a valuable tool in monitoring corneal ulcers and assessing for complications. While not the gold standard for diagnosis, USG can help visualize the posterior segment of the eyeball, identify vitreous fibrosis, and detect endophthalmitis, which can occur due to surgery or as complications of the disease itself. Close monitoring is crucial to assess the response to therapy and identify complications early. Various factors, including the lesion size, location, depth of infiltrate, and the timeliness of diagnosis and therapy, influence the prognosis of corneal ulcer cases with hypopyon. In patients with diabetes, prognosis is highly dependent on glycemic control. Management of blood glucose levels can slow the progression of diabetic complications and improve neuropathy symptoms.[26,29]

4. Conclusion

This case report presented a complex clinical scenario of a corneal ulcer with hypopyon in a patient with pre-existing diabetes, diabetic keratopathy, and a facial nerve lesion. The co-existence of these conditions posed significant challenges in managing the corneal ulcer, highlighting the intricate interplay between systemic and ocular health. The patient's diabetes likely contributed to delayed wound healing and increased susceptibility to infection, while the facial nerve palsy further compromised corneal integrity due to impaired eyelid closure and reduced tear film function. This case underscores the critical importance of a multidisciplinary approach in managing such patients.

5. References

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