

VIRAL KERATITIS ET CAUSA HERPES SIMPLEX VIRUS: A CASE REPORT

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ABSTRACT

Keratitis is an inflammation of the cornea characterized by acute pain in the eye, decreased visual acuity, corneal ulcers, and stromal infiltration that can potentially threaten vision. Herpes Simplex Virus (HSV) is one of the causes of viral keratitis. Continuous therapy is needed in the management of keratitis. This case report aims to discuss the clinical symptoms and management of keratitis caused by HSV. A 61-year-old man came with complaints of blurred vision in his right eye since 1 week ago. His symptoms worsened and accompanied by nausea, vomiting, and headaches. The results of physical examination of the eyes showed that the visual acuity in the right eye was 6/15 and the left eye was 6/20. CVI (+) dendritic lesions, central corneal infiltrate and senile arch (+) in right eye, normal left eye. Examination of both eyes revealed deep anterior chamber, regular round iris, normal (+) pupillary reflex, RAPD (-), clear lens. The patient had a history of herpes zoster infection since 2 months ago without any history of medication. The patient was diagnosed with Viral Keratitis et causa Herpes Zoster Virus in the right eye. The patient was treated with Acyclovir orally, Acyclovir eye drops, Gentamicin eye ointment, artificial tears, and other symptomatic medications with routinely control every 1 week. Viral keratitis is a disease that requires serious management. The success of therapy is influenced by the speed of early diagnosis and the determination of therapy to prevent permanent visual disturbances.

KEYWORDS: Viral Keratitis, Herpes Zoster Virus, Acyclovir.

INTRODUCTION

The cornea is a transparent and avascular eye structure that has an important role as a refractive medium. Inflammation of the cornea is called keratitis. Based on the etiology, keratitis is classified as infectious and non-infectious.^[1] Keratitis is very common eye disease and potentially vision threatening. This condition is characterized by acute pain in the eye, decreased visual acuity, corneal ulcers and/or stromal infiltration. Infectious keratitis is recognized as a silent epidemic in developing countries and has been proposed as a neglected tropical disease in ophthalmology. The etiology of infectious keratitis can be in the form of bacteria, viruses, fungi, or protozoa.^[2]

The incidence of infectious keratitis is estimated at 2.5-799 cases per 100,000 population per year depends on the study design and geographic location, especially in low-income countries. One study reported an estimated incidence of infectious keratitis of 2.5-27.6 per 100,000

population per year in the United States and 2.6-40.3 per 100,000 population per year in the United Kingdom. In contrast, the incidence is much higher in less resourced countries such as South India (113 per 100,000 population per year) and Nepal (799 per 100,000 population per year). The higher incidence in this region is mainly due to poorer environmental and personal hygiene, education level, agricultural industry, increased work-related risks, corneal trauma and poor sanitation.^[1]

Viruses are one of the most common etiologies of infectious keratitis besides bacteria and fungi. The most common viral keratitis is due to herpes simplex infection (HSV) and keratitis due to varicella zoster virus (HZV). A study shows that there are 1 to 1.5 million new cases and 9 million recurrent cases annually worldwide, resulting in at least 40,000 new cases of severe visual disability per year. However, the diagnosis often relies on non-specific clinical signs. The old notion that HSV-induced keratitis is the leading infectious cause of blindness in middle- to high-income countries stems

from epidemiological studies conducted in Denmark, Croatia, France, and the United States. The reported incidence rates of total cases (new and recurring) ranged from 4.1 to 31.5 per 100,000 people per year.^[3] HSV-induced keratitis is one of the most common eye disease which get the corneal transplant in the US. Another study conducted in China showed that viral keratitis was the most common cause as much as 46% was mainly associated with keratitis due to HSV (24%) and VZV (17%).^[4]

Several types of herpes viruses that can infect the eye are HSV virus type 1, HSV type 2, varicella zoster virus (VZV), Epstein Barr virus (EBV), CMV (cytomegalovirus), kaposissarcoma associated herpes virus or human herpes virus 8. As much as 60% cases of cornea ulceration in developing countries are caused by the herpes simplex virus. In the eye, HSV infection is more often caused by type 1 (>95%) than type 2, except in neonates, 75% is caused by HSV type 2.^[5]

Herpes simplex viral keratitis (HSV) is still one of the infectious etiologies that cause most common corneal blindness. HSV infection of the eye can be either primary infection or recurrent infection. Primary HSV infection is most often in the form of blepharoconjunctivitis, while for recurrent infections it can be epithelial keratitis, stromal keratitis (non-necrotizing stromal keratitis, namely interstitial keratitis and disciform keratitis and necrotizing stromal keratitis) and iridocyclitis.^[5] HSV infection of the eye is more common unilaterally, but 2-19% bilateral cases are also reported in immunocompromised patients. There is no clear evidence of differences in susceptibility to HSV infection by sex, but there are reports of an increased incidence in women and an increase in recurrence in men. Based on human and animal studies, males have a more intense response to viral infections but are more susceptible to reactivation. The opposite happened to women. Gender differences in these vulnerabilities may also affect response to therapy.^[6]

HSV keratitis has many manifestations that can be challenging for clinicians. As the population and ages increases, it is estimated that the burden associated with decreased visual function, lost productivity, and the need for continuous care also increases.^[3] Correct diagnosis and early treatment are very important in minimizing the occurrence of corneal scarring which can interfere with visual acuity. Therefore, this case report will discuss further about keratitis due to herpes simplex virus.

CASE REPORT

A man, aged 61 years, came to the Eye Polyclinic of Tabanan General Hospital, Bali, with complaints of blurred vision in his right eye since about 1 week ago. This complaint has been getting worse since 1 day ago. Complaints of blurred eyes are said to be like a cloud blocking the patient's vision. The complaint is felt all the time which is sometimes accompanied by other

symptoms. There is no condition that aggravates or relieves the patient's condition, but over time the complaints become worse.

Another complaints felt by the patient was that he often felt itchy, watery eyes, discharge from the eyes, a feeling of lump and a little glare. The patient also said that his complaints were accompanied by fever, nausea, vomiting, and headaches, causing the patient to be unable to sleep exactly 2 days before coming to the eye polyclinic, requiring him to come to the ER of a private hospital and receive symptomatic therapy. There was no other complaints like seeing black shadows, halos and curtains.

The patient had a history of herpes zoster 2 months ago where the disease attacked his right upper back region, shoulder, to the right upper chest which lasted approximately 1 month and he did not get proper treatment. The patient also has a history of controlled hypertension and kidney failure who is routinely dialysis until now.

On visual examination, visual acuity in the right eye was 6/15 and the left eye was 6/20. In the right eye there was corneal vascular injection (CVI). There were found dendritic lesions, infiltrate in the central cornea and arcus senilis in the right eye (Figure 1), while in the left eye was no abnormalities. In both eyes, the anterior chamber was deep, regular round iris, normal positive pupillary reflex, RAPD was negative (-), clear lens. Examination of the posterior segment of both eyes revealed no abnormalities. The nasolacrimal ducts of both eyes were within normal limits and the movement of the eyeballs in both eyes was good in all directions. Patients was diagnosed with Viral Keratitis et causa Herpes Zoster Virus in the right eye.

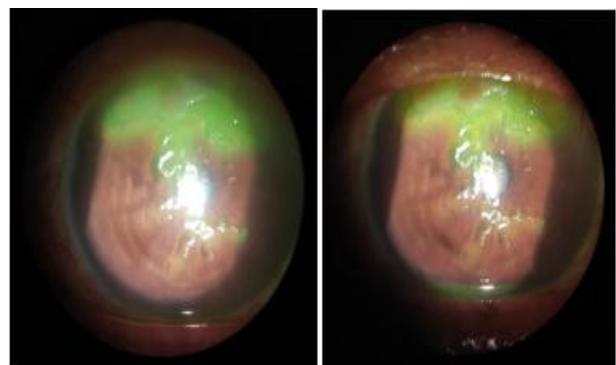


Figure 1: Clinical presentation of the patient's right eye cornea (with fluorescein test).

Treatment for this patient includes Acyclovir 400 mg orally for 2 weeks, CendoHervis (Acyclovir) eye drops in the right eye, Gentamycin eye ointment in the right eye, CendoLyteers (artificial tears) eye drops in the right eye, Paracetamol 500 mg orally (if necessary), Mecobalamin 500 mg orally, and did a routine control every 1 week.

One week later on June 3rd, 2021 the patient had his first control. The patient still complained of red eyes since 1 week ago, feels blurry, sometimes painful and minimal discharge in his right eye. On examination, the visual acuity in the right eye was 6/12F, while in the left eye it was 6/20. The right eye showed conjunctiva had CVI, and the cornea had minimal dendritic lesions and infiltrates (Figure 2).

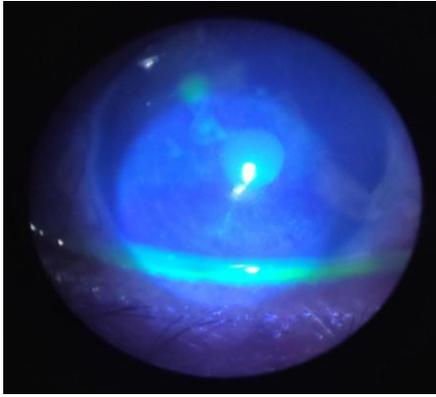


Figure 2: Clinical presentation of the patient's right eye cornea on June 3rd, 2021.

Patients were allowed to go home with the treatment given were CendoHervis (Acyclovir) eye drops in the right eye, CendoLyteers (artificial tears) eye drops in the right eye, Diclofenac sodium 50 mg orally (if necessary), Mecobalamin 500mg orally, Vitamin C orally, and control for 1 another week.

On June 10th, 2021 the patient came for a second follow-up. He complained a blurred vision in his right eye. On examination, the visual acuity in the right eye was 6/30, while in the left eye it was 6/20. In the right eye conjunctiva, CVI was found, and on the right eye cornea, dendritic lesions and ulcers were found in the central part of the cornea. The patient was allowed to go home with the treatment given were Gentamycin eye ointment, CendoHervis (Acyclovir) eye drops, CendoLyteers (artificial tears) eye drops, Paracetamol, Mecobalamin, Vitamin C, Acyclovir orally and control 1 week later.

The patient came for another follow up on June 17th, 2021, complaints in the right eye felt better. On examination, the visual acuity in the right eye was 6/20 while the left eye was 6/20. On the right eye conjunctiva, CVI was found, and the right eye cornea had dendritic lesions and ulcers on the central part of the cornea (Figure 3). The treatments before were continued and the patient must did a routine control 1 week later.

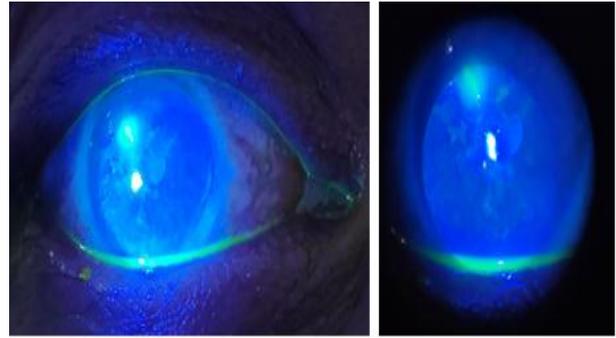


Figure 3: Clinical presentation of the patient's right eye cornea on June 17th, 2021.

On June 24th, 2021 the patient came for the fourth control. The patient complained of blurry vision in the right eye. On examination the visual acuity of the right eye was found to be 6/15 with corneal infiltrate (+) (Figure 4), whereas in the left eye it was 6/15. The treatment given were same as before, but Acyclovir oral and Mecobalamin was stopped. Patient came 1 week later for another routine control.

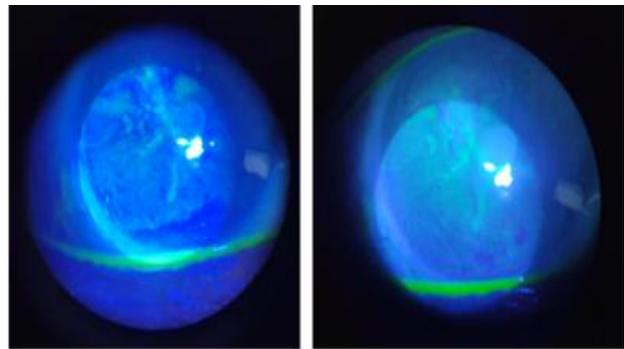


Figure 3: Clinical presentation of the patient's right eye cornea on June 24th, 2021.

On July 1st, 2021, the patient came back for control. He said that his right eye had improved. On examination, the visual acuity of the both eyes was 6/15 and the corneal infiltrate still shown but minimal. The treatment given were same as before, and control for 2 weeks.



Figure 5: Clinical presentation of the patient's right eye cornea on July 1st, 2021.

On July 15th, 2021, the patient's right eye was improved. On examination, the visual acuity of the both eyes was 6/15. On the right eye cornea, it was found there were cicatricial cornea, fluorescein was positive (+) peripheral cicatricial (Figure 6). The patient was diagnosed with

Follow Up Keratitis et causa HSV in the right eye. The treatment given was CendoHervis (Acyclovir) eye drops, Sanbe tears (artificial tears) eye drops, Vitamin C, Paracetamol, and control for 2 weeks later.

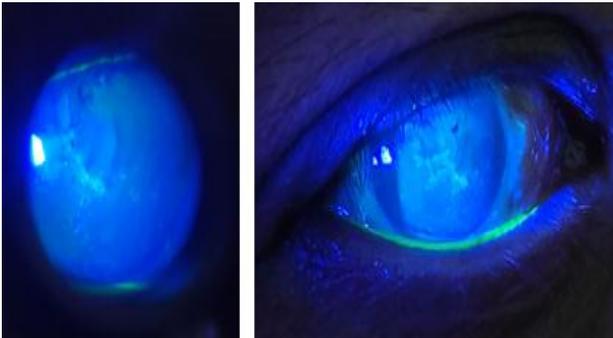


Figure 6: Clinical presentation of the patient's right cornea on July 15th, 2021.

DISCUSSION

Herpes simplex virus infection in the early stages is usually asymptomatic and occurs through direct contact with infected skin or through the mucosal epithelium. Virus enters epithelial cells on contact, replicates, enters sensory nerve endings, and travels retrogradely to the trigeminal ganglion, where it remains latent. After the initial round of replication in the trigeminal ganglion, the virus moves back to the nerves in an antegrade process, causing primary infection in about 6% of patients. Primary HSV infection is usually subclinical or causes only fever, mild symptoms of malaise and upper respiratory tract infection. Blepharitis and follicular conjunctivitis may occur but is usually mild. In recurrent infection, epithelial (dendritic/geographic) keratitis presents with symptoms of pain, foreign body sensation, light sensitivity, eye redness, and blurred vision.^[7]

Manifestations of infectious HSV keratitis can affect all layers of the cornea, from epithelial to endothelial layer.^[4] In this patient, the main symptom was blurred vision in the right eye since 1 week ago and worsened 1 day before coming to the hospital. Blurred vision is said to be like a cloud blocking the patient's vision. In addition, other complaints that the patient feels are right eye feel itchy, watery eyes, discharge from the eyes, a feeling of lump and a little glare. The patient also said that his complaints were accompanied by fever, nausea, vomiting, and headaches.

In 75% of patients, the diagnosis of HSV keratitis can be made based on the typical clinical features of a slit-lamp-assisted corneal defect and decreased corneal sensibility. Only in doubtful circumstances, laboratory tests can help to confirm the clinical suspicion in cases with atypical clinical features. Laboratory investigations that can be carried out are: Epithelial scraping with Giemsa and Papanicolaou staining, polymerase chain reaction (PCR), and viral culture as the "Gold Standard" which can determine the etiology of herpes simplex virus.^[4,8]

On the clinical picture there are some common symptoms including redness of the eyes, the presence of discharge, watery eyes, irritation, itching, pain, and photophobia. In most patients, symptoms begin to subside after the first 2 weeks. The most common subtype, epithelial keratitis, presents as coarse granular spots forming intermittent lesions, but these rapidly coalesce to form dendritic lesions. On physical examination, a white area was found. On slit-lamp examination, epithelial keratitis presents as a dendritic lesion with a terminal bulb, swollen margins, and intraepithelial cell infiltration. This was visualized by staining the lesions using lissamine green dye. In addition, to distinguish the location of infection can be done a simple test using fluorescein dye.^[8,9]

This patient underwent a physical examination, it was found that there was a decrease in vision in both the right and left eyes, but it was more worse in the right eye according to the location of the infection, with visual acuity of 6/15. In addition, the conjunctiva of the right eye has corneal vascular injection (CVI). During the follow-up examination, a fluorescein test and a slit lamp examination were performed. In the fluorescein test, a greenish color is obtained which indicates the presence of an infection in the cornea of the eye. On slit-lamp examination, the cornea of the right eye had dendritic lesions and an infiltrate in the central cornea. This indicates that the infected corneal layer is the epithelial layer.

Epithelial lesions of HSV initially appear as small lesions on the epithelium, which are referred to as punctate epithelial keratopathy (PEK). A common manifestation of HSV keratitis is dendritic ulcers, derived from the Greek word dendron, which means tree. The appearance of this dendritic ulcer is a branching, linear lesion with a rounded tip, which contains the virus. Widespread dendritic ulcers are called geographic ulcers. As with dendritic ulcers, these lesions are found in the epithelium that extends to the basement membrane. Another manifestation of HSV epithelial keratitis is marginal ulceration. The tip of this lesion is located at the limbus which is accompanied by blood vessels. These epithelial lesions are rapidly infiltrated by white blood cells from nearby limbal vessels.^[4]

Most herpes simplex keratitis infections subside on their own, even without treatment. However, healing takes a long time without proper treatment, and can become a worsened corneal inflammation and cause recurrent lesions, and also vision loss. In addition, other subtypes, such as geographic epithelial keratitis, are difficult to treat and require long-term therapy. Although self-limiting, it is important to treat the infection as early as possible to reduce viral replication, shorten the course of the disease, and maintain latency, to prevent further complications.^[8]

The use of antiviral therapy for HSV epithelial keratitis has been supported by several clinical trial data. In the

United States, the Food and Drug Administration (FDA) approved topical antivirals include trifluridine solution (1%), ganciclovir gel (0.15%), and acyclovir ointment (3%), while systemic therapies include acyclovir, valacyclovir, and famciclovir. The effectiveness of antiviral therapy for HSV epithelial keratitis was confirmed in an updated Cochrane systematic review and a meta-analysis by Wilhelmus, which included 137 randomized studies involving 8,333 eyes. Topical 1% trifluridine, 8 times daily, can be administered in dendritic and geographic epithelial keratitis.^[3]

Topical antiviral treatment is generally continued for 10-14 days to prevent toxicity to the ocular surface. Acyclovir salt is 3% more effective and has lower toxicity than Trifluridine and Vidarabine. Oral acyclovir is the most commonly used antiviral for ocular HSV and is as effective as topical. Oral antiviral treatment is penetrating and well tolerated and safe for the eyes, although dose adjustment is required in moderate to severe renal impairment and in the elderly. In contrast, topical antivirals are limited by their intraocular bioavailability and side effects such as ocular surface toxicity, allergic reactions, and punctal and nasolacrimal duct stenosis. For this reason, oral therapy is preferred by experts. Contraindicated topical corticosteroids in active epithelial herpetic keratitis. Therefore, patients on systemic corticosteroid treatment for other indications should be treated more aggressively with systemic antivirals.^[3,4]

In this patient, on arrival, several topical and systemic antiviral therapies were given and to reduce symptoms, namely: Oral acyclovir 400 mg 5 times per day orally for 2 weeks, CendoHervis (Acyclovir) antiviral eye ointment 5 times per day on the right eye, Gentamycin eye ointment 6 times per day on the right eye, CendoLyteers eye drops 6 times per day on the right eye, Paracetamol 500 mg 3 times per day (if needed), Vitamin mecobalamin 500 mg 3 times per day. This patient will be evaluated every 1 week for the next 7 weeks until the patient's complaints improve. As well as educating patients to use glasses to protect his eyes from exposure to light, dust, and unwanted things. And get enough rest, eat and drink nutritious food to increase the body's immunity.

In the first week of control until the fourth week, therapy was still continued. Oral antiviral use was continued for up to 1 month of treatment. At the fifth to last week of control, topical antiviral therapy and artificial eye drops and vitamins were continued until the patient's symptoms improved.

CONCLUSION

Keratitis is an inflammation of the cornea characterized by acute pain in the eye, decreased vision, corneal ulcers, and stromal infiltration. The most common viral keratitis is due to herpes simplex infection (HSV) and keratitis due to varicella zoster virus (HZV). HSV keratitis has

various clinical manifestations and can affect various layers of the cornea. Accurate diagnosis and prompt treatment are very important in minimizing the occurrence of corneal scarring or other complications that can occur which can threaten vision and cause permanent corneal damage.

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