



Case report

A unique case of herpetic keratitis manifesting as recurrent preseptal cellulitis

Emily Miller^{a,*}, Maxwell Ward^a, Tasaduq Fazili^b, Ekta Bansal^b

^a Department of Internal Medicine, Roanoke, VA 24014, United States

^b Department of Infectious Diseases – Virginia Tech Carilion School of Medicine, Carilion Clinic - 1906 Belleview Ave SE, Roanoke, VA 24014, United States

ARTICLE INFO

Keywords:

HSV keratitis
Immunocompromised
Preseptal cellulitis

ABSTRACT

Preseptal cellulitis is typically caused by nasopharyngeal bacteria and can usually be treated with empiric antibiotics. We present a case of herpes simplex virus (HSV) 1 keratitis manifesting as recurrent and treatment refractory preseptal cellulitis. This is a rare presentation that is infrequently reported in the literature. Due to the potential for permanent vision loss, it is important to consider herpes viruses as an etiology in immunocompromised patients with preseptal cellulitis not responding to standard treatment.

Introduction

Preseptal cellulitis is a skin and soft tissue infection around the eye that is anterior to the orbital septum. It is typically unilateral and presents as peri-orbital swelling, pain, and redness. It is commonly caused by the spread of bacteria from contiguous rhinosinusitis or direct trauma and therefore the most common pathogens are *staphylococcus* (including MRSA), *streptococcus*, and *H. influenzae* [2]. Typically, most cases occur in children and will resolve within 1 week given appropriate antibiotic therapy [2].

Viral etiologies are a very unusual cause of preseptal or orbital cellulitis. There are very few cases reported to date presenting as preseptal cellulitis caused by viruses. More commonly, viruses such as Herpes simplex virus (HSV) are known to cause keratitis, keratouveitis, blepharo-conjunctivitis or acute retinal necrosis. Viral keratitis is the most prevalent cause of keratitis with the global incidence of herpetic keratitis estimated at 1.5 million cases annually which corresponds to a 1 % lifetime risk worldwide [8].

We describe a case of HSV-1 keratitis presenting as recurrent and treatment-refractory preseptal cellulitis in an immunocompromised patient. This is notable as HSV keratitis is a leading cause of corneal blindness worldwide and may easily be overlooked if presenting in an atypical manner as was the case in our patient [5].

Case description

A 42-year-old male with end-stage kidney disease secondary to lupus nephritis (on hydroxychloroquine, mycophenolate and prednisone 80 mg daily) presented with recurrent unilateral left periorbital edema and erythema ongoing for the past 3 months.

He had an overly complex medical course in the preceding five months, starting with his diagnosis of lupus nephritis which required high doses of immunosuppressants. He was admitted several times at different local hospitals with worsening renal function, ultimately requiring dialysis, acute painful bilateral lower extremity edema, suspected due to nephrotic syndrome from lupus nephritis, acute left temporal stroke, acute left periorbital swelling, and seizures. Lumbar puncture was done during hospitalization for acute stroke, seizures and left periorbital swelling, with results (noted in Table 1) suggestive of traumatic tap.

Most recently, about 6 weeks prior (in Jan 2024), the patient was treated for Influenza A with secondary cavitory pneumonia (culture negative and no malignancy) with 6 weeks of broad-spectrum antibiotics. While on the antibiotics, he developed antibiotic associated diarrhea (negative for *Clostridioides difficile* infection) and recurrence of left eye swelling which “had been going off and on” for 3 months by this time. The patient denied visual changes or restriction of movement in the left eye but endorsed clear watery discharge and photophobia. He had significant swelling of L periorbital area (Fig. 1). Computed tomographic scan of the orbit supported preseptal cellulitis without evidence

* Corresponding author.

E-mail addresses: emmiller3@carilionclinic.org (E. Miller), mward@carilionclinic.org (M. Ward), tfazili@carilionclinic.org (T. Fazili), enbansal@carilionclinic.org (E. Bansal).

<https://doi.org/10.1016/j.idcr.2025.e02187>

Received 1 November 2024; Received in revised form 27 January 2025; Accepted 7 February 2025

Available online 9 February 2025

2214-2509/© 2025 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Table 1
CSF sample analysis suggestive of a traumatic tap.

CSF analysis	
Color Tube A	Colorless
Appearance Tube A	Clear
Tube A	1
WBC, CSF (0–10/mm3) Tube A	2
RBC count, CSF (/mm3) Tube B	246
Color Tube B	Colorless
Appearance Tube B	Turbid
Tube B	3
WBC Count, CSF Tube B	38
RBC Count, CSF Tube B (/mm3)	21,850
Glucose CSF	91
Protein CSF	60
CSF Neutrophils	88
CSF Lymphocytes	9
CSF Eosinophils	0
Albumin CSF	
Crypto Ag, Rflx, CSF	0
VDR, CSF	nonreactive



Fig. 1. Remarkable left eyelid edema.

of an abscess (Figs. 2a and 2b showing transverse and coronal views respectively). The patient had been receiving an empiric course of broad-spectrum antibiotics without any improvement. Infectious Diseases and Ophthalmology were consulted. The patient was then started on empiric systemic prednisone to reduce tissue swelling and allow for an eye exam to be completed. A trial of empiric valacyclovir was also initiated for consideration of possible herpetic etiology after noticing prior history of ‘cold sores’. Additionally, the left eye watery discharge and corneal swab were sent for PCR (Polymerase Chain Reaction) testing for HSV and VZV (varicella zoster virus). There was rapid improvement of tissue swelling (Fig. 3); PCR of the eye drainage resulted positive for HSV-1. Ophthalmologic exam also showed epithelial defect in upper cornea with extended dendrite pattern consistent with herpetic keratitis. Antibiotics were discontinued, and the patient was continued on valacyclovir and transitioned to lifelong suppressive therapy given his



Fig. 3. Resolution of edema after starting treatment with valacyclovir.

immunocompromised state. At the time of this writing – six months later, he had not had any recurrence of his left eye swelling and symptoms.

Discussion

HSV keratitis commonly presents with photophobia, severe pain, and watering due to involvement of the cornea as keratitis. Our patient exhibited photophobia and watering; however, this was overshadowed by significant periorbital swelling which led to three months of treatment with empiric antibiotics for presumed preseptal cellulitis. Lack of improvement on antibiotics initiated a search for alternative etiologies.

The presentation of herpes viruses (HSV-1/2 and VZV) as orbital or periorbital swelling is extremely rare. There have been only five cases reported so far in literature (Table 2). To our knowledge, our case is the sixth case to be reported with this atypical presentation.

Case 1

A 65-year-old female presented with over one week of pain and progressive periorbital edema sparing vision and extraocular muscles. She was initially treated with amoxicillin-clavulanate for three days with no response before the typical zoster rash appeared, bringing the diagnosis to light. Treatment with acyclovir was initiated [1].

Case 2

A 32-year-old female who presented with panophthalmitis affecting the optic nerve and surrounding tissue. She was treated with steroids and antibiotics with worsening of symptoms before HSV-2 was identified. She was treated with valacyclovir with a good response and transitioned to prophylactic valacyclovir [3].

Case 3

An 18-month-old male with diagnosis of cytokine 8 deficiency developed progressive periorbital erythema, swelling, and discharge

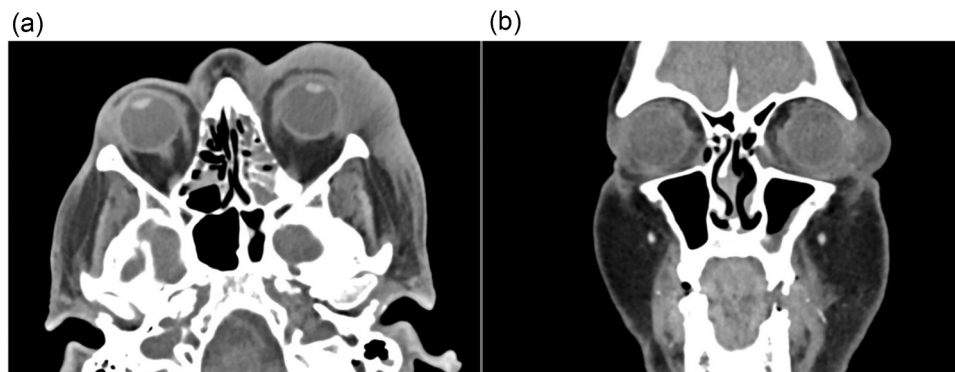


Fig. 2. a: Computed tomography image demonstrating left-sided preseptal edema; b: Computed tomography image demonstrating left-sided preseptal edema (coronal).

Table 2
Reported cases of Herpesviridae presenting with a component of extraocular edema.

	Presentation	Viral etiology	Immuno-compromised?	How diagnosis was made	Treatment administered
Case 1	65-year-old female with periorbital edema sparing vision and extraocular muscles	VZV	No	Clinical	Acyclovir
Case 2	32-year-old female with panophthalmitis and surrounding tissue edema	HSV-2	No	PCR	Valacyclovir followed by valacyclovir prophylaxis
Case 3	1-year-old male with progressive periorbital inflammation and ocular discharge	HSV-1	Yes	PCR	Acyclovir
Case 4	40-year-old female with recurrent pre-septal cellulitis	HSV-1	No	PCR	Valacyclovir followed by acyclovir prophylaxis
Case 5	4-year-old male who developed preseptal cellulitis in the setting of chickenpox	VZV	No	Clinical	No antiviral treatment

from the eye. He was initiated on teicoplanin with worsening of the symptoms on day three. This prompted consideration of nonbacterial causes and HSV-1 was identified, and the patient was treated with acyclovir [4].

Case 4

A 40-year-old female presented with recurrent, acute periocular swelling and tearing. This occurred yearly for 18 years before an etiology was established. Microbiologic testing confirmed HSV-1 as the culprit, and she responded to treatment with valacyclovir, and recurrence was prevented with acyclovir [6].

Case 5

A 4-year-old male presented with a vesicular rash which spread from the trunk to the face and limbs. After several days of this, the patient developed preseptal cellulitis of the R eye which did not respond to antibiotic therapy. Gram stain and cultures from an eventual incision and drainage were negative. VZV was suspected to be the ultimate etiology. But bacterial preseptal cellulitis that was slow to respond to antibiotics and ultimately treated with incision and drainage cannot be ruled out [7].

These presentations are unusual as herpes simplex typically causes keratitis (inflammation of the cornea) and spares the surrounding extraocular tissues from frank edema. Etiology is commonly due to the HSV reactivation from the ophthalmic branch of trigeminal ganglion and many times presents with a hallmark rash. Although there can be non-infectious causes of keratitis (such as eye trauma, chemical exposure, ultraviolet exposure, contact lens) or other viral infectious causes of keratitis (such as rhabdoviruses, coxsackieviruses etc), HSV remains the leading cause of infectious keratitis which makes it the most common infectious cause of corneal opacification and blindness in the US [5].

Our case is a unique presentation of HSV-1 keratitis masquerading as preseptal cellulitis. We purport that it is one of very few described cases of herpesviruses causing significant periorbital inflammation without a superimposed bacterial infection. The rapid improvement of our patient's condition after initiation of antiviral therapy supports the diagnosis of viral etiology, which was further solidified by confirmatory PCR testing and corneal dendritic pattern consistent with herpetic keratitis. Also, our patient's immunocompromised state could possibly be the reason the infection escalated to involve the preseptal tissues. Medications contributing to his immunocompromised state were prednisone, hydroxychloroquine, and mycophenolate mofetil along with the effects of lupus erythematosus itself on the immune system.

Alternative etiologies of a swollen eye should be considered in individuals not responding to treatment, especially individuals who are immunosuppressed as they will often present atypically with infections. Some differential diagnoses may include angioedema, insect bites, cavernous sinus thrombosis, chalazion, internal and external hordeola,

mucormycosis, nephrotic syndrome, orbital cellulitis, Pott's puffy tumor, and periorbital necrotizing fasciitis [2]. This case highlights the importance of not anchoring on a diagnosis as this can lead to delays in treatment and negative outcomes.

Ethical approval

IRB approval not needed for this case study.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Funding

Publication fees covered by Department of Infectious Diseases – Virginia Tech Carilion School of Medicine.

Disclosures

We have no disclosures.

Conflicts of interest

We have no disclosures.

CRediT authorship contribution statement

Bansal Ekta: Writing – review & editing, Supervision, Conceptualization. **Fazili Tasaduq:** Writing – review & editing. **Miller Emily:** Writing – review & editing, Writing – original draft, Resources, Conceptualization. **Ward Maxwell:** Writing – review & editing, Writing – original draft, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

- [1] Al-Rikabi A, Trotter MI, Khan H, Raut VV. A case of herpes zoster presenting as orbital cellulitis. *Kulak burun bogaz Ihtis Derg: KBB = J Ear Nose Throat* 2007;17(5):287–9.
- [2] Bae C, Bourget D. Periorbital cellulitis. [Updated 2023 Jul 17]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: (<https://www.ncbi.nlm.nih.gov/books/NBK470408/>).

- [3] Hassman LM, Chung MM, Gonzalez M, Bessette AP. Herpetic panophthalmitis: a diagnostic dilemma. *Ocul Immunol Inflamm* 2020;28(1):116–8. <https://doi.org/10.1080/09273948.2018.1546404>.
- [4] Pandrowala A, Ganatra P, Bodhanwala M, Sharma AN, Hiwarkar P. Periorbital cellulitis caused by herpes simplex virus in a child with dedicator of cytokinesis 8 deficiency. *Indian J Pediatr* 2022;89(7):723. <https://doi.org/10.1007/s12098-022-04108-0>.
- [5] Ahmad B, Patel BC. Herpes simplex keratitis. [Updated 2024 Jan 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. Available from: (<https://www.ncbi.nlm.nih.gov/books/NBK545278/>).
- [6] Khan SA, Hemming B, Babovic R, Imasogie Y. Recurrent unilateral preseptal cellulitis secondary to herpes simplex virus infection. *Eye News* 2023;29(6).
- [7] Qualickuz Zanan NH, Zahedi FD, Husain S. Varicella zoster causing preseptal cellulitis - uncommon but possible. *Malays Fam Physician* 2017;12(3):37–9 [PMID: 29527280; PMCID: PMC5842424].
- [8] Koganti R, Yadavalli T, Naqvi RA, Shukla D, Naqvi AR. Pathobiology and treatment of viral keratitis. *Exp Eye Res* 2021;205:108483. <https://doi.org/10.1016/j.exer.2021.108483> [Epub 2021 Feb 6. PMID: 33556334; PMCID: PMC8043992].