

case report

Title: **Recurrent Kerato-uveitis associated with Herpes Zoster Ophthalmicus**
Ophthalmoplegia

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Abstract:

Dendriform keratitis is a recurrent sequelae of herpes zoster ophthalmicus (HZO). A 76-year-old Indian male with HZO developed unilateral complete ophthalmoplegia following ~~Herpes Zoster Ophthalmicus~~ (HZO).

Complete resolution of ophthalmoplegia and ptosis was achieved with intravenous ~~aciclovir~~ acyclovir for a period of two weeks. His clinical course was complicated by nine recurrences of keratouveitis which was treated with topical aciclovir and steroids. The spectrum of corneal epithelial lesions included: (1) lacy branching pseudodendrites without true terminal bulbs (2) thickened grayish epithelium resembling mucous plaque keratitis, and (3) dot-like epithelial erosions in a linear configuration. ~~Each recurrence was treated with topical aciclovir and topical steroids only.~~

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HZO-associated complete ophthalmoplegia and keratouveitis are rare sequelae of HZO. Different corneal dendriform patterns can occur in the same patient with each recurrence of keratitis. Initiation of oral aciclovir 400 mg twice daily ~~for over nine month after the 6th recurrence resulted in a 24-month recurrence free interval till date prevented recurrence of symptoms.~~ This case ~~report~~ documents pleomorphic epithelial lesions in a patient with multiple recurrent dendriform

23 | keratitis. Oral aciclovir may have a prophylactic role against recurrent
24 | keratouveitis.

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27 | **Keywords:** Herpes zoster ophthalmicus; Complete ophthalmoplegia; Dendriform

28 | keratitis; [Aciclovir](#)

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Introduction

Late dendriform keratitis is a recognized sequelae of herpes zoster ophthalmicus (HZO). Epithelial recurrences are known to occur between 33% to 50% of patients with late dendriform keratitis.^{1,2} However, morphologic characterization of recurrent epithelial lesions, factors associated with recurrences, and optimal treatment strategies are unclear.³ In this case report, we describe a patient with HZO who developed recurrent anterior uveitis and late dendriform keratitis characterized by pleomorphic epithelial lesions. Recurrences were successfully managed with topical acyclovir and steroids, and initiation of oral acyclovir therapy resulted in no further recurrences to date.

Case report

A 76-year-old Indian male presented with a history of left-sided facial and periocular pain and erythema of 1 week duration. He had a history of hypertension, obstructive sleep apnea, a previous episode of lower limb cellulitis, and ~~was bilaterally pseudophakic, previously undergone cataract surgery in both the eyes with intraocular lens implantation.~~

On his first clinical evaluation he had a papulovesicular rash over the left side of his face and forehead. There were no vesicles at the tip of the nose or at the external auditory meatus. There was also no regional lymphadenopathy. Visual

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69 acuity was 20/30 in the right eye and 20/40 in the left eye. There was no relative
70 afferent pupillary defect, and color vision and confrontation visual fields were
71 normal. Extra-ocular motility was full, and the rest of the cranial nerves
72 examination was within normal limits. The applanation intraocular pressure was
73 37 mm Hg in the left eye and 20 mm Hg in the right eye. Slit-lamp examination
74 of the left eye revealed punctate epithelial erosions of the cornea, with a quiet
75 anterior chamber. Fundus examination was normal. A diagnosis of HZO¹ was
76 made and he was started on oral aciclovir 800 mg five-times a day and topical
77 timolol eye drops.

78
79 Fifteen days after the onset of HZO, the rashes had resolved with crusting. The
80 patient still had persistent left-sided periorbital pain. Evaluation of the left eye
81 showed visual acuity of counting fingers at 2 metres, conjunctival injection,
82 corneal epithelial edema and anterior uveitis with an intraocular pressure of 32
83 mm Hg. Fundoscopic examination was normal. There was also a superior
84 orbital fissure syndrome with V1, 3rd and 6th cranial nerve palsies with motility
85 examination revealing complete ophthalmoplegia in the left eye, — associated
86 with complete ptosis and a dilated pupil. The other cranial nerves were not
87 involved and there were with no clinical signs of meningitis or encephalopathy.

88 MRI revealed changes consistent with old infarcts in the corona radiata, but no
89 abnormalities were seen in the cavernous sinuses, orbits, meninges or central
90 nervous system. He was started on intravenous aciclovir at 500 mg thrice-daily,
91 oral gabapentin 300 mg once a day and a 3 hourly topical steroids to the left

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92 eye. There was improvement in ophthalmoplegia and ptosis within two weeks of
93 initiation of treatment. At 2 months follow up, there was a residual abduction
94 deficit and partial ptosis, and the left pupil remained dilated. There was complete
95 resolution of ophthalmoplegia and ptosis, and anterior uveitis 28 months after
96 the initial presentation.

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98 The patient's subsequent clinical course with varying keratitis patterns, treatment
99 and outcome has been outlined in Table –1. He had corneal epithelial
100 irregularities presenting as punctate epithelial erosions, pseudodendriform
101 patterns, dendrites, heaped up epithelium, coarse nodular opacities, nummular
102 keratitis, geographic patterns of radiating lines/dots and branches (Figure 1). He
103 also had corneal stromal edema, descemet membrane folds and endothelial
104 deposits, including pigmented keratic precipitates. Epithelial recurrences involved
105 paracentral and central lesions.

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106 Recurrence in our case was defined as a new dendriform corneal lesion after
107 resolution of previous lesions, with or without anterior chamber inflammation
108 consistent with previous reports.³. He had nine recurrences and remissions of
109 epithelial/stromal keratitis with or without anterior uveitis. Treatment involved
110 topical steroid eye drops, concurrently with aciclovir eye ointment and lubricant
111 eye drops. He subsequently had persistent raised intraocular pressure with
112 features of glaucomatous optic disc cupping 4 months after initiation of treatment.
113 Fortunately, from 9 months, IOP was consistently ≤ 21 mm Hg with IOP
114 medications and stable optic nerve head rim loss and visual fields on follow-up.

Discussion

To the best of our knowledge, this is the first case of multiple recurrent late dendriform keratitis and uveitis in a patient with HZO complicated by superior orbital fissure syndrome. This case demonstrates a spectrum of epithelial lesions over ~~four~~ five recurrence episodes. Both the duration of topical acyclovir therapy, and steroid usage for concurrent uveitic recurrences could explain these multiple recurrences. Lastly, this report suggests a possible prophylactic role for oral acyclovir against such recurrences. Anterior segment involvement has been documented in cases of HZO ophthalmoplegia. These clinical features include conjunctivitis, corneal epithelial defects, edema or keratitis and anterior uveitis. Corneal complications of HZO tend to occur in a temporal course related to virus infection and immune reactions, vasculopathy and neuropathy.⁴ Punctate epithelial keratitis and pseudodendrites are early and transient features. Keratouveitis/endotheliitis presents with localized stromal edema, keratic precipitates, anterior chamber cells and flare, and may represent direct viral infection or an immune reaction of the endothelium.¹ The release of viral antigens in the iris and ciliary body initiates a mild uveitis often accompanied by temporary elevation of the intraocular pressure that may become chronic.¹ Similarly, late complications in our case, i.e. recurrent VZV dendriform keratopathy, anterior uveitis, and superior orbital fissure syndrome could all be attributable to viral reactivation. There is evidence for an direct viral infection as a cause for keratopathy, particularly in immunosuppressed hosts, i.e. VZV DNA has been recovered in first-observed and recurrent corneal lesions.^{2,5} Our

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138 patient was immunocompetent, and although no microbiologic or serologic
139 investigations for VZV were conducted, there was a distinct complete resolution
140 of each recurrent episode to topical acyclovir, supporting an infective basis.

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141 Development of multiple cranial nerve palsies has been postulated to be due to
142 retrograde viral spread from the trigeminal ganglion to other ocular motor nerve
143 nuclei in the brainstem.⁶

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145 Hu et al³ described a spectrum of clinical features associated with the first-
146 observed epithelial lesions in HZO: there were branching forms with blunt ends
147 without true terminal bulbs, and comprising thickened and opaque epithelium.
148 This patient had lacy branching pseudodendrites, some of which assumed a
149 stellate configuration, grayish heaped-up epithelium, and dot-like epithelial
150 erosions (**Figure 1**). However, the recurrent lesions in our case appeared
151 coarser and larger. Our case provides further evidence that the well-described
152 mucous plaque keratitis sequelae of HZO is infective in origin, based on the
153 complete resolution of these lesions to topical acyclovir therapy.

154
155 The pathogenic mechanism for recurrent keratouveitis could be due to
156 persistence of viral genomes, most likely accompanied by gene expression or
157 slow viral replication.

158 This case may suggest that contributory factors towards multiple recurrences
159 include the use of topical steroids concurrently with topical acyclovir for epithelial
160 recurrences. To date, no study has identified any factor predisposing to

recurrence of late dendriform keratopathy. There was a treatment dilemma as our patient also had recurrent anterior uveitis and uveitic glaucoma, necessitating topical steroid therapy. In HSV concurrent epithelial and stromal keratitis, steroids are typically not started before closure of the epithelial defect, for fear of viral reactivation. medications individually or in combination at different stages in the clinical course.

Combined steroid and acyclovir is questionably better than steroid alone and causes marginally fewer rebound inflammations.⁷

Oral anti-viral prophylaxis was discussed with the patient in an earlier setting around the 4th month of his presentation with uveitis, however he did not wish to take long term systemic medication despite the risk of recurrence. Finally the oral acyclovir was started at the 19th month and continued beyond 28th month. The patient defaulted appointment and had stopped medications when he presented about 24 months later. He was apparently symptom free for about 2 years. Oral steroids were not considered in the patient's management as the keratouveitis was unilateral and most of the episodes of recurrence resolved with topical medication alone.

HZO ophthalmoplegia associated hypertensive keratouveitis with varied dendriform patterns can occur. Long term antiviral, anti-inflammatory and

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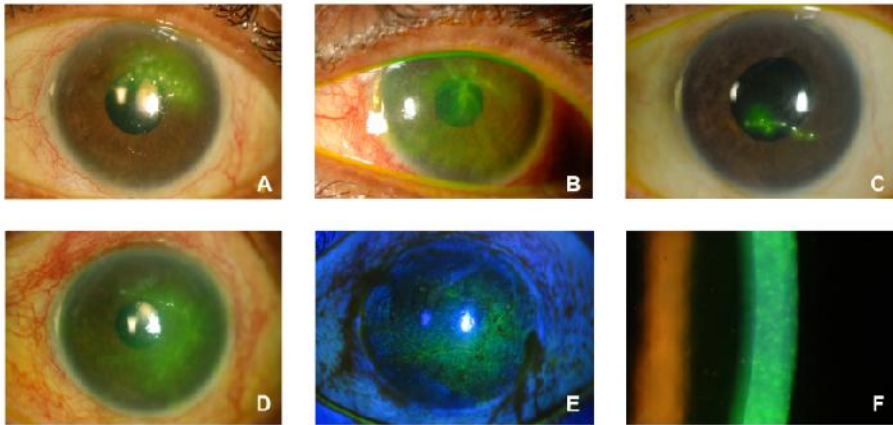
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antiglaucoma medications are necessary to prevent recurrences. There is a role for both topical aciclovir and steroid drops in managing this condition.

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208
209 **Legends for Figure 1**

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211
212 Figure 1: Slit-lamp biomicroscopic photographs of our patient with HZO keratitis
213 patterns with fluorescein staining

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215 A- Paracentral nodular epithelial lesions with thickened epithelium (4th month)

216 B- Central multiple, lacy branches (5^{1/2} month)

217 C- Inferior pseudodendriform lesions with peripheral bulbs(9th month)

218 D- Extensive superior and inferior dendriform lesions with punctate epithelial
219 erosions (15th month)

220 E- View with cobalt blue filter of fluorescein stained dendriform lesions illustrated
221 in D

222 F- Slit view showing coarse punctate epithelial keratitis.(19th month)

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Table-1 showing the clinical course, management and outcome in our patient

Time line	Symptoms	Presentin g VA	IOP (mmHg)	Signs	Intervention	Outcome	Remarks
0 days	Vesiculopapular rashes on left side of face and forehead	20/40	37	• PEE • Dilated pupil	• Oral aciclovir 800mg 5 times/day • G. timolol 0.5% bd • Artificial lubricants	Resolution of rashes	
15 days	• Drooping of left eyelid • Inability to move the LE	CF-2m	32	• Crusting of rashes • Corneal epithelial edema • Anterior uveitis • Complete ophthalmoplegia of the left eye	• IV aciclovir 500mg tds for 2 weeks • PO Gabapentin 300 mg OM • G. prednisolone acetate 1% qds • G. homatropine 2% bd • Artificial lubricants	Improvement in Ophthalmoplegia	• MRI Brain and anterior visual pathway - Normal
2 months	Partially able to open the LE	20/40	24	• Residual abduction deficit • Partial ptosis • Dilated pupil	• G. prednisolone acetate 1% qds tapered and stopped over a month		
4 months Fig 1A	• Decreased vision LE of two weeks duration • Pain in LE	CF-1m	31	• PEE • Corneal epithelial edema • Paracentral nodular epithelial lesions with thickened epithelium • Epithelial irregularities • Endothelial pigmentary deposits • Anterior uveitis	• G. prednisolone acetate 1% G. timolol 0.5% bd • G. brimonidine 0.15% bd • G. homatropine 2% bd • Artificial lubricants	Improvement in corneal surface	
5 months	• Pain in LE	20/50	24	• Pigmented KP	• G. timolol 0.5% bd • G. brimonidine 0.15% bd • G. prednisolone acetate 1% qds	• Resolution of corneal epithelial irregularities • Anterior uveitis resolution	

[illegible]

					▲ G. brimonidine 0.15% bd ▲ G. dorzolamide 2% tds ▲ Artificial lubricants		
52 month	Blurring of vision LE	20/60	16	- Cornea clear - AC quiet - Posterior capsular opacification -	. dexamethasone (preservative free) once at night ▲ G. timolol 0.5% bd	Patient had stopped T aciclovir after the last visit about 14 months and had defaulted follow up. As he was symptom free Feb Aciclovir 400mg bd	
53 month		20/25		Cornea clear - AC quiet	Artificial lubricants	Feb Aciclovir 400mg bd	

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Legend:

▲ HZO- Herpes Zoster Ophthalmicus VA- Snellen Visual acuity IOP- Intra ocular pressure in mm Hg LE- Left eye CF- Counting Fingers PEE- Punctate epithelial erosions bd- Twice a day ▲ IV- Intravenous	▲ Tds- thrice daily PO- Per oral ON- Once in the night time OM- Once in the morning Qds- four times daily MRI- Magnetic resonance Imaging KP- Keratic precipitates ERM- Epi-retinal membrane
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