Late dendriform keratitis in herpes zoster ophthalmicus: Evidence for late infection and management recommendations

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Abstract: Recent research suggests late dendriform keratitis following herpes zoster ophthalmicus is an active viral infection, responsive to systemic antiviral therapy. This report represents a case where oral antivirals lead to successful resolution of such lesions.

I. Case History
   a. A 62-year-old white male presented with a chief complaint of redness and irritation of his right eye that had been present for “a few days”.
      i. His ocular history was significant for herpes zoster ophthalmicus (HZO) OD, which was found to be completely resolved 1-month prior.
      ii. The presenting symptoms were similar to the eye irritation felt during the acute zoster infection.
      iii. He was using artificial tears every 2 hours as previously prescribed.
      iv. The acute HZO presentation was significant for the typical signs and symptoms of herpes zoster, including malaise, forehead pain, and erupting forehead and eyelid vesicles. While there was no Hutchinson sign, the eye was involved, manifesting a mild anterior uveitis and a dendritic/pseudodendritic keratitis. He was treated with oral valacyclovir for the zoster infection, topical steroid to remediate the uveitis, topical antibiotic ointment for prophylaxis, and artificial tears for lubrication.
      v. His ocular history was also significant for being functionally monocular (OD seeing) x 30 years due to an episode of endophthalmitis OS. There were no formal records of the cause, but the patient’s history of IV drug use and no prior ocular surgery leads one to believe it was an endogenous endophthalmitis.
      vi. He also had a history of category III dry age related macular degeneration in his right eye, having minimal affect on his visual acuity (20/25)

II. Pertinent Findings
   a. Entrance tests
      i. Uncorrected visual acuity was 20/25- OD and hand motion at 2’ OS with no improvement upon pinhole. OD pupil was round with a 3+ reaction to light. OS pupil was miotic, oval, and displaced superior temporally with little to no reaction to light. (+) APD OS seen by reverse pupillary testing. Confrontational visual fields were full to finger counting OU. Extraocular motilities were full with no restrictions OU.
   b. Anterior Segment
      i. Lids/lashes
         1. OU: tr flaking and lash debris
      ii. Conjunctiva
         1. OD: tr diffuse bulbar injection with tr-1+ inferior temporal limbal injection
         2. OS: clear and quiet
iii. Cornea
   1. OD: see pg 5, *figure 1*
      a. multiple midperipheral delicate dendriform lesions with no terminal end bulbs, some focal epithelial defects, all with (+) staining
      b. diffuse, mild, anterior stromal haze
      c. no keratic precipitates
   2. OS: clear and quiet, no staining
iv. Angle
   1. OS: ¾:1
   2. OD: 1:1
v. Anterior Chamber
   1. OU: deep and quiet
vi. Lens
   1. OD: tr nuclear sclerosis and tr psc
   2. OS: aphakic
vii. Iris
   1. OD: flat
   2. OS: concave, irregular pupil

c. Posterior Segment
   i. Posterior segment showed no signs of inflammation in either eye. The right eye showed category III AMD with confluent drusen and pigment at the macula, sparing the fovea. It was otherwise unremarkable. The macula in the left eye was fibrotic and atrophied s/p vitrectomy and endophthalmitis.
d. Physical Findings
   i. Corneal sensation was equal between the two eyes
   ii. Patient was immunocompetent and found to be HIV (-) 3 days prior to the exam.
   iii. He had very little post-herpetic pain, reporting an occasional shooting pain on the right side of his head.
   iv. The patient is currently being treated for a cellulitis of his right lower extremity secondary to a broken foot.

III. Differential Diagnosis
   a. Herpes simplex epithelial keratitis
      i. The lesions in this case were dendritic in nature with (+) staining. This presentation is often associated with a herpes simplex epithelial keratitis. The lesions in this case appeared in a more delicate pattern without terminal end bulbs. The recent history of HZO in a relatively quiet eye supported the conclusion that the lesions were not simplex. Rose Bengal staining could have been used for confirmation but was not deemed necessary at time of presentation.
      ii. Regardless, it has been shown that a 1 gram dose of valacyclovir produces a peak plasma concentration of 5-6μg/ml of acyclovir which is a therapeutic dose for both varicella zoster virus (VZV) and herpes simplex virus (HSV). Therefore, had the keratitis been simplex in nature, the treatment would have been adequate.
IV. Diagnosis and Discussion
   a. Late dendriform keratitis OD, secondary to recent HZO
   b. Early pseudodendrites occur in approximately one third of HZO infections. They have been shown to contain active virus during their initial presentation and typically resolve spontaneously within a few days. The lesions in this case were discovered 2 months after the acute onset of the condition. Therefore, the presentation is considered one of late dendriform keratitis.
   c. The occurrence of late lesions is reported in 4-13% of HZO patients.
   d. These late lesions have been described as pleomorphic and transient in appearance. They often have multiple components varying between dots, lines and branching lesions with blunt ends. The lesions can be discontinuous and the branching lesions have been described as more course or more delicate than HSV dendrites. The VZV branching lesions tend to be irregular in appearance as opposed to the more discreet lesions caused by HSV. Some of the late VZV lesions have presented with an associated stromal keratitis or iritis.
   e. In the past, it has been proposed that late dendriform lesions were non-infectious in origin. More recently, it has been shown that VZV DNA can be detected via polymerase chain reaction (PCR) in late dendriform lesions. Due to the presence of the VZV DNA and the response to antiviral therapy, current literature suggests that there is active VZV in the lesions.

V. Treatment and Management
   a. The following treatment was initiated:
      i. valacyclovir, 1000mg, po, tid, to treat the active viral component
      ii. polytrim, 1 gt, OD, qid, for prophylaxis from bacterial co-infection
      iii. preservative free carboxymethylcellulose 0.5%, 1 gt, q3hr while awake for lubrication to promote corneal healing
   b. The patient returned to clinic 6 days after initiation of treatment, see pg 5, figure 2
      i. The majority of dendriform lesions were completely resolved. There was one residual linear area of staining inferiorly. Otherwise, the OD cornea showed diffuse superficial punctate keratitis, suspected to be secondary to corneal toxicity from the antibiotic drops, but no distinct lesions or frank epithelial breaks were present.
   c. Hu et al report approaching all cases of late dendriform keratitis by starting antiviral medication and reducing iatrogenic immunosuppression. Following this approach, they found a consistently shorter time to resolution after initiating therapy than the duration of the lesions prior to initiating therapy. While not definitive, this suggests that their approach was successful. With the presence of symptoms and the risk of concurrent stromal keratitis and/or iritis, they suggest that all cases of late dendriform keratitis should be treated.
   d. According to a case study by Pavan-Langston, topical trifluridine (Viroptic) has little to no effect on these types of lesions. Topical vidarabine (which is no longer commercially available in the US) and oral acyclovir proved to be the most efficacious.
VI. Conclusion

Although sparse, current literature suggests that late dendriform keratitis following HZO is an active viral infection. Pulling from a number of articles on the topic, it seems the current best treatment of these lesions is with oral antiviral agents.

It has been shown through case reports that topical trifluridine is not effective in these cases. Topical vidarabine has shown some success but is no longer commercially available in the US. There is merit to the idea that topical gancyclovir (Zirgan) may show promise as an alternative to oral therapy but there is currently no literature to support this hypothesis.

Some say the incidence of HZO may increase by as much as 42% in coming years due to varying factors in immunity and vaccinations. Therefore, it is becoming more imperative for us as primary eye care providers to familiarize ourselves with the current research regarding the complications and treatments associated with herpes zoster ophthalmicus. This case presents just one of many complications we should be clinically equipped to address.

Sources:


Figure 1. OD cornea appearance pre-treatment

Figure 2. OD cornea 6 days after initiation of treatment