

Reactivation of herpes simplex keratitis following vaccination for COVID-19

James Richardson-May ¹, Alice Rothwell,¹ Mohammed Rashid²

¹Ophthalmology, University Hospital Southampton NHS Foundation Trust, Southampton, UK

²Ophthalmology, University Hospitals Dorset NHS Foundation Trust, Bournemouth, UK

Correspondence to

Dr James Richardson-May; jamesrichardsonmay@gmail.com

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SUMMARY

An 82-year-old man with a history of herpes simplex keratitis 40 years previously presented with recurrence, 1 day following vaccination for novel COVID-19. His condition worsened despite topical treatment with ganciclovir gel. A diagnosis of herpetic stromal keratitis was made, requiring systemic aciclovir, topical prednisolone, moxifloxacin and atropine, and oral doxycycline. He improved clinically on treatment, with some residual corneal scarring. Visual acuity improved from 6/36 corrected at presentation, to 6/24 following treatment. Clearly, public and personal health benefits from vaccination are hugely important and we would not suggest avoiding vaccination in such patients. It is, however, important for ophthalmic providers to be aware of the rare potential for reactivation of herpetic eye disease following vaccination to enable prompt diagnosis and treatment.

BACKGROUND

Herpes simplex keratitis is a common ocular condition regularly presenting to ophthalmic emergency services. While epithelial disease is usually treatable with topical antivirals, occasionally it can be more aggressive and require more intensive treatment to avoid visual complications. With a national vaccination programme underway for the novel COVID-19 pandemic, we feel it important to highlight this case in which there is a likely temporal association between vaccination and reactivation of herpes simplex keratitis, more than 40 years since the patient's last episode.

CASE PRESENTATION

An 82-year-old man presented to the ophthalmic emergency department with a painful, watering and red left eye. His symptoms had begun 1 week previously, the day after his first dose of vaccination for novel COVID-19 (AstraZeneca). Visual acuity (VA) at presentation was 6/36 in the left eye, improving to 6/24 with pinhole. On examination, the eye was significantly hyperaemic with reduced corneal sensation and multiple corneal dendrites. There was evidence of previous corneal scarring. He had a history of herpes simplex keratitis, which had been quiescent for 40 years. His right eye was unremarkable with VA of 6/9.

INVESTIGATIONS

Initially, our patient was diagnosed clinically. As described below, later deterioration in the clinical appearance led to microbiological investigation with corneal scrapes.

DIFFERENTIAL DIAGNOSIS

On the basis of his ocular history, along with classical corneal findings of epithelial dendritic ulcer, he was diagnosed with herpes simplex epithelial keratitis.

TREATMENT

This patient was initially started on ganciclovir 0.15% gel, five times a day.

OUTCOME AND FOLLOW-UP

Despite this treatment, he returned 1 week later with worsening pain and vision. His VA was reduced to hand movements in the left, with diffuse hyperaemia, corneal haze and mild anterior chamber inflammation. There was evidence of geographical ulceration and corneal neovascularisation ([figure 1](#)). Corneal scrapes were taken for microbiology, including viral PCR, and a diagnosis of herpetic stromal keratitis was made. He was started on acyclovir 800 mg orally five times a day, doxycycline 50 mg orally once a day, preservative free prednisolone phosphate 0.5% once a day, atropine 1% once a day and moxifloxacin 0.5% four times to the left eye. Ganciclovir gel was continued five times a day.

The patient continued to improve; 2 weeks later, vision was significantly improved to 6/24 corrected, 6/18 with pinhole. He was much more comfortable. Microbiological results were positive for herpes simplex virus-1 (HSV-1), as well as the presence of diphtheroids. The epithelial defect was noted to have healed, with a quiet anterior chamber. Treatment was continued with plans to reduce ganciclovir gel to three times a day after 1 week.

This patient underwent planned review 2 weeks later. Best-corrected VA in the affected eye was 6/24. The eye was quiet with central corneal scarring and mild nuclear sclerotic cataract ([figure 2](#)). Topical treatment was tapered off and aciclovir reduced to a prophylactic dose of 400 mg two times a day, to continue.

DISCUSSION

HSV-1 and HSV-2 are common, double-stranded, non-enveloped DNA viruses. Ocular infection can cause a range of conditions. In the cornea, this includes epithelial, stromal and disciform keratitis. Other ocular conditions include blepharoconjunctivitis, iridocyclitis and retinal infection such as acute retinal necrosis.¹ Approximately 52%–84% of adults demonstrate latent infection to HSV-1.² Latent infection within the trigeminal ganglia, along with recurrent episodes of viral replication,



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Figure 1 The patient's clinical appearance 1 week after beginning topical treatment. The eye is significantly inflamed, with corneal neovascularisation, epithelial defect and stromal opacity. The pupil is pharmacologically dilated.

can lead to recurrent clinical disease; this can include corneal infection, as in our patient.

Hassman and DiLoreto described a patient with previous HSV-1 encephalitis, who later developed acute retinal necrosis 1 day following an influenza vaccine. PCR of the aqueous fluid was positive for HSV-1.³ Reactivation of cutaneous HSV-2 has been reported in a patient with transverse myelitis following influenza vaccination.⁴ Grillo and Fraunfelder, identified 24 causes of keratitis following vaccination for varicella zoster; most of these occurred within days, and resolved with topical steroid and oral aciclovir. They suggested that persistent viral antigens within the cornea may be the underlying mechanism.⁵ Walter *et al* described reactivation of herpes virus infection in mostly healthy subjects with no relevant comorbidity following vaccination.⁶

Possible mechanisms for reactivation of HSV following vaccination include molecular mimicry, in which the host proteins



Figure 2 The same eye following treatment. The inflammation has settled and the epithelial defect has closed. There is evidence of corneal scarring inferiorly which is encroaching on the visual axis.

are mimicked by those within the vaccine, thus triggering a host response. A further proposed mechanism includes autoinflammation triggered by the vaccine, with possible reduction in neurotrophin allowing HSV replication; this has been demonstrated within the brain following intranasal H1N1 influenza vaccination.^{3,7} Further, distraction of humoral response due to the vaccination may lead to loss of immunological control of HSV.³

To our knowledge, this is the first reported case of reactivation of herpes simplex keratitis following vaccination for COVID-19, with a clear temporal relationship. Given the significant personal and public health benefits in receiving vaccination for COVID-19, as well as the apparently rare occurrence, we do not suggest withholding vaccines in this population. However, providers should be mindful of the possible association and encourage patients to seek ophthalmic review should they develop new ocular symptoms.

Learning points

- ▶ Herpes simplex keratitis is a common eye condition presenting to ophthalmic emergency services.
- ▶ When treatment with topical antivirals fails, further investigations (such as corneal scrapes) should be sought and treatment escalated.
- ▶ Close follow-up for such patients is important to assess for potential visual complications.
- ▶ Ophthalmic providers should be aware of the potential for reactivation of herpes simplex following vaccination.

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ORCID iD

James Richardson-May <http://orcid.org/0000-0002-8223-3101>

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