

## CASE REPORT

## Lamellar macular hole after intravitreal ocriplasmin injection

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## SUMMARY

Intravitreal ocriplasmin was recently approved by the Food and Drug Administration to achieve medical vitreolysis in the setting of vitreomacular adhesion (VMA). We report a case of a 76-year-old woman who developed a lamellar macular hole following treatment with intravitreal ocriplasmin injection for VMA. A pathophysiological mechanism to explain this previously unreported complication of ocriplasmin injection is proposed.

## BACKGROUND

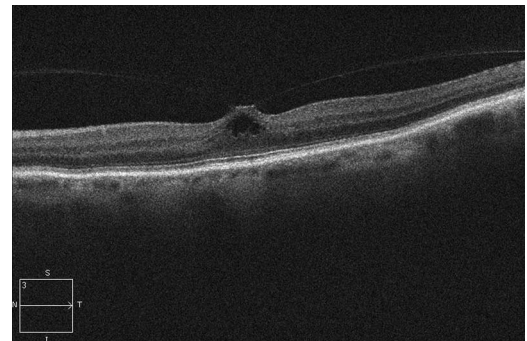
Physiological liquefaction and contraction of the vitreous body commonly cause disruptions in the connections between the hyaloid membrane and the internal limiting membrane of the retina. This process leads to posterior vitreous detachment (PVD). Vitreomacular adhesion (VMA) and vitreomacular traction (VMT) are observed when sub-total PVD occurs and a portion of the posterior hyaloid face remains attached at the macular centre.<sup>1</sup> In such instances, VMA, VMT, as well as full-thickness and lamellar macular holes may result at the fovea.<sup>1-2</sup> Pars plana vitrectomy remains the gold standard of care when these processes become visually significant.<sup>3</sup> Ocriplasmin, an intravitreal agent approved by the Food and Drug Administration (FDA) in 2012, provides a pharmacological alternative to surgical release of symptomatic VMT.<sup>4</sup>

Ocriplasmin is a low-molecular-weight recombinant molecule consisting of the catalytic domain of the human serine protease, plasmin.<sup>5</sup> The activity of this molecule is utilised for its ability to cleave glycoproteins, specifically fibronectin and laminin,<sup>6-7</sup> which comprise much of the molecular connection at the vitreoretinal interface.<sup>8</sup> As such, ocriplasmin is injected intravitreally to induce medical vitreolysis and release of VMT.<sup>9</sup> At the FDA recommended dose of 0.125 mg/0.1 mL intravitreal injection, however, this treatment has been shown to successfully achieve VMT release in only 31% of patients.<sup>10</sup>

We present an interventional case report describing a patient with VMT who developed a lamellar macular hole 7 months after failed intravitreal ocriplasmin injection.

## CASE PRESENTATION

A 76-year-old woman with a history of surgically repaired macular hole of the right eye was noted to have an asymptomatic VMT with impending macular hole in the left eye, with best corrected



**Figure 1** Spectral domain optical coherence tomography demonstrating vitreomacular traction at presentation, prior to injection of ocriplasmin.

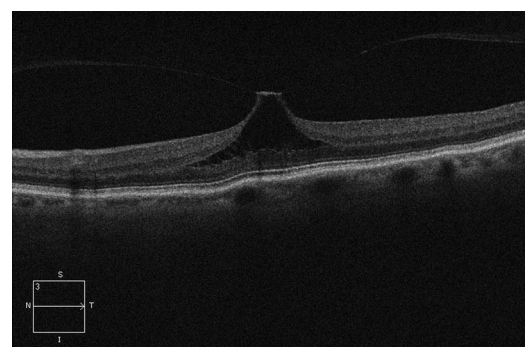
visual acuity (BCVA) of 20/25 in the affected eye (figure 1). Given the asymptomatic nature of the macular hole and good visual acuity in the left eye, observation was recommended. Twenty-one months later, follow-up spectral domain optical coherence tomography (SD-OCT) imaging showed progression of the VMT (figure 2). After a thorough discussion of therapeutic options, including continued observation, the patient elected to undergo injection of ocriplasmin.

## TREATMENT

The patient received one intravitreal injection of ocriplasmin at the recommended dose (0.125 mg in 0.1 mL diluted solution).

## OUTCOME AND FOLLOW-UP

At first follow-up, 8 days after the injection, the patient denied improvement in vision and denied visual side effects. BCVA of the left eye was noted

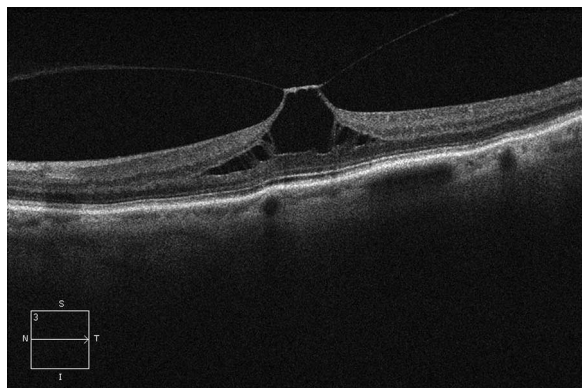


**Figure 2** Spectral domain optical coherence tomography demonstrating progression of vitreomacular traction prior to injection of ocriplasmin.



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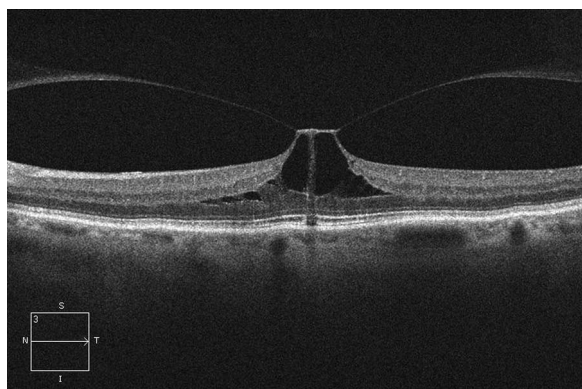
**Figure 3** Nearly unchanged appearance of vitreomacular traction 1 week after ocriplasmin injection.

to be 20/20, however, SD-OCT imaging demonstrated an unaltered appearance of the VMT (figure 3). At next follow-up, 1 month postinjection, the VMT persisted with minimal change in appearance on SD-OCT imaging (figure 4). Seven months after injection, the patient continued to deny any changes in vision or visual symptoms. BCVA was noted to be 20/20 in the left eye. Clinical examination and SD-OCT demonstrated the formation of a lamellar hole of the macula with operculum of inner retinal tissue persistently adherent to the posterior hyaloid membrane (figure 5).

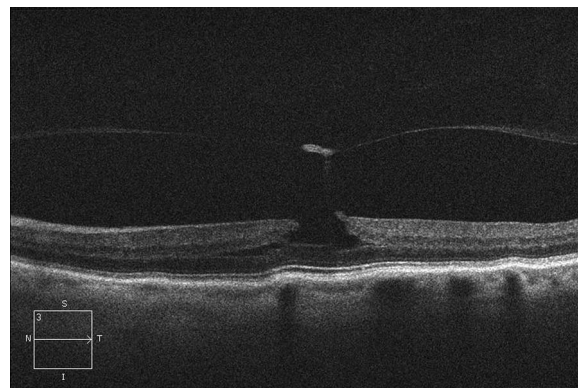
## DISCUSSION

Our patient's imaging illustrates foveolar VMT with poor response to ocriplasmin injection. Seven months after injection, however, SD-OCT demonstrated a lamellar macular hole corresponding to the previous site of VMT.

The activity of ocriplasmin presumably has the potential to affect all of the vitreoretinal attachment points within the eye. Furthermore, availability of the drug to the entire continuum of vitreoretinal interface may be affected by various clinical parameters: drug distribution within the vitreous cavity, heterogeneity of vitreoretinal attachment integrity, epiretinal membranes and other pathophysiological variabilities. Additionally, mechanical forces inherent in the act of performing intravitreal injections, including possible vitreous incarceration at the injection site, might also increase the anteroposterior traction on the target VMT.



**Figure 4** Nearly unchanged appearance of vitreomacular traction 1 month after ocriplasmin injection.



**Figure 5** Lamellar macular hole with retinal operculum observed 7 months after the injection of ocriplasmin for vitreomacular traction.

As is believed to be the case with our patient, if intravitreal ocriplasmin injection fails to induce successful vitreofoveal release, the use of this medication may actually result in increased anteroposterior forces concentrated at the target VMT. Such forces might be great enough to overcome the intrinsic strength of the retinal tissue, thereby causing a lamellar macular hole. Further, peripheral retinal breaks have been reported after intravitreal ocriplasmin injection.<sup>11</sup>

The MIVI-TRUST trial demonstrated that the effect of ocriplasmin on VMT plateaus by day 28, however, it could not account for the pharmacokinetic activity of ocriplasmin at non-target areas of vitreoretinal adherence. Despite failure of the target VMT to release, one can safely assume that drug action was fulfilled elsewhere within the eye. While the natural history of VMT includes progression to macular hole,<sup>12</sup> the kinetic changes resulting at the site of VMT after intravitreal ocriplasmin injection might accelerate this process. Such a possibility would be a cause for caution in the use intravitreal ocriplasmin for the treatment of symptomatic VMT.

In summary, we present the case of a patient who sustained a lamellar macular hole following injection of ocriplasmin for VMT. To our knowledge, this complication of ocriplasmin injection has yet to be reported. Notably, the patient suffered no vision loss from this event. We do not have peripheral optic coherence tomography (OCT) imaging to confirm peripheral vitreoretinal release. Further studies with peripheral OCT, including three-dimensional and en-face imaging,<sup>13</sup> may be warranted to investigate extrafoveal vitreomacular release after ocriplasmin injection.

## Learning points

- ▶ Intravitreal ocriplasmin injection has become a therapeutic option for the treatment of symptomatic vitreomacular traction.
- ▶ Intravitreal ocriplasmin injection is not always successful in affecting release of vitreomacular traction.
- ▶ More is being learned about the risks of performing intravitreal ocriplasmin injection, including the possibility of lamellar macular hole and other retinal breaks.

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**Competing interests** None.

**Patient consent** None.

**Provenance and peer review** Not commissioned; externally peer reviewed.

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