

## Herpes Simplex Negative Trabeculitis Responsive to Anti-Viral Mediation: A Case Report

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### Abstract

**Background:** Patient's that present with unilateral ocular hypertension can create a diagnostic challenge for the clinician. This observational case reports of a patient who initially presented with unilateral eye pain, whose HSV PCR was negative, however still appeared to respond to anti-viral treatment. The patient had a unilateral intraocular pressure spike that only decreased with addition of topical steroid, thus was presumed to be secondary to trabeculitis.

**Case Presentation:** This case reports a healthy 47-year-old male, who initially presented with unilateral eye pain (44 mmHg). The patient's IOP was unresponsive to pressure-lowering medication, but was eventually normalized with topical steroid. Despite negative PCR sampling of aqueous humor, the patient's ocular exam and subjective symptoms normalized after a course of acyclovir.

**Conclusion:** This case highlights an unusual presentation of a unilateral IOP spike, which was only responsive to topical steroid, supporting the idea of an inflammatory origin. However, the subsequent development of anterior chamber reaction infers a potential infectious etiology. Although the patient's HSV PCR was negative, a course of acyclovir did appear to resolve the patient's inflammation, IOP increase, and subjective symptoms. In this patient, it is not certain if HSV was the causative agent involved. Though even with a negative anterior chamber sample, suspicion for HSV remains high, as the patient appeared to improve with antiviral treatment. This case has significant clinical relevance for the clinician managing unilateral ocular hypertension seemingly resistant to initial pressure-lowering treatment, a somewhat uncommon but not scarce case.

**Keywords:** Trabeculitis; Ocular Hypertension; Herpes Simplex Virus (HSV); PCR, Case Report

### Abbreviations

IOP: Intraocular Pressure; PCR: Polymerase Chain Reaction; HSV: Herpes Simplex Virus; mmHg: Millimeters Mercury; SD-OCT: Spectral Domain Optical Coherence Tomography; NFL: Nerve Fiber Layer; BID: Twice a Day; TID: Three Times a Day; OD: Right Eye; OS: Left Eye; OU: Both Eyes

### Background

Patient cases that present with unilateral intraocular pressure (IOP) spikes involve a wide range of differential diagnoses. Often times, structural features of the hypertonic eye, such as a mature lens, angle abnormalities, anterior chamber reaction, optic disc characteristics, or neovascularization can suggest an underlying etiology. However other times, an eye that appears structurally similar to its fellow eye can present with a largely disparate IOP, thus presenting a challenging diagnosis and management choice for the clinician.

Previous cases have been reported in which unilateral ocular hypertension in structurally normal eyes were later proven to be due to Herpes Simplex Virus, thus implicating trabeculitis as the source of the IOP increase [1,2]. In cases such as these, in which samples

are positive for an implicating viral source, the decision to treat with anti-viral agents is rather clear. However, in other cases, in which no confirmative data or clinical signs are present, the treatment decisions are less apparent.

We report a patient who presented with unilateral ocular hypertension, who responded to anti-viral treatment, despite PCR negative for Herpes Simplex Virus (HSV).

### Case Description

A healthy 47-year-old male from Senegal, living in the United States for four years, presented from the emergency room with right eye pain and photophobia for three days. A complete and thorough medical history was obtained, which was negative. The patient conveyed an ocular history of a right eyelid lesion removed five years ago in his native country; it was unknown if pathological analysis was performed. A full review of systems was conducted, which was also negative.

On examination, the patient's vision was 20/20- in the right eye, and 20/20 in the left eye, with an IOP of 44 mmHg and 13 mmHg, respectively; pupils were equal and briskly reactive. Slit lamp examination of the right eye was notable for trace conjunctival injection, with a deep and quiet anterior chamber. The cornea was clear of edema or fluorescein staining; an age-appropriate nuclear sclerotic lens, equivalent to the fellow eye, was present. Gonioscopic examination showed an open anterior chamber angle x 360 degrees. Dilated fundus examination showed a 0.6 cup:disk ratio in the right and 0.55 in the left; otherwise unremarkable. Central corneal thickness was measured at 510 and 491 nm, respectively. An SD-OCT of the optic nerve was performed, which did not show superior or inferior nerve fiber layer (NFL) thinning in either eye. The patient's ocular hypertension was treated with topical Dorzolamide-Timolol (Cosopt) in the office, and the patient was discharged on Cosopt BID OD.

The patient followed up four days later, with reported compliance with topical medications, presenting with sustained, although improved, eye pain. The eye was again free of anterior chamber reaction, and the IOP was measured at 26mmHg; Brimonidine 0.2% TID OD was added to the patient's drop regimen. Ten days later, the patient returned, at that time on Brimonidine TID and Cosopt BID, and right eye pressure was found to be 27 mmHg. At this point, as the pressure appeared minimally responsive to topical pressure-lowering medications, it was thought that the patient's IOP spikes might have been due to an occult inflammatory trabeculitis. Topical prednisolone acetate 1% (Pred Forte) TID was added to the drop regimen. The patient followed up four days later (now off Brimonidine due to expense) with a dramatic improvement in intraocular pressure (14 mmHg). The patient was instructed to continue the topical steroid TID for one week, followed by a taper. Two weeks later, the IOP was measured at 9 mmHg, thus Cosopt was stopped and Pred Forte decreased to once daily. Upon follow-up one week later, now on only Pred Forte just once daily, the IOP increased to 19 mmHg, thus Pred Forte was again increased to TID.

Fourteen days later, the patient came in prior to his scheduled follow up with right eye pain. The IOP was still well controlled on Pred Forte TID (8 mmHg), however the patient now had 1+ anterior chamber cell; corneal exam was still normal. With new anterior chamber reaction, the decision was made to perform an anterior chamber tap for HSV PCR. Oral anti-viral medication (acyclovir 400 mg 5x/day) was also started.

The patient returned seven days later after one week of oral acyclovir. The IOP was 20 mmHg, and the anterior chamber was now quiet; results from the HSV PCR returned as negative. With a resolved inflammatory reaction and asymptomatic patient, the Pred Forte was again tapered over four weeks. On latest follow-up, after completing a full course of acyclovir and topical steroid course, the patient was asymptomatic with exam revealing an IOP of 16 mmHg and a quiet anterior chamber.

### Discussion

This case reports a patient with an initial presentation of isolated trabeculitis, who presented approximately eight weeks later with presumed HSV uveitis. This patient presentation mirrors other published cases in which patients initially presented with trabeculitis.

Carrillo-Arroyo, *et al.* report a case which also initially presented with unilateral ocular hypertension controlled with steroids; this patient presented five weeks later with an ulcer that was positive for HSV PCR [1]. Prokopich, *et al.* similarly report a patient presenting with a unilaterally elevated IOP and corneal edema, which eventually developed into stromal keratitis and ulceration, positive for HSV [2]. In the above cases, the intraocular pressure increases were proven to be secondary to HSV-related trabeculitis.

Our case also presents with unilateral ocular hypertension responsive to steroids, but with negative PCR for HSV. Two pieces of evidence support a herpetic etiology of the unilateral ocular hypertension. The first is the fact that steroid therapy was the first to successfully lower the patient's eye pressure. The patient's unilateral ocular hypertension was unresponsive to three pressure-lowering medications, however dramatically decreased with topical steroids. This is compelling evidence that the underlying etiology for the increased eye pressure was not structural or related to aqueous production, but rather inflammation. As clinicians, we must be aware of cases such as these, in which seemingly resistant IOP spikes are actually due to inflammation. A second point that should be stressed is that the patient's subjective complaints and clinical ocular findings did appear to respond to anti-viral medication. The acyclovir was able to quiet the anterior chamber reaction, and allowed the patient's Pred Forte to be weaned off with a maintained normal IOP. As mentioned, previous cases have eventually yielded HSV-related ocular findings and associated positive samples. However, in cases like our patient, one should still maintain a suspicion for underlying viral infection even before the onset of overt findings, or even with negative sampling. This patient, although with negative viral PCR, responded well to oral anti-viral medication, with a quieting of the anterior chamber and an ability to maintain normal IOP off steroids. Thus, in cases of unilateral trabeculitis, the index of suspicion for HSV related disease must remain high.

This patient's initial examinations did not show any anterior chamber reaction or corneal findings, which may lead clinicians to preclude certain infectious etiologies. It is extremely common for HSV related IOP spikes to present with corneal findings, with one study reporting the rate up to 96% [3]. Additionally, this patient had a negative aqueous humor PCR for HSV. However, the sensitivity of HSV PCR was found to be only 75% - 85% with CSF samples; the exact test parameters for aqueous humor sampling is unknown, and may be lower as the volume of sample collected is considerably less [4]. Also, previous HSV cases have yielded a negative initial aqueous humor sample, but positive cultures on a subsequent sampling [5].

In this patient, it is not certain that the cause of his symptoms was HSV-related trabeculitis. Yet, with his symptoms resolving with anti-viral medication, the decision to start anti-viral medication did appear to hasten recovery. To our knowledge, there are no established guidelines for cases of initial trabeculitis. It may be reasonable in such suspected cases to prophylactically start anti-viral treatment prior to any overt herpetic ocular manifestation. This may be especially useful when treating with a steroid regimen, which can unmask an underlying infection. Although this does pose the problem of suppressing a possibly diagnostic clinical feature, the concurrent use of anterior chamber sampling at that time of treatment initiation can counteract this issue. Additionally, it is prudent to monitor these patients closely, as their initial presentation may not reveal ocular manifestations that may be looming.

The final point to consider is non-herpetic etiologies for the unilateral pressure spike. With the very dramatic and abrupt response to topical steroids, the index of suspicion for an inflammatory etiology is very high. Although trabeculitis is often thought of related to HSV, it is possible that an alternate agent, perhaps another viral pathogen, was responsible. However, as acyclovir is a specific inhibitor of the herpesvirus DNA polymerase, it would be less plausible that the medication helped remedy our patient's case [6]. Perhaps an alternate organism was the underlying source, and played out its self-remitting course. Further testing that could help elucidate the etiology include corneal sensation with a Cochet-Bonnet aesthesiometer, which would show decreased corneal sensation in the case of herpetic disease. Additionally, in indeterminate cases such as this one, a Goldmann-Witmer coefficient, comparing aqueous and serum levels of anti-herpetic antibody can aid in the diagnosis.

### Conclusion

HSV is an extremely commonly harbored virus in the US, with 58% and 17% of the country being seropositive for HSV-1 and HSV-2, respectively [7]. Cases in which HSV is a suspected underlying etiology will continue to be a frequently encountered scenario in oph-

thalmology practices. This case illustrates an example of when HSV PCR was negative in a patient with steroid-responsive trabeculitis, however anti-viral medication appeared to aid in recovery. We are not suggesting the use of anti-viral therapy on every patient with an unexplained unilateral trabeculitis picture, as each case must be individualized. We, however, do recommend keeping antiviral treatment as a consideration, even with a lack of overt herpetic features.

### Conflict of Interest

No conflicting relationship exists for any of the authors.

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