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LETTER TO THE EDITOR

Combined Intravitreal and Systemic Antibiotic Therapy in a Patient with Syphilitic Uveitis

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ABSTRACT

Purpose: To report the novel use of combined intravitreal and systemic antibiotic therapy in a patient with syphilitic panuveitis and discuss the management of ocular syphilis.

Methods: Case report

Results: A 45-year old heterosexual male with human immunodeficiency virus (HIV) presented with 1 month of blurry vision in both eyes. Clinical examination revealed a bilateral panuveitis. The patient denied history of genital lesions or rash, but did complain of difficulty hearing bilaterally. Treponemal EIA was positive, the RPR titer greater than 1:512 dilution, and CSF VDRL 1:4. A diagnosis of neurosyphilis and ocular syphilis was made based on the clinical and laboratory findings. The patient was admitted for systemic intravenous antibiotic therapy, but was noted to have a penicillin allergy. Intravitreal ceftazidime was promptly administered bilaterally to achieve treponemacidal levels of antibiotic therapy. After penicillin desensitization protocol, the patient received 14 days of intravenous penicillin with clinical resolution.

Conclusions: There are increasing reports of ocular syphilis in the United States and delay in diagnosis and management can lead to severe visual impairment and blindness. We report the first case of adjunct intravitreal antibiotic therapy in a penicillin allergic patient. As ocular syphilis is a form of bacterial endophthalmitis, combination intravitreal and systemic antibiotics may be considered.

Keywords: Infectious Uveitis, syphilis, Panuveitis, Endophthalmitis

Syphilis is an infectious disease caused by the organism *Treponema pallidum* and is most commonly spread by sexual transmission.¹ This infectious disease has afflicted humans for centuries, however, with the introduction of penicillin in the 1940s, the neurologic and ocular complications arising from chronic infection have declined.² Recently, however, the Centers for Disease Control (CDC) has reported an increasing number of ocular syphilis cases in the United States resulting in severe visual impairment and blindness.³ The recommended treatment of ocular syphilis per

the CDC STD Treatment guidelines is 18 to 24 MU of intravenous aqueous crystalline penicillin G for 10–14 days.⁴ In this report, we present a unique case of bilateral syphilitic panuveitis treated initially with intravitreal ceftazidime until systemic intravenous penicillin therapy could be initiated in a penicillin allergic patient. We discuss the management of ocular syphilis and neurosyphilis and suggest a continued role for combined intravitreal and systemic antimicrobial therapy that may improve visual outcomes.

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CASE REPORT

A 45-year-old African American male with HIV infection and CD4 count of 132 presented to the emergency room complaining of 1 month of decreased vision in both eyes associated with redness, pain, and light sensitivity. Visual acuity was 20/400 in the right eye and 20/100 in the left eye. Intraocular pressures were 14 in both eyes. Anterior segment exam was notable for 2+ cell and nearly 360 degrees of posterior synechiae in the right eye and 1+ cell in the left eye. There was no view of the fundus in the right eye. A B-scan ultrasound was performed and showed an attached retina with dense vitreous debris. Fundus examination of the left eye showed vitritis with a placoid area of deep retinal whitening in the macula (Figure 1).

The clinical presentation was consistent with a bilateral panuveitis. The review of systems was positive for difficulty hearing bilaterally. He denied fevers, chills, nausea, vomiting, or diarrhea. Social history was notable for recent incarceration. He denied any sexual contact with men or intravenous drug use. Physical examination was remarkable for diffuse lymphadenopathy, subtle pigmented rash on the palms and absence of genital lesions. Serologic evaluation demonstrated a RPR titer > 1:512 and a positive treponemal EIA. Cerebrospinal fluid (CSF) evaluation revealed a VDRL of 1:4 with WBC count 92, glucose 39 mg/dl and protein 76 mg/dl. A diagnosis of ocular and neurosyphilis was made and systemic intravenous penicillin was recommended; however, the patient reported a history of penicillin allergy as a child. Therefore, intravitreal ceftazidime 2.25 mg/0.1mL was administered in both eyes given the location of active infection and concern for sight threatening disease. Improvement in the retinitis was noted within 1 day of intravitreal antibiotic therapy. The infectious disease service administered intravenous (IV) Ceftriaxone 2 grams daily for

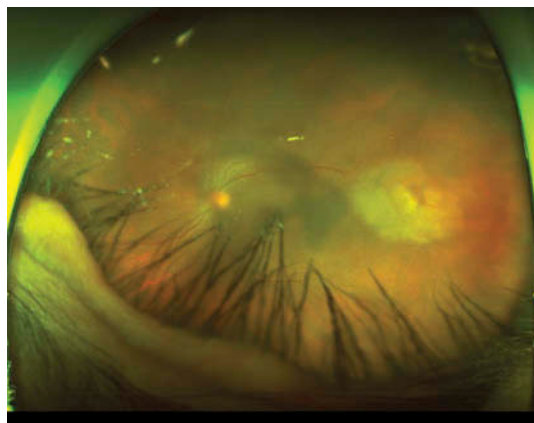


FIGURE 1. Optos Fundus Photo of left eye. There is vitritis with a placoid area of deep retinal whitening in the macula extending temporally.



FIGURE 2. Optos Fundus Photo of left eye. Clear media with resolution of retinal whitening and residual chorioretinal atrophy.

3 days while the patient underwent penicillin desensitization. Following desensitization, the patient was transitioned to 24 MU of intravenous aqueous crystalline penicillin G for 14 days by continuous infusion. Ocular inflammation was also managed with topical prednisolone acetate 1%, and 40mg oral prednisone once a demonstrable clinical response was confirmed. Uncorrected visual acuity at last follow-up was 20/30 in both eyes with complete resolution of the panuveitis (Figure 2).

DISCUSSION

To our knowledge, the case presented herein represents the first report of combined intravitreal and systemic antibiotic therapy for syphilitic uveitis in a penicillin allergic patient. Syphilis is caused by the bacterial spirochete *Treponema pallidum* and is most commonly spread via sexual transmission.¹ The organism can disseminate systemically hours to days after inoculation, and early invasion of the central nervous system occurs in many patients.⁵ Therefore, ophthalmic manifestations of syphilis can occur at any stage of infection and affect any part of the eye, with the most common presentation being syphilitic uveitis.^{1,6}

Penicillin was the first antibiotic discovered in the 1940s and remains the primary treatment for all stages of syphilis, including ocular and neurosyphilis, both of which are treated with the same regimen. The initial management of neurosyphilis in the 1940s was benzathine penicillin 2.4 MU by intramuscular (IM) injection.⁵ The treatment evolved over the next several decades in large part due to treatment failures. In the 1970s, 3 weekly doses of 2.4MU of Benzathine Penicillin G IM was a recommended treatment option for neurosyphilis. However, further investigation noted that this dosing did not consistently achieve treponemacidal levels in the CSF and treatment

failures were reported.⁵ As a result, treatment recommendations for neurosyphilis have continued to evolve over the last 40 years. The ideal dose for neurosyphilis remains unknown as no randomized comparative trials have been done.

Today, the CDC recommends treating neurosyphilis with intravenous aqueous crystalline penicillin G 18–24 MU daily for 10–14 days to maintain adequate treponemacidal levels in the CSF.⁴ The CDC also recommends treating ocular syphilis with the same regimen as neurosyphilis, even if a CSF examination is normal.⁴ Our patient had a penicillin allergy as a child and the CDC recommends penicillin desensitization in these situations. There is limited data that ceftriaxone IV 2 grams daily (third-generation cephalosporin) can be used as an alternative neurosyphilis treatment regimen in the penicillin allergic patient.⁴ Agostini et al. reported good outcomes with ceftriaxone IV (varying dose and duration) daily in syphilitic uveitis due to unavailability of penicillin.⁷ After discussion with our patient, we proceeded with intravitreal ceftazidime (2.25mg/0.1mL) to both eyes while awaiting penicillin desensitization. There is no previous data on the use of local or systemic ceftazidime in ocular syphilis, but given this medication is safe and routinely used for bacterial endophthalmitis, we elected to use it in our patient. It is noteworthy that improvement of the retinitis was seen after intravitreal injections and prior to systemic antibiotic therapy.

There is increasing evidence for combination local and systemic therapy in other infectious entities, including viral retinitis, ocular toxoplasmosis, fungal endophthalmitis and endogenous bacterial endophthalmitis.⁸ While the tempo and rate of progression in ocular syphilis is typically slower compared to the aforementioned infectious uveitides, there remains a number of patients with ocular syphilis who develop severe visual impairment and/or blindness.³ Hoogewoud et al. published a retrospective study looking at predictors of treatment success in syphilitic uveitis and found that early improvement is the strongest predictor of ophthalmological recovery in syphilitic uveitis.⁹ Furthermore, since syphilitic uveitis is an acquired bacterial infection caused by the hematogenous spread of *Treponema pallidum* to the eye, we believe ocular syphilis should be considered a form of endogenous bacterial endophthalmitis

and be treated as such with local therapy. The adjunctive role for intravitreal drug administration in ocular syphilis should be strongly considered for patients with poor prognostic factors, including low vision on presentation, retinitis, severe panuveitis and optic nerve involvement. Further research is necessary and warranted to validate this novel approach given the rise in ocular syphilis globally and its serious consequences.

DECLARATION OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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