## A masquerader epidemic: five heterogeneous ocular syphilis presentations

Syphilis is a spirochete infection transmitted through intercourse or congenital infection. Despite declining incidence since the 1990s, ocular syphilis has re-emerged in developed countries.[1] We describe 5 distinct presentations of ocular syphilis to promote recognition of this increasingly prevalent disease.

Case 1, a 58-year-old man, presented with 3 weeks of worsening vision. Initial assessment showed best-corrected visual acuity (BCVA) of 20/260 OD and 20/800 OS with bilateral subfoveal fluid and trace vitreous cells. Oral prednisone 60mg daily was initiated for presumed Vogt–Koyanagi–Harada disease, and the patient was referred when poor vision persisted despite improved subretinal fluid.

Fundus examination showed bilateral yellow-white macular lesions with submacular fluid and attenuation of the ellipsoid zone (Fig. 1A–C). Detailed history taking elicited unprotected same-sex intercourse, oral ulcers (previously biopsied by an oral surgeon), and hearing loss. Acute syphilitic posterior placoid chorioretinitis was diagnosed following positive anti-treponema IgG and IgM titres, rapid plasma reagin (RPR) titres of 1:128 units, and reactive *Treponema pallidum* particle agglutination (TP-PA). Intravenous aqueous crystalline penicillin G was initiated, and prednisone was tapered over 2 months. Vision improved to 20/25 OD and 20/30 OS.

Case 2, a 56-year-old HIV-positive man on antiretroviral therapy (ART), presented with 1 week of blurred vision OD. BCVA was 20/200 OD with anterior chamber inflammation, moderate vitritis, and peripheral granular retinal infiltrates (Fig. 1D). Acute retinal necrosis was suspected, and oral valaciclovir was initiated alongside difluprednate eye drops. Serum testing for syphilis was performed given the patient's HIV-positive status. Aqueous aspiration was negative for herpes simplex virus, varicella-zoster virus, and cytomegalovirus infection by polymerase chain reaction (PCR). Within 1 week of presentation, blood work showed positive RPR titres of 1:256 and reactive TP-PA and syphilis IgG titres. Valaciclovir was discontinued and intravenous aqueous crystalline penicillin G treatment commenced. Final BCVA measured 20/25 OD with resolution of inflammation.

Case 3, a 45-year-old man, presented with 2 weeks of painful vision loss OS. BCVA measured 20/200 OS with hypopyon, retinal whitening, and vasculitis concerning for viral retinitis (Fig. 1E). Aqueous humour was sampled for viral PCR, and oral valaciclovir was initiated with difluprednate eye drops. Retinitis progression was noted the following day, prompting intravitreal ganciclovir 2mg/0.05mL. Blood work identified acute syphilis infection with an RPR titre of 1:512, and HIV infection with 201 CD4+ cells/uL. Lumbar puncture demonstrated pleocytosis with reactive RPR and TP-PA titres. The patient disclosed heterosexual extramarital intercourse associated with previous pruritic eruptions on his scrotum, torso, and palms. Aqueous PCR was negative for viruses, and valacyclovir was discontinued. Retinitis stabilized following intravenous aqueous crystalline penicillin G treatment and highly active ART (HAART) initiation. The patient required topical steroids to treat persistent cystoid macular edema (CME). Final BCVA was 20/30 OS.

Case 4, a 35-year-old man, presented with 1 week of blurred vision OD. BCVA measured 20/60 OD. Fundus examination demonstrated diffuse dot-blot hemorrhages, dilated retinal veins, optociliary shunt vessels, and severe CME, consistent with chronic central retinal vein occlusion (Fig. 2A). The presence of vitritis promoted investigation for infectious or inflammatory etiologies. Intravenous fluorescein angiography displayed macular, peripapillary, and peripheral vascular leakage (Fig. 2B).

On further questioning, the patient disclosed intercourse with an HIV-positive male partner 3 months prior associated with acute penile rash, maculopapular eruption, persistent joint pain, and a self-limited episode of blurred vision OD. Syphilis testing revealed acute syphilitic infection: RPR titre 1:64 with reactive TP-PA and IgG titres. HIV testing was positive with a CD4+ count of 971 cells/$\mu$L. The patient received aqueous crystalline penicillin G treatment as well as intravitreal ranibizumab 0.5mg for CME and HAART initiation. Vision improved to 20/20 OD.

Case 5, a 59-year-old man, was referred with several months of vision loss OU. Past history included a frontal lobe mass containing spirochetes, resected 6 years prior. The patient was diagnosed with syphilitic gumma and received multiple courses of intravenous aqueous crystalline penicillin G but suffered recurrent ischemic strokes secondary to syphilitic vasculitis. Interestingly, no laboratory markers of syphilis or other infectious, inflammatory, or neoplastic processes were identified despite repeated testing. Risk factors included only a remote unspecified sexually transmitted infection. He had no ocular symptoms or eye examinations during previous hospitalizations.

On presentation, the patient's BCVA was 20/400 OU. Optic disc pallor, vascular sheathing, and retinal neovascularization with vitreous hemorrhage were noted bilaterally, consistent with syphilitic vasculitis (Fig. 2C, 2D). The patient underwent bilateral panretinal laser photocoagulation and intravitreal ranibizumab 0.5mg injection. Six months later, retinal neovascularization had regressed, but poor vision persisted.

We describe 5 heterogeneous presentations of ocular syphilis seen by a single ophthalmologist between September and December 2018 at a Canadian hospital. In all cases,

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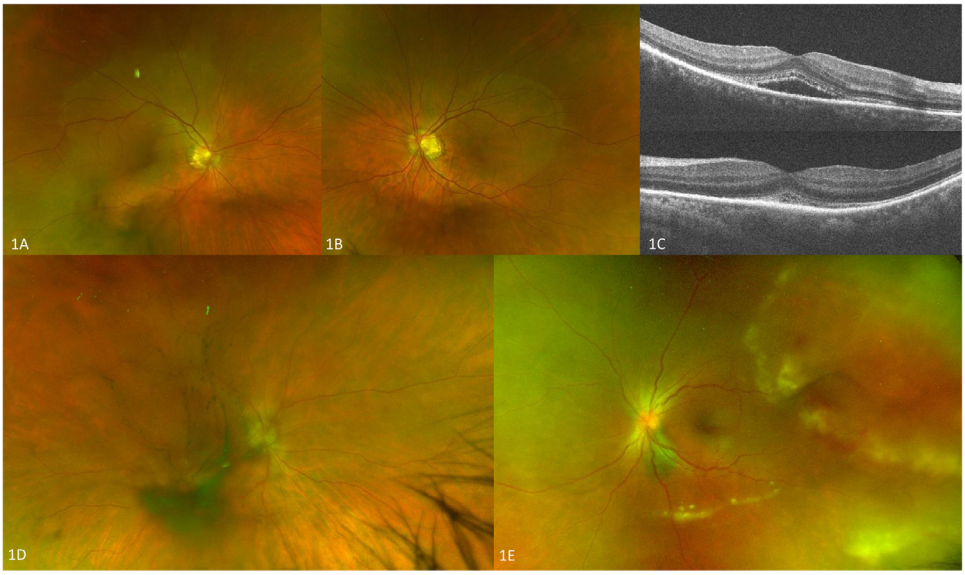


**Fig. 1—Case 1 demonstrates acute posterior placoid syphilitic chorioretinitis. Bilateral symmetric yellow-white macular lesions (A, B) were seen in the posterior pole. Optical coherence tomography demonstrates subfoveal fluid with disruption of the retinal pigment epithelium and outer retinal layers in both eyes (C). Case 2 (D) and case 3 (E) presented with syphilitic retinitis displaying vitritis, retinal whitening, and anterior chamber inflammation. Part D shows right eye vitritis and peripheral granular retinal infiltrates (not visible here). Part E shows temporal retinitis with associated retinal hemorrhage with inflammatory precipitates along the posterior hyaloid.**

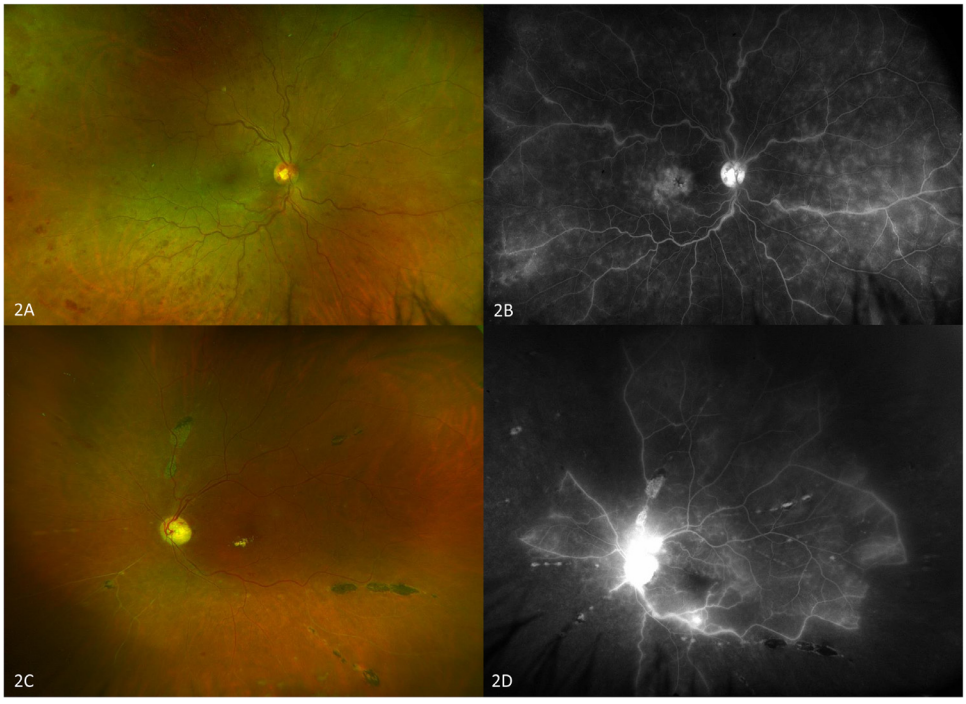


**Fig. 2—(A) The classic features of a central retinal vein occlusion including engorged, tortuous veins in all retinal quadrants and diffuse intraretinal hemorrhages, as observed in case 4. Intravenous fluorescein angiography (B) demonstrated delayed venous filling with associated macular edema, as well as a mild degree of retinal vasculitis with a venular predilection. The presence of optociliary shunt vessels at the optic disc suggests central retinal vein occlusion chronicity. Part C shows occlusive retinal vasculitis OS, as observed in case 5. Optic disc pallor, vascular sheathing, peripheral retinal vessel attenuation, and areas of retinal and subretinal pigmentary scarring suggest long-standing disease. Intravenous fluorescein angiography OS (D) displays extensive retinal nonperfusion and associated neovascularization, which regressed following panretinal laser photocoagulation and intravitreal ranibizumab.**

an alternate diagnosis was indicated on referral, including Vogt–Koyanagi–Harada syndrome, viral retinitis, retinal vein occlusion, and bilateral optic neuritis, underscoring syphilis as the "great masquerader." Early recognition of ocular syphilis is important given the rising incidence across North America.[1,2] Nevertheless, misdiagnosis delays

treatment in more than two-thirds of cases and contributes substantially to adverse outcomes.[3]

Ocular syphilis occurs most commonly during secondary infection but may present at any stage.[2,4] Manifestations include conjunctival chancre, keratitis, iridocyclitis, optic neuritis, chorioretinitis, vasculitis, and retinal vessel occlusion, with panuveitis as the most frequent.[5] Syphilis screening therefore should be considered in all patients presenting with uveitis, retinitis, or vasculitis, particularly in high-risk individuals. HIV infection, male homosexuality, and age greater than 40 years are associated with ocular syphilis in urban North American centres.[1] In our all-male cohort, 3 of 5 patients were HIV positive, 3 endorsed sex with men, and all but 1 were older than 40 years. However, patients may be reticent to disclose sexual history or unaware of partner-incurred exposure. In 2 patients, ocular symptoms occurred months to years following initial infection, highlighting the importance of syphilis testing even in cases without known or recent exposure.

Investigations should include enzyme immunoassay, followed by RPR and TP-PA titres.[4] Negative serology despite strong clinical suspicion should prompt retesting in 2–4 weeks to identify early seroconversion.[4] One patient displayed persistent seronegativity despite biopsy-proven syphilitic gumma. Gumma is an exceedingly rare presentation of late tertiary syphilis and likely reflects inadequate treatment for a primary infection.[2]

Ocular syphilis is a subtype of neurosyphilis. Cerebrospinal fluid pleocytosis and positive RPR titres occur in up to 79% of ocular syphilis patients. Lumbar puncture is universally recommended because further treatment is required if cerebrospinal fluid abnormalities persist beyond 2 years.[4] Lumbar puncture was deferred in 3 patients at our centre because they lacked neurologic symptoms.

Ocular syphilis treatment parallels neurosyphilis protocols. Aqueous crystalline penicillin G 3–4 million units should be administered intravenously every 4 hours for 10–14 days.[4] Penicillin desensitization is strongly preferred over use of alternate agents in patients with penicillin allergy.[4] Visual prognosis is favourable following treatment: a recent study reported 65% recovery at 1 month, with early improvement as the strongest prognosticator.[5] In our patients, 4 demonstrated a final BCVA of 20/30 or better, whereas 1 demonstrated persistent vision loss owing to optic atrophy and chronic vasculitis.

Our series illustrates the heterogeneous nature of syphilitic uveitis and emphasizes the importance of syphilis screening when faced with unexplained or refractory ocular inflammation. Rapid recognition of syphilis can save vision, prevent systemic sequalae, and reduce transmission of a growing epidemic.

**Seema Emami,* Panos G. Christakis*,†**
*University of Toronto, Toronto, Ont.; †Toronto Western Hospital, Toronto, Ont.

Correspondence to Panos G. Christakis; panos.christakis@uhn.ca.

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## Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this correspondence.

# Multiple myeloma with concurrent herpes zoster ophthalmicus: a case report

Hyperviscosity syndrome, which typically results from elevated serum levels of monoclonal protein, can present with bleeding, retinopathy, and neurologic symptoms.[1] We present a case of hyperviscosity syndrome confounded by herpes zoster reactivation in a patient with newly diagnosed multiple myeloma.

A 71-year-old male presented to the urgent care clinic with a chief complaint of left eyelid swelling and redness. Ocular history was significant for V1 herpes zoster cellulitis OS 1 year prior. Medical history was significant for idiopathic pulmonary hypertension, chronic kidney disease, dyslipidemia, and depression. On presentation, visual acuity was 20/20 OD and 20/200 OS. The patient had an irregular pupil OS but no relative afferent pupillary defect. The intraocular pressures were 12 and 38 mm Hg in the right and left eyes, respectively. Slit-lamp examination of the anterior segment was remarkable for 1+ nuclear sclerosis OD. The left eye demonstrated eyelid edema, 2+ conjunctival injection, corneal haze, 3+ flare with a deep anterior chamber, numerous pigmented keratic precipitates, posterior synechiae, and punctate epithelial erosions but no dendrite or pseudodendrite. The dilated fundus examination was normal OD, with