

## CLINICAL VIGNETTE

---

# Headache and Blurry Vision in a Patient with Uncontrolled Gout

---

Thanda Aung, MD, MS

### *Introduction*

Gout is the most common form of inflammatory arthritis in the United States, characterized by the deposition of monosodium urate into joints and other organs including the eye.<sup>1</sup> This is a case of unilateral optic disc edema in the setting of poorly controlled chronic gout with a surprisingly final diagnosis.

### *Case*

A 54-year-old male with history of gout, hypertension, hyperlipidemia, obstructive sleep apnea and obesity, presented to rheumatology for evaluation and treatment of gout. He reported numerous gout flares up affecting big toes and ankles for the last 5 years. He had been treated intermittently with short courses of allopurinol and febuxostat. He expressed dislike of taking them because they triggered acute gout attacks and also abdominal cramps that he believed were medication side effects. At the time of presentation, there was no acute joint issue and he was not taking any regular gout medication. His last gout attack was about two weeks prior, which was successfully treated with a course of oral steroid. His gout arthritic attacks occur once or twice every month. He also suffered from chronic headache, evaluated by a neurologist a few years ago. He recalled that his MRI brain was unremarkable and was he treated with amitriptyline. He also noticed worsening of headache more on the left side and intermittent blurry vision in his left eye for a few weeks. He questioned that if his headache and vision change were due to gout since they seemed to bother him more during acute gouty arthritic attacks.

He denied chest pain, abdominal pain, jaw claudication, weight loss, fever or other neurological symptoms. His other review of system was negative. He denied history of any recent infection or recent travelling. Physical exam was unremarkable except mild eye congestion more on the left. His initial labs revealed normal complete blood count and comprehensive metabolic panel, elevated uric acid of 9.6 mg/dl and high inflammation markers ESR 69 mm/hour, CRP 2.0 mg/dl. Giant cell arteritis was a concern although his presentation was not typical. Ocular manifestation of gout was also considered.

He was urgently evaluated by ophthalmology and subsequently neuro-ophthalmology. He was found to have unilateral left optic disc edema with subhyaloid bleed. Other rheumatology tests included negative anti-nuclear antibody, vasculitis markers (ANCA, cryocrit), but all three anti-phospholipid antibodies (DRVVT, anti-cardiolipin IgG and IgM, beta 2 glycoprotein

IgM) were positive. MRI brain and orbit did not show any space occupying lesion. Fluorescein angiogram did not reveal retinal vasculitis. Infection evaluation returned with negative hepatitis B, hepatitis C and MTB quantiferon gold, but positive RPR. Subsequent confirmation TP-PA (specific treponemal test) was reactive and confirmed the diagnosis of ocular syphilis. The case was reported to the health department. Further CSF analysis revealed elevated protein, elevated white count and CSF VDRL positive; negative CSF fungal, HSV and bacterial culture. HIV was negative. He was treated with parenteral Penicillin G, 24 million units every 24 hours for 2 weeks with resolution of headache and significant improvement in vision changes. Ophthalmology exam showed significant improvement in optic disc edema after completion of 2-week antibiotics. Allopurinol with colchicine prophylactics were also started with improvement in his serum urate level.

### *Discussion*

This case highlights a few learning points. First, gout can affect the eye as an extra-articular manifestation. Gout is a systemic disease characterized by recurrent arthritic attacks, chronic tophaceous gout, tophi in soft tissue and gouty nephropathy.<sup>2</sup> Ocular involvement in patients with gout include deposition of urate crystals in multiple ocular structures resulting in conjunctivitis, uveitis, scleritis, blurred disc margins and elevated intraocular pressure.<sup>2</sup> Patients with ocular gout can present with wide range of manifestations from recurrent red eyes due to scleritis, episcleritis and uveitis to vision loss due to elevated intraocular pressure or optic disk edema.<sup>3</sup> This patient's optic disc edema have been due to uncontrolled gout, however, his dramatic response to antibiotics suggests ocular syphilis as the final diagnosis.

Second learning point of the case is that although the incidence of syphilis has dramatically decreased since advent of penicillin in the mid-20th century, it remains a large global problem, especially in developing countries.<sup>4</sup> There is also an increased incidence of primary and secondary syphilis in developed countries, especially in young men.<sup>5</sup> The majority of cases have been reported among HIV-infected MSM. However, other cases have occurred among HIV-uninfected persons including heterosexual men and women.<sup>5</sup> Ocular manifestations of syphilis are rare, representing less than 5 percent of all cases of uveitis.<sup>6,7</sup>

Ocular syphilis can involve almost any structure in the eye, but posterior uveitis and panuveitis are the most common.<sup>8</sup> Additional manifestations may include anterior uveitis, optic neuropathy, retinal vasculitis and interstitial keratitis. Ocular syphilis may lead to decreased visual acuity including permanent blindness. Ocular syphilis can be associated with neurosyphilis. Both ocular syphilis and neurosyphilis can occur at any stage of syphilis, including primary and secondary syphilis.<sup>8</sup>

The diagnosis of ocular syphilis depends largely on serologic testing. Centers for Disease Control currently recommends analysis of cerebrospinal fluid (CSF) should be performed in all cases of ocular syphilis. Persons testing positive for syphilis should also be tested for HIV. Cases of ocular syphilis should be reported to your state or local health department within 24 hours of diagnosis per CDC recommendations.<sup>8,9</sup>

Penicillin is the treatment of choice for all stages of syphilis. Acquired syphilis with ocular involvement should be treated as neurosyphilis with intravenous penicillin G, 18 to 24 million units (MU) daily for 10 to 14 days, followed by intramuscular procaine penicillin, 2.4 MU weekly for three weeks.<sup>9</sup> In patients with penicillin allergy, several therapeutic alternatives are available, including tetracycline, doxycycline, chloramphenicol, ceftriazone and the macrolide antibiotics.<sup>9</sup> Common long-term complications of syphilitic uveitis include glaucoma, cataract, epiretinal membrane and macular edema.<sup>10</sup> Widespread chorioretinal scarring and permanent blindness can occur in some patients.<sup>10</sup>

A final learning point is related to positivity of antiphospholipid antibodies in active syphilis infection. A positive antiphospholipid antibody test can be expected in syphilis due to the cross-reactivity of the reagin antibodies found in syphilis with phospholipids.<sup>11</sup> In addition to syphilis, there are a great variety of infections that are associated with increase in antiphospholipid antibodies.<sup>12</sup> They include viral infections (e.g EBV, CMV, Hepatitis C), bacterial infections (e.g TB, leprosy), parasitic infections (e.g malaria), and spirochaetal infections (e.g syphilis, leptospirosis).<sup>12</sup>

## Conclusion

This case illustrates that ocular syphilis should be considered as a possible etiology in any inflammatory eye conditions. Clinicians should have a low threshold for checking syphilis serology because it is often curable and also accurate diagnosis and prompt treatment prevents further spread of the infection. Additionally, recognition that gout is a systemic disease, that can potentially affect the eye.

## REFERENCES

1. **Zhu Y, Pandya BJ, Choi HK.** Prevalence of gout and hyperuricemia in the US general population: the National Health and Nutrition Examination Survey 2007-2008.

- Arthritis Rheum.* 2011 Oct;63(10):3136-41. doi: 10.1002/art.30520. PMID: 21800283.
2. **Yülek F, Cağil N, Orhan N, Midillioğlu IK, Erten S, Simşek S.** Gout attack with unusual ocular complications. *Rheumatol Int.* 2009 Mar;29(5):557-9. doi: 10.1007/s00296-008-0736-z. Epub 2008 Oct 9. PMID: 18841369.
3. **Burgos F, Capone RC.** Ocular and systemic manifestations of gout. *Clin Eye Vis Care.* 1996;8:155-63.
4. **Centers for Disease Control and Prevention (CDC).** Primary and secondary syphilis--United States, 2003-2004. *MMWR Morb Mortal Wkly Rep.* 2006 Mar 17;55(10):269-73. PMID: 16543880.
5. **Peterman TA, Su J, Bernstein KT, Weinstock H.** Syphilis in the United States: on the rise? *Expert Rev Anti Infect Ther.* 2015 Feb;13(2):161-8. doi: 10.1586/14787210.2015.990384. Epub 2014 Dec 9. PMID: 25487961; PMCID: PMC6750765.
6. **Barile GR, Flynn TE.** Syphilis exposure in patients with uveitis. *Ophthalmology.* 1997 Oct;104(10):1605-9. doi: 10.1016/s0161-6420(97)30089-x. PMID: 9331198.
7. **Davis JL.** Ocular syphilis. *Curr Opin Ophthalmol.* 2014 Nov;25(6):513-8. doi: 10.1097/ICU.0000000000000099. PMID: 25237932.
8. **Wender JD, Elliott D, Jumper JM, Cunningham Jr. ET.** How to recognize ocular syphilis. *Rev Ophthalmol.* 2008.
9. **Centers for Disease Control.** STD Facts – Syphilis (Detailed). Syphilis.
10. **Halperin LS, Lewis H, Blumenkranz MS, Gass JD, Olk RJ, Fine SL.** Choroidal neovascular membrane and other chorioretinal complications of acquired syphilis. *Am J Ophthalmol.* 1989 Nov 15;108(5):554-62. doi: 10.1016/0002-9394(89)90433-9. PMID: 2479270.
11. **Noakes D, Evans K, Pathansali R.** The return of a former foe: syphilis with antiphospholipid syndrome as a cause of acute stroke. *JRSM Open.* 2017 Sep 5;8(9):2054270417725498. doi: 10.1177/2054270417725498. PMID: 28904807; PMCID: PMC5588799.
12. **Asherson RA, Cervera R.** Antiphospholipid antibodies and infections. *Ann Rheum Dis.* 2003 May;62(5):388-93. doi: 10.1136/ard.62.5.388. PMID: 12695147; PMCID: PMC1754545.