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BILATERAL SYPHILITIC OPTIC NEURITIS

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ABSTRACT
Background: Ocular syphilis is an uncommon clinical condition. There are no specific clinical pattern nor pathognomonic signs. The visual prognosis for patients with syphilis and optic neuritis is good if properly treated.
Case Presentation: A 28-year-old man presented with gradually worsening blurred vision in both eyes, especially the left, over six weeks. Visual acuity in the left eye was reduced to counting fingers at 2 meters, and a relative afferent pupillary defect was positive in the left eye. Fundus examination of the right eye shows blurred margin in superior, inferior, and nasal quadrans with slight hyperemia in color but no elevation, while the left eye's posterior segment was obscured by vitreous opacities. Ultrasonography of both eyes showed echogenic membrane-like lesions with normal retinal attachment. No restriction and pain on ocular motility both eyes. He had rash in both plantar of hand and foot. OCT examination shows thickening of retinal nerve fiber layer on both eyes. Serological tests were positive for TPHA and HIV; C-reactive protein was normal.
Discussion: Syphilitic optic neuritis can be unilateral or bilateral, often presenting with eye pain and rapid vision loss. Treatment includes antisyphilitic antibiotics with adjunctive oral or intravenous corticosteroids for posterior uveitis and optic neuritis. Ocular syphilis is highly suggestive of central nervous system involvement (neurosyphilis). Secondary optic atrophy does not respond to antisyphilitic therapy.
Conclusion: Careful history taking and physical examination are essential to diagnose optic neuritis etiology. Early and appropriate treatment can improve visual outcomes in syphilitic optic neuritis.
Keywords: syphilitic optic neuritis, ocular syphilis, secondary syphilis

BACKGROUND

Syphilis is a sexually transmitted disease caused by spirochete, *Treponema pallidum*. Syphilitic infection is commonly associated with human immunodeficiency virus (HIV) infection. One retrospective study reported 49.3% of syphilitic cases were known to be HIV positive.[1] Ocular involvement in acquired syphilis is rare and occurs mainly in secondary and tertiary syphilis. Although the ocular manifestation of syphilis can affect any structures of the eye, including keratitis, scleritis, episcleritis, anterior and posterior uveitis, optic nerve involvement is not a common presentation and can be found in only 20%.

The worldwide incidence of syphilis is increasing and is now approximately 8.7/100,000 population in North America. It is most frequently seen among men who have sex with men, with human immunodeficiency virus (HIV) co-infection often present. There has been a corresponding increase in reported ophthalmic manifestations of syphilis including keratitis, anterior and posterior segment inflammation, syphilitic optic neuropathy (SON), and neuro- syphilis.

Ocular syphilis is an uncommon clinical condition: only in 3% cases of neurosyphilis ocular structures are involved, but when the eye is affected there

does not exist any specific clinical pattern nor pathognomonic signs. Optic nerve abnormalities in an ophthalmological examination in a patient with diagnosis of syphilis is highly suggestive of central nervous system involvement and it should be considered as neurosyphilis for its treatment[6].

The diagnosis of optic neuritis is based on a constellation of symptoms and signs. The onset is usually with pain on eye movement in one eye and subacute visual loss. In unilateral optic neuritis, the direct pupillary light reflex is weaker in the affected eye. One-third of patients with optic neuritis have a mild edematous optic disc. The visual disturbance resolves in 95% of cases. A less favorable course may be evidence of neuromyelitis optica, and macular involvement may be evidence of neuroretinitis. High-dosed intravenous methylprednisolone therapy speeds recovery but does not improve the final outcome.

The interaction of syphilis and HIV has stimulated renewed interest in this ancient disease and has challenged some of the long held ideas about the investigation and treatment of syphilis.

A case of secondary syphilis is presented in which a gradually loss of vision occurred as the first manifestation. The natural history, investigation, treatment and follow up for ocular syphilis are discussed.

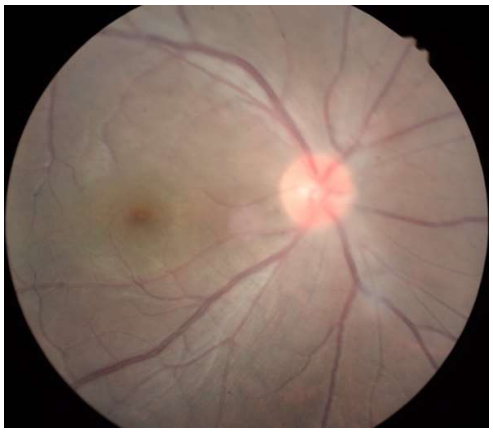
CASE PRESENTATION

A 28 year-old unmarried man came to outpatient clinic with chief complain vision loss on both eyes especially on his left eye since one and half months before first admission. He complained gradually blurred vision without any other accompanied symptoms like photophobia, tearing, and pain. Recurrent red eye in both eyes was denied. No other systemic disease was complained. Patient did not consume long term medication. He was a smoker for almost 10 years.

The best corrected visual acuity right eye was 5/6,5 and two meters finger counting in left eye. Intraocular pressure on both eyes were within normal limits. Anterior segment was within normal limits only relative afferent pupillary defect on left eye was positif. No flare and cell on anterior chamber both eyes. Posterior segment examination right eye shows blurred margin in superior, inferior, and nasal quadrans with slight hyperemia in color but no elevation, retina within normal limit. Left eye posterior segment was difficult to evaluate due to obscura corpus vitreous. Ultrasonography both eyes show echogenic lesion membrane shape mobility low to medium with echospike 10-20% RCS complex and retina on place. Left eye showed more lesion than in right eye. No restriction and pain on ocular motility both eyes. Ishihara examination showed decreasing in left eye and normal in right eye. OCT examination showed thickening of retinal nerve fiber layer on both eyes.

We found rash in both plantar of hand and foot, then we ask more detail history about his sexual life. He admitted that he had sexual intercourse with his ex-girlfriend who is a widow. But he has no complain about the rash, no itchy, no pain. He said his rash appear 1 week prior to admission and after consume medication from previous doctor. He was given methyl prednisolone which already tappered off 8 mg twice daily and p-pred eye drop 6 times daily. Then we treated this patient with methyl prednisolone 16 mg 3 times daily, laboratory testing, and consultation to dermatovenerology department. Multiple macula erythematosus, sharp margin, size lenticular-numular, white thin squama in part of macula was found, also some lesion in regio genitalia with description macula eritematous, blurred margin, size

lenticular, serous in the middle. They diagnosed this patient with secondary syphilis and follow up every week. The ancillary test came up positive on TPHA, and HIV, CRP level was 0,2, other item was within normal limit.



a

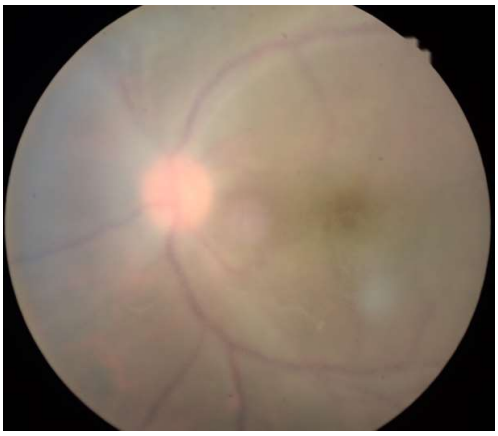


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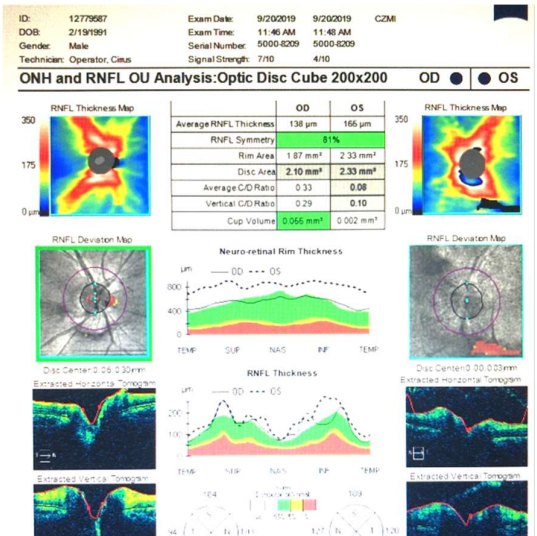
Figure 1. fundus photograph at first admission (a) right eye showed blurred margin in superior, inferior and nasal quadrans with slight hyperemia in color but no elevation (b) left eye was difficult to evaluate due to obscura corpus vitreous



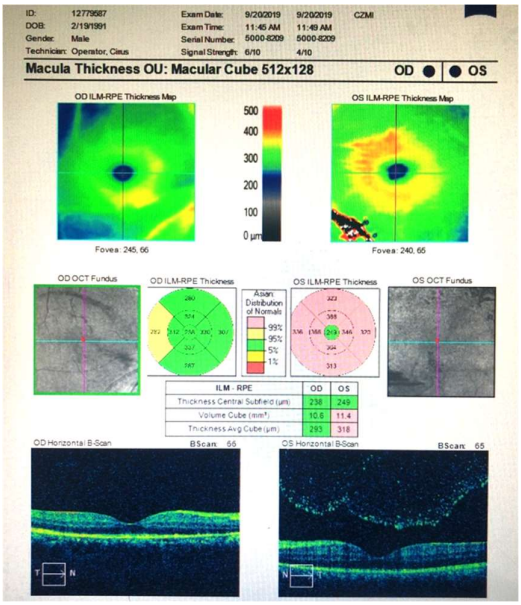


Figure 2. OCT of posterior segment at first admission (a) right eye (b) left eye showed thickening of retinal nerve fiber layer on both eyes and thinning of macula in the left eye

Dermatovenerology department treated this patient with penicillin single dose intramuscular. One week after that, patient came back for follow up and still no improvement on ophthalmic examination then the methyl prednisolone dosage increase became 32 mg twice daily. 2 weeks after that the ophthalmic examination revealed improvement visual acuity right eye become 5/5 and left eye 4 meters counting finger. Ishihara color test left eye much improvement become 36/38. While the posterior segment of left eye still obscura corpus vitreous.

DISCUSSION

A healthy 28-year-old patient presented with a complaint of gradually vision loss in his both eyes 6 weeks prior admission. No associated symptoms were noted.

The pain and worsening of vision are so disturbing that hardly any affected person waits to see whether they will improve spontaneously; patients tend to find their way to an ophthalmologist very

early in the course of the disease. Pain on eye movement is absent in the 8% of patients whose inflammatory focus lies in the intracranial portion of the optic nerve and thus proximal to its mobile portion.

In a patient with syphilis the presence of ocular involvement is strongly suggestive of involvement of the CNS and should be considered synonymous with neurosyphilis. The spirochaete *Treponema pallidum* enters via an abrasion during sexual contact. During this primary infection there is rapid lymphatic and haematological spread. After an incubation of three weeks (range: 9–90 days) an infectious painless ulcer (primary chancre) develops at the site of sexual contact. The genitalia, anus, and mouth should all be examined. The primary lesion heals in two to six weeks even without treatment.

Secondary syphilis occurs four to eight weeks after the chancre. In secondary syphilis early dissemination of the organism frequently includes the CNS.[3] Among patients with secondary syphilis about 18% may have neurological (including ophthalmological) signs or symptoms.[3] Ocular involvement may be silent or present as anterior uveitis, choroiditis, interstitial keratitis, retinal vasculitis, retinitis, optic neuritis, dacryoadenitis, or scleritis.[2,4] In this case the presenting symptoms of neurosyphilis were non-specific.

Optic nerve involvement may be unilateral or bilateral and manifest as perineuritis, anterior or retrobulbar optic neuritis or papilloedema,. Optic perineuritis is usually asymptomatic, in optic neuritis however, there is usually rapid visual failure.The optic neuritis is rare and there is no specific characteristic about its appearance to distinguish it from non-syphilitic involvement of similar distribution.[5] Anterior optic neuritis showed the optic nerve head appears inflamed and there is often cellular activity in the posterior vitreous,[5] there may be patchy diffuse neuroretinitis with areas of haemorrhage. Retrobulbar neuritis, showed the optic nerve head may appear normal, but a RAPD and poor colour vision indicate poor optic nerve function. The history may not suggest a diagnosis of syphilis so patients with optic neuritis should be tested for syphilis.

Visual acuity in optic neuritis can range from 0, i.e., no light perception, to 1.5; in two-thirds of patients, it is below 0.5. The affected eye is blind in 3% of cases but has an acuity of 1.0 or better in 11% of cases. Most patients have central and centrocecal scotomata. One-third have mild deficits on the opposite side as well, which one might be tempted to attribute to inattentiveness during perimetry

The optic disc usually appears normal but is mildly edematous in one-third of cases. Impaired color perception is best tested by having the patient look at a colored object first with the right eye, then with the left (or vice versa). The object's color should seem equally saturated and bright in the two eyes; if one eye is affected by optic neuritis, that eye perceives a darker, desaturated color.

The clinical constellation of pain on eye movement, a relative afferent pupillary defect, and a normal or mildly edematous optic disc is pathognomonic for optic neuritis and suffices to establish the diagnosis. Macular inspection is important for the exclusion of neuroretinitis.

The specific antitreponemal tests such as TPPA, microhaemagglutination (MHA), and FTA-ABS (fluorescent treponemal antibody) are said to be sensitive, and specific in all stages of syphilis.[4] However, treponemal test reversion ($\leqslant$16%) after treatment[6] and false positive (2%) syphilis serology may occur during pregnancy or because of infection with non-venereal spirochaetes, for example, *Borrelia bergdorferi*.

Lipid antigen tests such as VDRL (venereal disease research laboratory) or

RPR are a better reflection of disease activity and are important for assessing the patient's response to treatment. The VDRL turns positive one to two weeks after chancre formation. However, false positives because of cross reaction with cardiolipin may occur in pregnancy, after vaccination, after myocardial infarction, or any febrile illness. False negatives (⩽32%) can occur in early primary, latent, or late syphilis and with concomitant HIV infection.[2,4] A specific antitreponemal test and a lipid antigen test should be performed together and all patients with syphilis should be evaluated for HIV and vice versa.[2,4] In some cases more elaborate tests and variables may be useful.[7, 8]

The HIV status of the patient is important because patients with concurrent HIV have a higher incidence of neurosyphilis, including ocular complications, which are more likely to be bilateral.[4,10]Neurosyphilis in patients with HIV infection may follow a more aggressive course because of the reduced immunological response found in these patients.[4] Occasionally the serological response may be reduced, delayed, or absent making diagnosis difficult.[6,7,8]

Benzathine penicillin intramuscularly is used because it is simple, cheap, can be given on an outpatient basis, and is less susceptible to patient non-compliance than oral treatment. However, there are concerns that useful levels may not be achieved in the CSF or eye.[9,10,11,12] The addition of probenecid to penicillin G increases the ocular concentration of penicillin in proportion to the rise in serum level of penicillin and increases the intraocular half life of penicillin.[11]

The CSF and aqueous levels of penicillin may not be vital. There are few treatment failures with benzathine penicillin despite its failure to reach treponemocidal levels in the CSF, possibly because the pathology is at the endarterial level where it is the serum level that is more important. None the less persistence of *T pallidum* in CSF and aqueous after penicillin treatment has been reported,[12] and may have occurred in this case. Although tetracycline and doxycycline are used as alternative treatments for syphilis there is less experience with their use, and patients receiving these regimens should be closely monitored.[2,7,8,13,14] The oral administration of tetracycline or doxycycline, which are less lipophilic than minocycline, results in a low concentration in the spinal fluid. There is little information on the ocular penetration of doxycycline. Oral minocycline penetrates well into the eye achieving vitreous levels of about 50% of the plasma levels.[15] This patient still manifested neurosyphilis despite benzathine penicillin and doxycycline. Doxycyline interferes with the bacterial protein synthesis by binding to the bacterial S30 ribosomal unit. It is treponemostatic and its effects are reversible when the drug is stopped. Although penicillin is treponemocidal it is only effective against multiplying organisms. It may be that simultaneous administration of doxycycline and penicillin was in part responsible for the treatment failure. Prolonged treatment with intravenous penicillin was required. Similarly azithromycin and penicillin probably should not be used together in patients with non-gonococcal urtheritis.[16] However, quinolones, which are inactive against spirochaetes, may be the best treatment choice for patients with syphilis and non-gonococcal urtheritis.

Properly treated the visual prognosis for patients with syphilis and optic neuritis is good.[5] Oral and intravenous corticosteroids are an appropriate adjunct for posterior uveitis, scleritis, and optic neuritis.[4]Secondary optic atrophy is uninfluenced by antisyphilitic treatment.

The neurological and ophthalmological guidelines state that optic neuritis should be treated with

methylprednisolone at a dose of 500–1000 mg/day for 3–5 days. During steroid treatment, a proton-pump inhibitor is also given to prevent peptic ulcers. Osteoporosis prophylaxis, in contrast, is not necessary, because steroids are only given for a short time. The complete blood count, serum glucose, and electrolyte levels are checked before the first intravenous dose of methylprednisolone and on the third and (sometimes) fifth day of treatment.

Acquired immunity develops three to six months after infection. This immunity is incomplete and re-exposure to syphilis can bring about asymptomatic re-infection. Therefore after treatment the VDRL should be repeated at one, three, six, and 12 months. A persistent fall in VDRL titre after treatment provides essential evidence of an adequate response to therapy. HIV positive patients may relapse even after treatment with high dose intravenous penicillin. Lumbar puncture should be repeated every six months for two years in patients who have had neurosyphilis. The CSF VDRL titre should decrease fourfold, typically within the first 6 to 12 months. An increased CSF protein falls more slowly. If these parameters do not fall as predicted then re-treatment may be indicated.

CONCLUSION

Optic neuritis as a complication of syphilis is rare and there is no specific characteristic about its appearance to distinguish it from non-syphilitic involvement of similar distribution. Careful history taking is needed to find its etiology. Patient with immunocompromised condition need a special treatment due to its condition. The visual prognosis for patients with syphilis and optic neuritis is good if properly treated. A careful physical examination is needed that we might missed if we only see the ophthalmology status.

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