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CASE REPORT

Presentation of Ocular Syphilis with Bilateral Optic Neuropathy

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ABSTRACT

A 60-year-old otherwise healthy male presented with a 1 year history of bilateral progressive visual loss. His best-corrected visual acuity was counting fingers at 2 m with his right eye and counting fingers at 0.5 m with his left eye. Visual field testing revealed bilateral near-total loss of visual fields. Slit-lamp examination was unremarkable, apart from bilateral grade two nuclear sclerotic cataracts. Both optic discs were pale-looking with some retinal pigment epithelial alterations at the left papillomacular region. Enhanced depth imaging optical coherence tomography depicted punctate hyperreflective dots at the inner choroidal level corresponding to the retinal pigment epithelial changes in the left eye. Fundus autofluorescence imaging revealed patchy hyper-autofluorescent and hypo-autofluorescent areas, and there was mild staining in the early and late phases of the fluorescein angiogram at the papillomacular region in the left eye. A diagnosis of bilateral optic neuropathy was made. A full systemic work-up was carried out, and serological tests pointed out the presence of syphilis with normal cranial magnetic resonance imaging. He was treated accordingly. Our case clearly demonstrates the importance of a high clinical suspicion for syphilis in cases of optic neuropathy.

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Introduction

Syphilis is an infectious systemic disease caused by the spirochaete *Treponema pallidum*. Although syphilis is known as a sexually transmitted disorder, the spirochaete can be transmitted from mother to baby during the pregnancy or delivery and also via blood transfusions.[1] The incidence of syphilis ranges between 2.5/100.000 and 8.7/100.000 per year in different publications from different regions.[2,3]

Syphilis has four disease stages: primary; secondary; latent; and tertiary and can affect almost any organ or system in the body such as skin, eyes, cardiovascular system, musculoskeletal system, and nervous system. Although eye involvement may occur in all stages, at an average of 10% of cases, it is frequently encountered in the secondary stage.[4]

Ocular syphilis may present with a variety of manifestations and involve anterior and/or posterior segments of the eye. Syphilis is named as the 'great imitator' and may masquerade as many ocular diseases.[5,6]

We report a case of bilateral syphilitic optic neuropathy (ON) and remind the clinicians not to forget syphilis in the differential diagnosis of ON. Written informed consent for publication was obtained from the patient.

Case report

A 60-year-old otherwise healthy male presented with a 1 year history of visual deterioration in both eyes. The visual disturbance was more prominent in his left eye and had gradually worsened, especially in the previous month. He smoked one packet of cigarettes per day and consumed alcohol once per week. His past medical history and family history were unremarkable.

On examination, his best corrected visual acuity (BCVA) was counting fingers at 2 m with his right eye and counting fingers at 0.5 m with his left eye. Mild anisocoria was present (right pupil was 3 mm and left pupil was 2.5 mm in diameter). Both pupils were unresponsive to light, whereas miosis was observed bilaterally with accommodation. His colour vision was 0/21 bilaterally with the Ishihara pseudoisochromatic plates. Slit-lamp examination was unremarkable except for grade 2 nuclear sclerotic cataracts bilaterally. His intraocular pressures

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were 15 mmHg in each eye. Fundoscopy revealed pallid optic discs and slight patchy retinal pigment epithelial (RPE) alterations in the left papillomacular area (Figure 1a,b). Enhanced depth imaging (EDI) optical coherence tomography (OCT) (Heidelberg Spectralis, Heidelberg Engineering, Heidelberg, Germany) sections showed no significant pathological changes in the right eye (Figure 1c), but there were punctate hyperreflective dots at the inner choroidal level and disorganisation of the outer retinal layers in the papillomacular region of the left eye (Figure 1d). Bilateral near-total atrophy was observed of the peripapillary retinal nerve fibre layers in both eyes (Figure 1e,f). There was bilateral asymmetrical near-total visual field loss that was more prominent in the left eye on the Humphrey 30-2 Swedish interactive thresholding algorithm (SITA) visual field test (Figure 2a,b). Right fundus autofluorescence (Heidelberg Spectralis, Heidelberg Engineering, Heidelberg, Germany) was normal (Figure 3a), but there were patchy hyper-autofluorescent and hypo-autofluorescent areas in the left papillomacular region (Figure 3b). While fluorescein angiography (FA) (Heidelberg Spectralis, Heidelberg Engineering, Heidelberg, Germany) showed no abnormality in the right eye (Figure 3c,e), there was some staining in the left papillomacular region in the early and late phases (Figure 3d,f).

A full systemic work-up was performed including complete blood count, routine biochemistry, sedimentation rate, C-reactive protein level, full infectious panel and rheumatological panel to investigate the aetiology as the clinical presentation was compatible with bilateral ON. The non-specific anti-treponemal test of the venereal disease

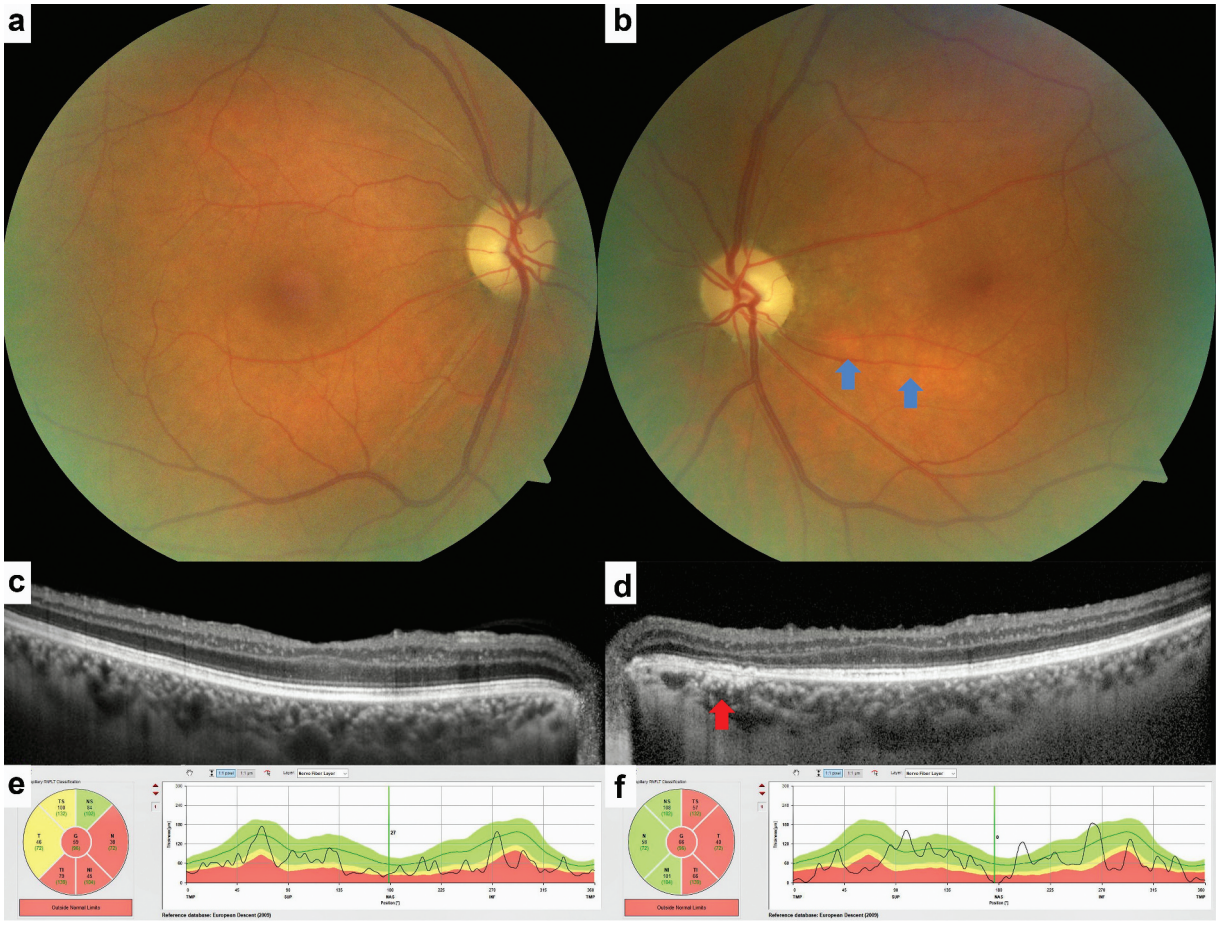

Figure 1. Colour fundus pictures on admission (a, right and b, left eye) showing bilateral pale optic discs and patchy retinal pigment epithelial alterations (blue arrows) in the left papillomacular region. Enhanced depth imaging optical coherence tomography sections depicting a normal right eye (c) and punctate inner choroidal hyperreflective dots (red arrow) in the left papillomacular region together with the disorganisation of the outer retinal layers (d). Retinal nerve fibre layer thickness measurements revealing near-total atrophy in both eyes (e, right and f, left eye).

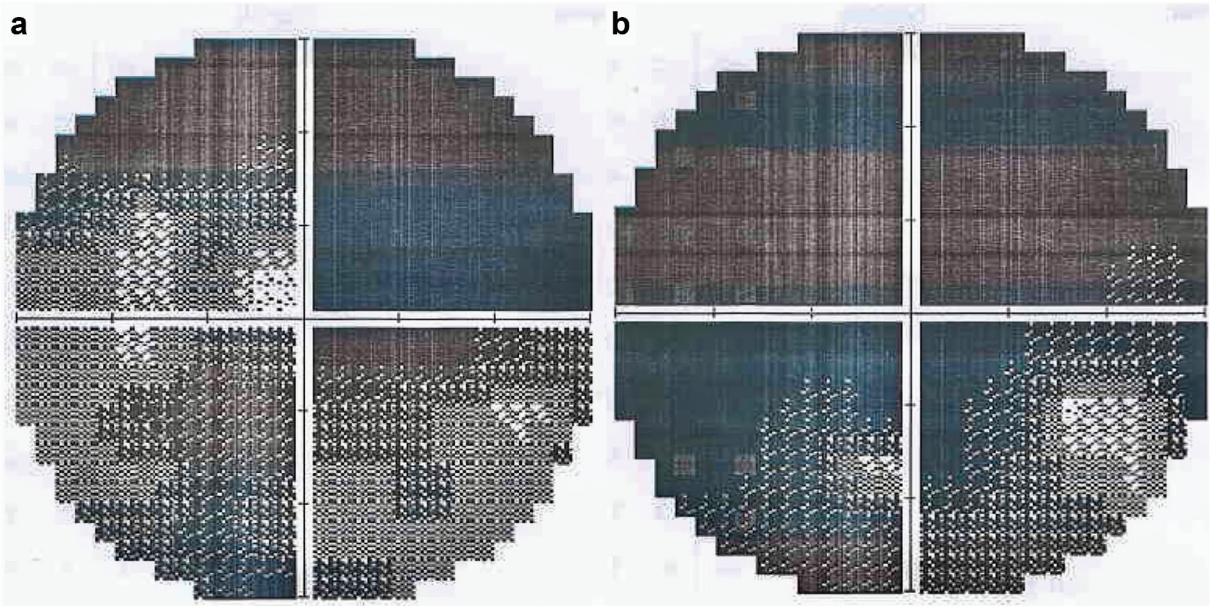

Figure 2. 30-2 Humphrey visual field tests of the left (a) and right (b) eyes with bilateral asymmetrical near-total visual field loss.

research laboratory (VDRL) and rapid plasma reagin (RPR) tests turned out to be positive (RPR titre: 1/16). He tested negative for other infectious agents including human immunodeficiency virus. Cranial and orbital magnetic resonance imaging (MRI) with gadolinium showed no abnormal changes. Thus, a diagnosis of bilateral syphilitic ON was made. A lumbar puncture was offered to evaluate the cerebrospinal fluid (CSF) for central nervous system (CNS) involvement, but he refused to have the procedure.

Although, intravenous crystalline penicillin G is the standard recommended ocular syphilis and/or neurosyphilis treatment, we could not administer it due to its absence in the country at the time of diagnosis. He was treated with a total of 7.2 million units (MU) of benzathine penicillin G, administered as three intramuscular doses of 2.4 MU each at one-week intervals in a care unit that was determined by Provincial Health Directorate.

Seven months after the diagnosis, the right BCVA improved to 0.05 on Snellen chart, the left BCVA remained as counting fingers at 0.5 m. The right central visual field defect slightly improved in the Humphrey 30-2 SITA visual field test, parallel to the visual acuity improvement. Fundoscopic and multimodal imaging findings were almost similar to those at the time of diagnosis except for slightly reduced hyperreflective dots at the papillomacular region in the left eye. The RPR titre was 1/16 at the last visit.

Discussion

All segments and layers of the eye as well as the optic nerve can be affected in ocular syphilis. Optic nerve involvement has been diagnosed in 12% to 78% of ocular syphilis cases[6] and can present as inflammatory optic disc oedema, optic neuritis, optic disc gumma formation, neuroretinitis, perineuritis, optic chiasmal syndrome or optic atrophy accompanying uveitis.[7–10]

Ocular syphilis and syphilitic ON cases have been reported more frequently in recent years. Apinyawasisuk et al. reported seven patients diagnosed with syphilitic ON in a 2-year period in their clinic.[11] Kowalski et al. published a case of a 65-year-old male who presented with horizontal diplopia and pale optic discs and received the diagnosis of bilateral syphilitic ON.[3]

Klein et al. studied 32 eyes out of 23 patients diagnosed with ocular syphilis and reported that syphilitic optic nerve involvement was detected in 25 eyes (78%) and syphilitic ON was detected in 11 eyes (44%).[6] In this study, syphilitic optic nerve involvement was defined as optic disc oedema and/or optic disc leakage on FA with or without uveitis. Syphilitic ON was defined as the presence of a relative afferent

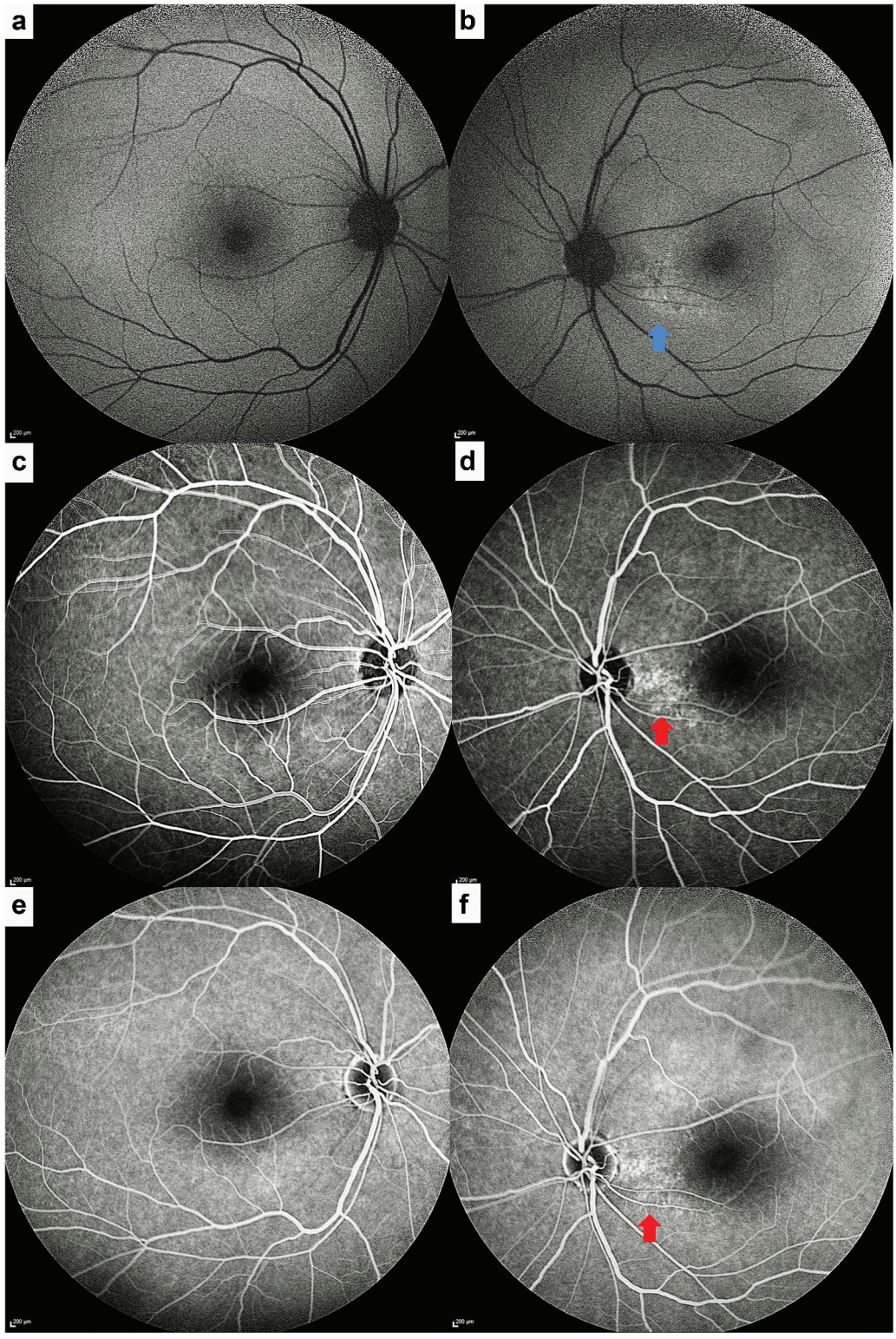

Figure 3. Fundus autofluorescence imaging was normal in the right eye (a) but patchy hyper-autofluorescent and hypo-autofluorescent areas (blue arrow) were present in the papillomacular region in the left eye (b). Early and late phase fluorescein angiographic images showing no abnormal findings in the right eye (c and e), however there is some staining (red arrows) at the left papillomacular region (d and f).

pupillary defect in unilateral cases, or visual loss, visual field defect and decreased colour vision, unexplained by any other findings, in bilateral cases.[6]

Syphilis, one of the leading infectious causes of intraocular inflammation, can present with a variety of clinical appearances. Anterior/intermediate/posterior uveitis, interstitial keratitis, papule formation on the iris, chorioretinitis, retinal vasculitis, scleritis, and episcleritis are among the reported ocular manifestations of syphilis.[12–14]

Acute posterior placoid chorioretinopathy is considered a characteristic presentation of ocular syphilis but this is also an unusual type of disease presentation.[15] Tongue-like projections between the nerve fibre layer (NFL) and the inner plexiform layer, rounded spots in the NFL and ganglion cell layer, disruption or loss of the ellipsoid zone, hyperreflective dots in all retinal layers and in the choroid, vitreous hyperreflectivity, mottling of the RPE and outer retinal discoloration are the previously described OCT findings of ocular syphilis.[16,17] EDI-OCT is a useful imaging method to detect the hyperreflective dot-like lesions at the inner choroidal and outer retinal layers. These lesions are thought to represent the inflammatory foci in the choroid vasculature since the circulating *Treponema pallidum* spirochaetes enter the outer retina through the choroidal circulation.[18] In our case, the presence of these lesions on EDI-OCT supported the diagnosis of syphilis.

Ocular syphilis is considered as part of the spectrum of neurosyphilis. CSF evaluation has been generally recommended in cases of ocular syphilis in order to look for possible CNS involvement, even in the absence of neurological symptoms or signs.[19] However, in the latest guideline for the treatment of sexually transmitted diseases, which was published in 2021 by The United States Center for Disease Control and Prevention, it was recommended that among the individuals with isolated ocular symptoms (i.e., no cranial nerve dysfunction or other neurological abnormalities), confirmed ocular abnormalities on examination, and for reactive syphilis serology, a CSF examination was not necessary before treatment.[20] Additionally, involvement of the brain also can be depicted on cranial MRI and computed tomography imaging even in neurologically asymptomatic cases.[7] The absence of neurological symptoms in the medical history and clinical signs do not exclude neurosyphilis in cases with ocular syphilis.[7] A lumbar puncture was not performed in our patient as he refused the procedure. However, cranial and orbital MRI with gadolinium showed no pathological findings.

Treponema pallidum is a pathogen which cannot be cultured in vitro. Therefore, the diagnosis is based on the relevant clinical findings and appropriate serological examinations. Two groups of tests, nontreponemal and treponemal, are utilized. Besides the frequently used non-treponemal tests VDRL and RPR, treponemal tests including fluorescent treponemal antibody absorption (FTA-ABS) and treponema pallidum particle agglutination (TP-PA) are also employed. Serological test positivity with any type of ocular involvement points out the diagnosis of ocular syphilis. However, some autoimmune diseases may interfere with the non-treponemal tests and cause false positivity. Also, treponemal tests may give false positive results in several conditions, such as other spirochaete infections and malaria.[21]

Treatment of ocular syphilis cases, including syphilitic ON, should be administered in accordance with the neurosyphilis protocol. In this context, it is recommended to administer 18–24 MU of intravenous crystalline penicillin G treatment per day for 10–14 days.[20,22] Although its benefit has not been proven in randomised controlled studies, some authors recommended supportive corticosteroid therapy, especially in cases with intense inflammation.[11,23]

Serological follow-up is recommended for all cases with syphilis following the treatment to evaluate the treatment response. Appropriate serological treatment response is defined as ≥ four-fold decline from the baseline nontreponemal antibody titres or seroreversion to non-reactive.[20] The RPR titre is commonly used to evaluate the treatment response in cases with syphilis.[20] However, some patients, as in our case, have been reported to have persistent low-level titres over time with lack of complete seroreversion during the follow-up despite the proper treatment.[24]

Syphilis is considered as the ‘great imitator’ as the disease can present with various clinical presentations and can easily be misdiagnosed. Our

case is a clear example of why the possibility of syphilis should always be kept in mind in the differential diagnosis of ON, even though there may be no direct history or systemic finding.

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