

# Syphilitic Chorioretinitis – Two Case Reports and Literature Analysis

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## Abstract:

**Introduction:** Syphilis, a systemic, sexually transmitted inflammatory disease caused by *Treponema pallidum*, presents challenges in diagnosis due to its varied manifestations. Ocular syphilis often presents with non-specific symptoms. This study aims to elucidate the diagnostic process through the analysis of two patient cases, including one with HIV co-infection.

**Material and Methods:** The study evaluated two ocular syphilis cases, diagnosed using comprehensive treponemal (fluorescent treponemal antibody absorption test, *Treponema pallidum* hemagglutination assay, enzyme immunoassay) and nontreponemal (venereal disease research laboratory test, rapid plasma reagin test) testing. Factors such as uveitis symptoms, sexual behavior, drug use, previous treatments, and available medical history were considered.

**Results:** The results highlight the complexity of ocular syphilis diagnosis. Both cases underscored the need to include ocular syphilis in differential diagnoses for eye infections or inflammations, especially in patients with high-risk behaviors, drug use, or a history of syphilis. The non-specific nature of symptoms necessitates comprehensive testing for accurate diagnosis.

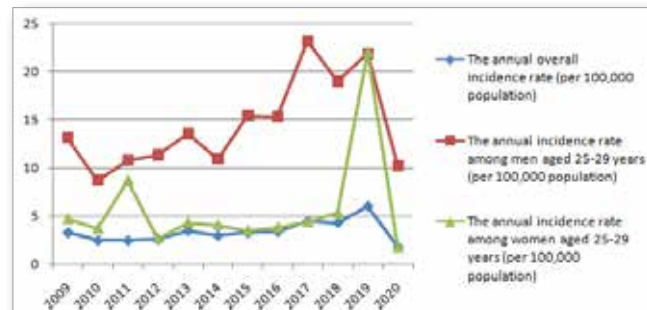
**Conclusions:** This study reinforces the importance of considering ocular syphilis in the differential diagnosis of inflammatory eye diseases. A meticulous approach combining both treponemal and nontreponemal tests is crucial for accurate diagnosis. These findings emphasize the need for thorough clinical evaluation and history-taking in patients presenting with ocular symptoms.

## Key words:

syphilitic chorioretinitis, uveitis, *Treponema pallidum*, uveitis, acute posterior placoid chorioretinopathy.

## Introduction

Syphilis is a sexually transmitted disease caused by the bacterium *Treponema pallidum* ssp. *pallidum*, for which humans are the only reservoir. According to data from 2018, there are 18 million new cases of syphilis reported globally each year, an increase of 8 million from 2008 (1, 2). A particularly noticeable increase in cases is seen among homosexual men and patients infected with the HIV virus. In Poland, the incidence in the general population decreased from 3.3/100,000 in 2009 to 1.85/100,000 in 2020. The highest incidence trend was noted in the age group 25–29 years. Statistical data on incidence in Poland from 2009–2020 are shown in the chart (Fig. 1) (3). The incubation period for the disease ranges from 4 weeks to 3 months (4). The frequency of ocular symptoms in syphilis patients is estimated at 0.6–1.0% of all infection cases.



**Fig. 1.** Incidence of syphilis in the Polish population between 2009–2020, detailing the incidence in the general population as well as in the age group 25–29 years, separately for women and men

Ocular symptoms can occur at all stages of the disease and can vary greatly in clinical presentation (5). However, they most often relate to secondary syphilis, developing about 6 months after infection and manifesting as panuveitis or posterior uveitis.

In primary syphilis, ocular symptoms are rare. They appear at the site of direct contact with the pathogen and manifest as ulcers of the eyelids or conjunctiva (6), as well as of the lacrimal gland (7). Untreated cases of primary syphilis progress to secondary syphilis within 4–10 weeks, presenting skin symptoms in the form of rashes and itching, sometimes involving the eyelids. In addition, there have been cases of madarosis (eyelash loss), inflammation of the conjunctiva, sclera, cornea, iris, ciliary body, and choroid. Anterior uveitis is usually unilateral, granulomatous or non-granulomatous in nature, and may manifest as tyndallization in the anterior chamber, dilation of the iris vessels (iris roseola), and an increase in intraocular pressure (IOP) (7–9).

Inflammation involving the posterior segment of the uvea is characterized by the presence of exudate in the vitreous body and multifocal inflammation of the retina and choroid with accompanying serous retinal detachment. The disease can also manifest as retinal vascular inflammation and optic nerve inflammation. Inflammatory changes can resemble acute retinal necrosis (ARN), but in syphilis (syphilitic retinal necrosis – SRN), it most often primarily appears in the posterior pole, with the retina having a marbled appearance, unlike the homogeneous changes in ARN. Another characteristic of syphilitic chorioretinitis is the presence of numerous small, round, whitish opacities in the vitreous. These symptoms occur bilaterally in 50% of cases (7).

A common form of secondary syphilis or late latent syphilis is acute posterior placoid chorioretinopathy (APPC), which is associated with damage to the retinal pigment epithelium (RPE) and the outer layers of the retina. It manifests as a yellowish, single or multifocal placoid lesion with round borders located in the macula. Additionally, changes can involve vessels – both arteries and veins – causing inflammation and thromboembolic changes. These changes often accompany retinal ground-glass inflammation (10).

Neuro-ophthalmic changes may include optic disc edema secondary to increased IOP, optic neuritis, and the presence of the Argyll Robertson sign (11).

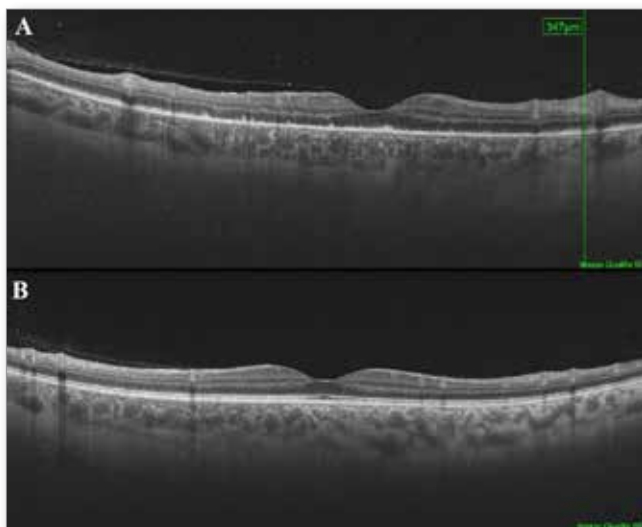
## Case Descriptions

### Case 1.

A 35-year-old patient presented to the ophthalmology emergency department due to visual disturbances in the right eye (RE) in the form of blurred vision with a dark spot in the field of vision, which had intensified over 5 days. The patient denied any eye pain. He had a history of an upper respiratory tract infection accompanied by fever three weeks prior to presentation. The patient had not previously been treated by an ophthalmologist, denied any complaints or systemic diseases, and also denied contact with tuberculosis patients, tick bites, and past or current skin changes. BMI was 27.5. During the ophthalmic examination, the best-corrected visual acuity (BCVA) for distance was 1/50 in the RE and 1.0 in the left eye (LE). Intraocular pressure (IOP) in the RE and LE was 17 mmHg and 18 mmHg, respectively. The anterior segment of both the RE and LE showed no deviations from the norm. In the vitreous body of the RE, the presence of fine particulate exudate and condensations in the posterior layers of the vitreous (SUN 1+) were observed. The fundus of the RE appeared foggy. The optic nerve disc had slightly blurred boundaries, and the blood vessels appeared normal. The macular reflex was absent. Both the anterior segment and fundus examination of the LE showed no abnormalities.

In the spectral domain optical coherence tomography (SD-OCT) examination of the RE, a well-defined area of outer limiting membrane atrophy and damage to the outer photoreceptor segments (absence of the ellipsoid and interdigitation zones) was observed. These changes were accompanied by hyperreflective foci of increased RPE thickness and scattered tiny hyperreflective granules within the choroid. Numerous hyperreflective opacities were visible in the vitreous and on the retinal surface. SD-OCT images of both eyes are shown in Figure 2.

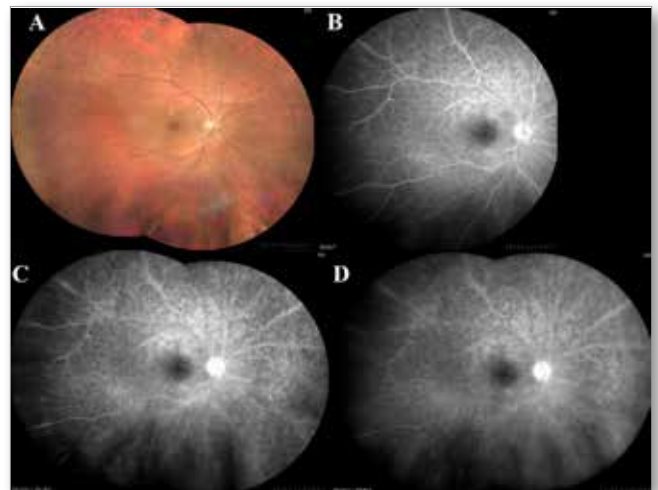
Late-phase fluorescein angiography (FA) performed three months after the onset of symptoms revealed, in the RE, leakage from large and medium-sized arterial and venous vessels of the



**Fig. 2.** A – horizontal SD-OCT scan of the right eye centered on the macula showing a localized area of external limiting membrane atrophy and damage to the outer photoreceptor segments. Visible hyperreflective foci of increased RPE thickness. Numerous hyperreflective opacities in the vitreous body. B. Horizontal SD-OCT scan of the left eye displaying a retina with a normal structure at the macular center.

superior and inferior temporal arcades and peripheral vessels, as well as dye pooling in the optic nerve disc.

Both the fundus image of the LE and the results of SD-OCT and FA were within normal limits. FA results and color fundus photographs are shown in Figure 3.



**Fig. 3.** Color fundus photograph of the right eye and FA in early and late phases. A. – Color fundus photograph with visible abnormal reflex. B. – FA image of the right eye at 36 seconds after fluorescein injection. C. and D. – Late phase FA images of the right eye, taken at 3 minutes and 9 minutes respectively, showing leakage from large and medium-sized arterial and venous vessels of the superior and inferior temporal arcades, as well as peripheral vessels, and dye pooling at the optic disc.

During hospitalization, a panel of tests was conducted to search for infectious agents causing inflammation. Blood morphology, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), AST, ALT, and ionogram were all within normal limits. Chest X-ray showed no deviations. Urinalysis revealed a slightly increased number of leukocytes and erythrocytes. In the RE, BCVA improved to 0.3 without treatment. The patient was discharged with a preliminary diagnosis of acute posterior multifocal pigment epitheliopathy and scheduled for monthly outpatient ophthalmic checks. During the first follow-up visit, additional diagnostic tests for HIV and syphilis were ordered.

During the next visit, the patient reported deteriorating vision and flashes in the affected eye. Follow-up SD-OCT showed increased inflammatory infiltrates and macular edema. During subsequent visits, peribulbar steroid injections were administered twice, resulting in BCVA improvement to 0.5 and a subjective improvement in color vision. Tests for infectious diseases such as antibodies against *Toxoplasma gondii* and *Borrelia burgdorferi*, as well as the Quantiferon test to rule out tuberculosis, were negative. However, antibodies against HIV were detected, and a positive result was obtained from the syphilis screening test venereal disease research laboratory (VDRL) and the fluorescent treponemal antibody absorption test (FTA-ABS). HIV infection was confirmed with an HIV confirmation test. The patient was diagnosed with syphilitic posterior uveitis and HIV infection. The patient, with a diagnosis of acute posterior placoid chorioretinitis and retinal vasculitis of syphilitic etiology, was referred to a clinical hospital for infectious diseases. During hospitalization in the immunodeficiency department, the patient was treated with penicillin and antiretroviral drugs were introduced. Test results indicated HIV carriage without immune disorders.

### Case 2.

A 36-year-old patient presented to the ophthalmology emergency department due to deteriorated vision, floaters, and flashes in the

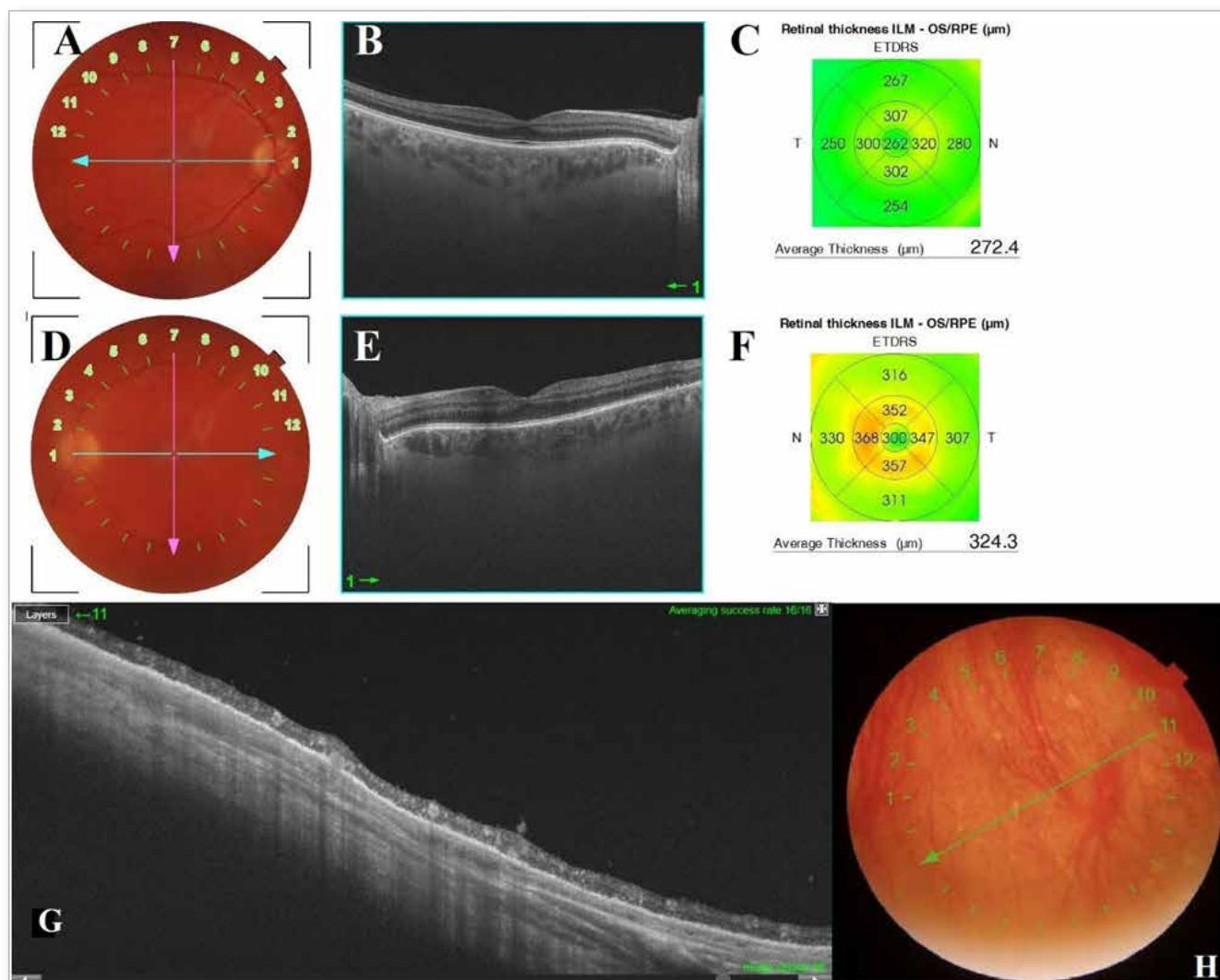
field of vision of the left eye (LE). The complaints had persisted for 1.5 months. The patient had no history of eye-related diseases. He reported a fever with a skin rash that he had experienced 3 months ago, a skin infection with *Staphylococcus* in the lower abdomen treated with oral antibiotics, and a recent urinary tract infection treated with Augmentin (2 times 1.0 g p.o.) a week ago. Additionally, he mentioned recurrent herpes outbreaks (last one year ago). BMI was 20.5. Body temperature was within the normal range.

During the ophthalmic examination, BCVA for the RE and LE was 1.0 and 0.8, respectively, and IOP was 17 mmHg for RE and 13 mmHg for LE.

The anterior segment and fundus of the RE were within normal limits, with no vitreous haze. In the LE, the conjunctiva was injected, the cornea was clear with deposits extending up to 2/3 of the cornea from the bottom, the deposits were of medium intensity and varied in size. The anterior chamber showed tyndallization (SUN +0.5). The iris was normal, the pupil was constricted without synechiae, and reactive. The lens was clear. In the vitreous, inflammatory cells (SUN 1+) and a dense pre-retinal exudate were observed.

The fundus examination of the LE showed slightly blurred boundaries of the optic nerve disc and minor macular edema. Numerous small, creamy, flat retinal foci were seen peripherally from the bottom and temporally, partially obscured by a dense, lumpy, white pre-retinal exudate. The ultrasound of the LE revealed an organized hyperechoic conglomeration attached to the peripheral retina. SD-OCT of the RE showed no deviations from the norm. The retinal structure in the macula was normal, but its thickness was slightly increased compared to the RE. Peripheral foci in the OCT cross-sectional image appeared as areas of inner retinal layer atrophy. Adjacent to the foci, the vitreous showed hyperreflective granular densification. The choroid was thickened. The patient's imaging results are shown in Figure 4.

Blood tests: blood morphology with smear, ESR, blood sugar level, AST, ALT, HIV Combo test, HBs antibody levels, HCV, *Borrelia burgdorferi*, *Chlamydia*, and Quantiferon were all negative. Elevated levels of IgG against *Toxoplasma gondii* and *Cytomegalovirus* (CMV) were observed, but IgM was within normal limits. Blood and urine cultures were negative. FTA-ABS and VDRL tests were ordered.



**Fig. 4.** Fundus photographs of both eyes, along with SD-OCT imaging, retinal thickness maps as well as a color photograph of the peripheral retina with its corresponding SD-OCT scan. A. – Color fundus photograph of the right eye. B. – Right eye B-scan SD-OCT showing a normal retinal appearance. C. – Retinal thickness map of the right eye with an average retinal thickness of 272.4  $\mu\text{m}$ . D. – Color fundus photograph of the left eye showing blurred appearance of the optic disc and vessel outline due to vitreous opacities. E. – Left eye B-scan SD-OCT showing individual hyperreflective RPE thickening temporally from the fovea, along with disruption of the outer retinal layers and shadowing from vitreous opacities. F. – Retinal thickness map of the left eye with an average retinal thickness of 324.3  $\mu\text{m}$ . G. – SD-OCT scan of the retinal periphery showing numerous hyperreflective foci of inflammatory infiltration across various retinal layers, hyperreflective opacities in the vitreous body and on the retinal surface, disturbances in the inner retinal layers, and localized areas of RPE atrophy. H. – Color photograph of the left eye's peripheral retina displaying multiple whitish hyperreflective foci.

During hospitalization, a deterioration in BCVA of the LE to 0.6 and an increase in exudation were noted. During the stay, the patient was treated topically with injections of atropine, epinephrine, Dexaven and gentamycin subconjunctivally to the LE, and periocularly with Depo-Medrol.

After receiving positive FTA–ABS and VDRL results, the patient was referred to a dermatology and venereology clinic for further treatment.

## Discussion

Ocular syphilis is often referred to as the “great imitator” because its symptoms can affect both the anterior and posterior segments of the eyeball, as well as the eye’s protective apparatus, and can resemble uveitis of various etiologies. The conditions that most closely resemble the changes in the posterior segment are acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and atypical serpiginous choroidopathy. Other diseases that can mimic syphilis symptoms in the posterior segment include intermediate uveitis, non-infectious posterior uveitis (e.g., related to sarcoidosis, systemic lupus erythematosus, and rheumatoid arthritis), ARN, progressive outer retinal necrosis (PORN), other infectious retinitis (e.g., due to CMV, toxoplasmosis, and tuberculosis), and Behcet’s disease.

In this paper, we present two cases of the disease with very different clinical presentations. In the first case, symptoms primarily concerned the posterior segment of the eye, characteristic of acute posterior placoid retinitis and choroiditis. In contrast, the second case primarily presented features of anterior uveitis. This vast range of potential clinical forms suggests that syphilis diagnostic tests should be performed in all cases of uveitis. Serological tests, which include treponemal (specific) and non-treponemal (cardiolipin, non-specific) tests, are the primary tool for confirming syphilis. Among the non-treponemal reactions, the most commonly used are the VDRL tests – the microflocculation test with cardiolipin antigen and the RPR. These detect anti-cardiolipin antibodies 1-2 weeks after infection with a sensitivity of up to 99% in patients with secondary syphilis. For tertiary syphilis patients, sensitivity drops to 70%, and after treatment, these tests become non-reactive. Treponemal reactions include the FTA–ABS test, the *Treponema pallidum* hemagglutination assay (TPHA), the enzyme immunoassay (EIA), and the less frequently performed immunoblot. Treponemal reactions remain positive throughout a patient’s life and are required to confirm a positive VDRL/ RPR

result. The frequently used FTA–ABS test is highly specific, but false-positive results can occur in patients with various diseases, e.g., rheumatoid arthritis (RA), HIV infections, systemic lupus erythematosus, infectious mononucleosis, scarlet fever, rickettsiosis, and in pregnant women. The Centers for Disease Control and Prevention (CDC) propose two algorithms for serological syphilis testing: the traditional screening algorithm and the reverse sequence screening algorithm; both are shown in Figure 5.

Due to similar risk factors, syphilis often coexists with HIV infection. Although epidemiological data do not indicate differences in clinical presentation between patients with concurrent HIV and those without this infection, it has been proven that in the group of HIV-infected patients, ocular syphilis presenting as posterior uveitis or panuveitis is more common.

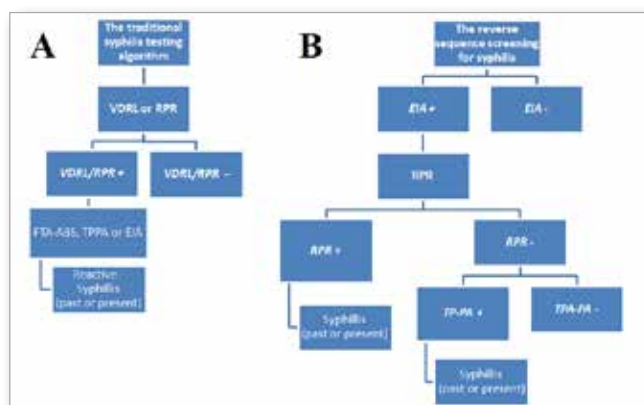
In conclusion, it should be emphasized that in every case of uveitis, serological tests should be performed to rule out infection with *Treponema pallidum*. In the event of a positive result, HIV diagnostics should be carried out.

## Disclosure

The authors declare no conflict of interest.

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**Fig. 5.** A. – Traditional syphilis testing algorithm: A non-treponemal test (VDRL/ RPR) is used as the first screening test. Reactive samples are subjected to a second, confirmatory treponemal test: FTA–ABS, TPPA, or EIA. B. – Reverse sequence syphilis testing algorithm: Initial screening is done with a specific test such as enzyme immunoassays (EIA) and chemiluminescent immunoassays (CIA). Samples that show a reaction are then subjected to a non-treponemal test, such as VDRL or RPR. If the non-treponemal test does not show a reaction, a second treponemal test (such as FTA–ABS) is conducted to confirm the disease.

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