Letter to the Editor

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A rare case of syphilitic uveitis in a 61-year-old non-HIV woman

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To the Editor:

Syphilis is a multisystemic infection caused by the spirochete *Treponema pallidum* and characterized by a wide clinical variance of symptoms.[1] It is most commonly transmitted sexually. The clinical course of acquired, untreated syphilis can be divided into four distinct stages depending on its severity: primary, secondary, latent, and tertiary.[2]

In any of these stages, without treatment, syphilis can spread to the central nervous system—neurosyphilis. This may be asymptomatic or present with vasculitis, stroke, dementia, meningitis, psychosis, and ocular involvement.[3] Ocular syphilis can affect any ocular structure, with posterior uveitis and panuveitis being the most common manifestations.[4-6] The disease occurs predominantly bilaterally in men, especially men who have sex with men, with an average age of 43 years. HIV coinfection is also common.[1] Diagnosis of ocular syphilis is challenging because there are no specific diagnostic criteria.[7]

Uveitis is a common inflammatory eye disease that threatens vision. The most common form of uveitis is anterior idiopathic uveitis. Noninfectious causes of uveitis, such as autoimmune diseases, are more common in developed countries.[8] Infectious causes contribute for 30–60% of the cases, with Herpes simplex and toxoplasmosis being the most common agents of uveitis, especially in developing countries. Recently, an increase in the prevalence of infectious causes, including tuberculosis and syphilis, has been observed.[8,9]

Although the incidence of acquired syphilis has increased significantly in several countries, syphilitic uveitis is a rare condition, accounting for 1–2% of all uveitis cases.[5,9,10] Laboratory diagnosis is crucial to clarify the etiology of the disease.[11] The present case report deals with a 61-year-old non-HIV woman who was diagnosed with syphilitic uveitis.

A 61-year-old woman had been examined at a private consultation and diagnosed with anterior uveitis. At that time, she was advised to have a blood test to determine the cause and treated for the anterior uveitis with various collyrium solutions. Despite medical advice, the patient did not fully follow the treatment plan or undertake further investigations to clarify the cause.

Owing to the worsening of this medical condition, she went to the emergency department complaining of low visual acuity in her right eye that has progressively developed over a two-month period.

Medical history revealed exotropia and hypovision of the left eye, which had developed over 10 years. The patient was undergoing rheumatologic treatment for oligoarthralgia and polymyalgia (under investigation) and had received hydroxychloroquine three months previously.

On physical examination, vital signs were stable and no neurologic deficits were noted. Ophthalmologic examination included routine eye acuity and eye fundus observation. Eye acuity examination confirmed hypovision which had worsen on the right eye to 4/10 (previously 8/10). Eye fundus observation showed vitritis on the right eye. Ocular biomicroscopy showed pigmented granulomatous in the left eye. Further ophthalmologic workout included optical coherence tomography to both macula and papilla which revealed choroidites and edema of the left eye; fluorescein angiogram revealed bilateral papillary diffusion, with hypofluorescence on the early phases. Indocyanine green angiography revealed hypocyanescence in all phases of the angiogram. Fundus autofluorescence showed multiple macular hypofluorescent dots. No other findings were reported on ophthalmologic examination. A computed tomography (CT) scan of the brain excluded parenchymal changes suggestive of vascular or space-occupying lesions.

Blood examination revealed a normal blood count, a leukogram with neutrophilia, and positivity for lysozyme. Blood serology revealed positive IgG for herpes simplex virus-1 (HSV-1) and *Toxoplasma gondii*, positive IgM for herpes simplex virus-2 (HSV-2), reactive treponemal test (chemiluminescent immunoassay—CLIA—IgG), and positive VDRL (Veneral Disease Research Laboratory) − 512 dilution titer. She tested negative for HIV (human immunodeficiency virus). These and all other results obtained are listed in Table 1.

Cerebrospinal fluid (CSF) analysis revealed discrete pleocytosis (13 cells), with proteins and glucose within the normal range; a treponemal test (immunoblot assay IgG) and VDRL were positive, with a VDRL titer of two dilutions; molecular testing for *T. pallidum* was negative.

She was hospitalized and received intravenous benzathine penicillin G 2.4 million units for 14 days, oral prednisolone 1 mg/kg/day, and collyrium solutions 48 hours after starting antibiotic therapy. During hospitalization, she underwent ophthalmologic examination, and papilledema improved.

After hospitalization, the patient was treated with a single intramuscular dose of benzathine penicillin G 2.4 million units 1 week after discharge and began de-escalation of corticosteroid therapy with oral prednisolone 0.5 mg/kg/day for five days and 0.25 mg/kg/day for 1 month.

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Table 1

Values of the analytical parameters assessed

Exam	Patient result	Reference value
Hemoglobin	13.2 g/dL	12.0–16.0 g/dL
Platelets	249 × 10^9/L	150–400 × 10^9/L
Leukocytes	6.45 × 10^9/L	4.00–11.00 × 10^9/L
Creatinine	0.49 mg/dL	0.51–0.95 mg/dL
Sodium	141 mEq/L	135–147 mEq/L
Potassium	4.3 mEq/L	3.5–5.1 mEq/L
Chlorides	104 mEq/L	101–109 mEq/L
Angiotensin-Converting Enzyme	49 U/L	20–70 U/L
Lysozyme	30.0 mg/L	4.0–13.0 mg/L
Antiherpes virus I IgG	Positive	—
Antiherpes virus I IgM	Negative	—
Antiherpes virus II IgG	Negative	—
Antiherpes virus II IgM	Positive	—
Antitoxoplasma IgG	Positive	—
Antitoxoplasma IgM	Negative	—
HIV (1 and 2)	Negative	—
CLIA Antitreponema IgG	Reactive	—
VDRL	Positive—512 Dilutions	—
CSF Cytology	13 cells, 300 erythrocytes	<5 cells
CSF Total Proteins	0.41 g/L	0.15–0.45 g/L
CSF Glucose	57 mg/dL	60–70% serum Glucose
CSF Western blot TP IgG	Positive	—
CSF VDRL	Positive—2 Dilutions	—
CSF DNA Treponema pallidum	Negative	—
CSF Bacteriology	Negative	—

CLIA = chemiluminescent immunoassay; CSF = cerebrospinal fluid; IgG = immunoglobulin G; IgM = immunoglobulin M; TP = Treponema pallidum; VDRL = veneral disease research laboratory.

At the 1-month follow-up, the patient stated that her visual acuity had recovered. Ophthalmologic examination revealed improvement of most ocular changes.

The multiple clinical manifestations of syphilis often interfere with diagnosis and allow progression of the disease.[3] Laboratory diagnosis of syphilis is made by serologic treponemal and nontreponemal tests. Treponemal tests are specific for *T. pallidum* and indicate the presence of serum antibodies (IgG) to treponemal antigens, but the result is only qualitative.[12] Nontreponemal tests are less specific but allow for semiquantitative results that are essential for monitoring disease activity and treatment.[1,12]

Despite the lack of specific guidelines for the management of uveitis, serologic screening for syphilis is always recommended, and it is important to rule out neurosyphilis.[7,11] This requires standard criteria including serologic testing, analysis, and response to antimicrobial treatment in the context of consistent clinical symptoms. Among all diagnostic tests for neurosyphilis, CSF-VDRL is considered the gold standard.[3,6] CSF analysis in patients with ocular syphilis is extremely important, as findings of neurosyphilis include pleocytosis and elevated proteins.[3] Other CSF tests may be useful, including Western blot and molecular assays.[11]

As recommended by the Centers for Disease Control and Prevention and European guidelines, treatment of ocular syphilis should be the same as to neurosyphilis (crystalline penicillin), even in the absence of CSF abnormalities.[2,3,6,12,13]

In the case presented, the patient was a 61-year-old woman whose only symptoms were acute visual acuity deterioration. Although all causes of uveitis, including infectious causes, must always be considered, in this case, gender, age, geographic epidemiology (industrialized country), and clinical history may suggest a noninfectious cause as the initial diagnostic hypothesis.[8]

Initial ophthalmologic examination revealed changes suggestive of anterior uveitis. With no other clinical symptoms and failure to follow medical advice, the diagnosis of syphilis was made after a delay of almost two months, with progressively worsening visual acuity and further damage to ocular structures.

The diagnosis of syphilitic uveitis was made only after clinical progression and high suspicion because the development of panuveitis required further investigation.

The potential neurosyphilis development was investigated by CT and CSF analysis. It was confirmed by CSF VDRL which was positive titer in two dilutions, titer in 512 dilutions in serum and by immunoblot, although molecular testing was negative for Treponema pallidum, CSF showed only mild pleocytosis, with protein and glucose levels in the normal range, and the CT scan was benign.

As recommended in the Centre of Disease Control and European guidelines,[14] the treatment regimen for syphilitic uveitis and neurosyphilis is the same since the common CSF abnormalities found in patients with syphilitic uveitis support the diagnosis of neurosyphilis in most cases.[6,7] Therefore, the patient started treatment even before neurosyphilis was confirmed.

Syphilitic uveitis is an infectious form of uveitis that should be included in the differential diagnosis of any ocular inflammation. Regardless of gender, age, and geographic epidemiology, all causes of uveitis should be investigated. Because the eye is an extension of the central nervous system, it is recommended that ocular syphilis always be investigated to exclude neurosyphilis. Although the treatment regimen is the same for both entities, the consequences of developing neurosyphilis are more severe, and thus, follow-up strategies may differ.

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