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When Ocular Syphilis Masquerades as Rheumatic Disease

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Abstract

Ocular syphilis is a rare but critical manifestation of systemic infection that can mimic various rheumatic diseases, often leading to delays in appropriate treatment. We report two cases where ocular syphilis presented similarly to giant cell arteritis and sarcoidosis, respectively. These cases highlight the need for a high index of suspicion and inter-specialty collaboration to avoid misdiagnosis and prevent irreversible vision loss.

Keywords: Ocular Inflammation; Papillitis; Uveitis; Giant Cell Arteritis; Sarcoidosis; Syphilis.

Introduction

Syphilis, caused by Treponema pallidum, is known as "the great masquerader" due to its diverse clinical manifestations. Ocular involvement is a sight-threatening complication that can mimic rheumatologic diseases, leading to unnecessary immunosuppressive therapy and delays in curative treatment. Given the rising incidence of syphilis globally, clinicians must maintain vigilance when assessing intraocular inflammation, as early recognition is crucial in preventing irreversible blindness.

Case Presentation

Case 1

Our first patient is a 52-year-old male with type 2 diabetes mellitus who presented with a two-week history of decreased vision in his left eye and a six-month history of bilateral hand pain. His review of systems was otherwise unremarkable. Ophthalmologic examination revealed reduced visual acuity in the left eye, a trace afferent pupillary defect on the left, and bilateral optic disc swelling, more pronounced on the left. Musculoskeletal examination showed no evidence of active synovitis. Laboratory evaluation demonstrated an elevated erythrocyte sedimentation rate (74 mm/hr) and C-reactive protein (4 mg/dl; reference cut-off: 0.6 mg/dl). He was mildly anemic, with a hemoglobin of 12.7 g/dl. Given the presence of papillitis and elevated inflammatory markers, arteritic ischemic optic neuropathy was strongly considered. Other differential diagnoses of papilledema included inflammatory, infectious and compressive or neoplastic causes. Temporal artery Doppler ultrasound demonstrated bilateral halo signs; therefore, a temporal artery biopsy was ordered. Corticosteroid treatment was discussed but deferred pending further work-up. MRI and MR angiography of the head and neck were unremarkable. A positron emission tomography (PET) scan revealed nonspecific hypermetabolic cervical, axillary, and inguinal lymphadenopathy. Autoimmune work-up- including anti-nuclear antibody, extractable nuclear antigen panel, double-stranded DNA, anti-neutrophil cytoplasmic antibody, rheumatoid factor, cyclic citrullinated peptide antibody, antiphospholipid antibodies, and a CNS demyelinating panel (aquaporin-4 antibodies and myelin oligodendrocyte glycoprotein antibodies)- was negative. Notably, both rapid plasma regain (RPR) and Treponema pallidum particle agglutination (TTPA) tests were reactive, with an RPR titer of 1:128. The combination of vision loss, joint pain, lymphadenopathy and positive treponemal and non-treponemal tests supported a diagnosis of syphilis. The temporal artery biopsy was subsequently cancelled. Given the ocular involvement, a lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis was suggestive of probable neurosyphilis, showing 6 white blood cells (WBCs) with

lymphocytic predominance (83%) and elevated protein (66 mg/dl), although the CSF Venereal Disease Research Laboratory (VDRL) test was negative. The patient was treated with intravenous penicillin, resulting in marked improvement in vision and hand pain as well as adequate serologic response.

Case 2

Our second patient is a 49-year-old female who had been diagnosed with sarcoidosis 18 years earlier, based on the presence of lower extremity erythema nodosum and mediastinal lymphadenopathy on chest-X-ray. She was treated with a course of steroids, leading to symptom resolution. Six months prior to current presentation, she developed joint pain and progressive vision loss. An ophthalmologic evaluation confirmed bilateral panuveitis, and she was started on oral and topical steroids, as well as methotrexate, for a presumed sarcoidosis flare. However, her vision continued to deteriorate. Escalation of immunosuppression with tumor necrosis factor-alpha inhibitors was considered, but the patient opted to seek a second opinion at our institution. When evaluated in our emergency department, she reported a rash on the palms and soles that had persisted for several months and had previously been diagnosed as eczema, in addition to joint pain and vision changes. Examination revealed bilateral panuveitis and erythematous plaques on the palms and soles. Given her worsening symptoms despite immunosuppression, alternative diagnoses were considered. Serologic testing showed a reactive RPR with a titer of 1:512, and a positive TTPA test. CSF analysis was consistent with neurosyphilis, revealing 123 WBCs with lymphocytic predominance (87%) and a positive VDRL test. She was treated with intravenous penicillin, which led to partial improvement in vision and complete resolution of the rash and polyarthralgia.

Ocular layer involved in syphilis	Ocular manifestation(s)	Rheumatic differential diagnosis
Eyelid	Blepharitis	None
Conjunctiva	Conjunctivitis	SICCA syndrome, sarcoidosis
Lacrimal gland	Dacryoadenitis	Sjogren syndrome, sarcoidosis, IgG4 related disease, AAV
Extraocular muscles	Orbital myositis	GCA, sarcoidosis, IgG4 related disease, SLE, RA, AAV, Cogan syndrome, Behcet
Cornea	Keratitis	RA, AAV, Sjogren syndrome, sarcoidosis, relapsing polychondritis, Cogan syndrome, Behcet, SLE
Lens	Cataract	None
Sclera, episclera	Scleritis, episcleritis	AAV, RA, reactive arthritis, relapsing polychondritis, Cogan syndrome
Uveal tract	Anterior, intermediate, posterior uveitis or panuveitis	HLA-B27-associated conditions, sarcoidosis, Behcet, Cogan syndrome, relapsing polychondritis, SLE, Sjogren syndrome, VKH
Retina	Retinitis, retinal vasculitis	Behcet, SLE, GCA, PAN, HLA-B27-associated conditions, relapsing polychondritis, sarcoidosis, AAV, Susac syndrome, VKH
Optic nerve	Optic neuritis, papillitis, papilledema, optic atrophy	Giant cell arteritis, SLE, Sjogren syndrome, sarcoidosis

AAV, ANCA-associated vasculitis; GCA, giant cell arteritis; PAN, polyarteritis nodosa; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; VKH, Vogt-Koyanagi-Harada syndrome

Table 1: Ocular syphilis and its rheumatic differential diagnoses.

Discussion

These cases illustrate how ocular syphilis can closely mimic rheumatic diseases, underscoring the importance of maintaining a broad differential diagnosis when rheumatologists evaluate intraocular inflammation. This is particularly critical, as clinical examination often reveals few distinguishing features to suggest ocular syphilis over other causes [1]. Moreover, ocular manifestations can occur in the absence of systemic signs further complicating the diagnosis [2].

Ocular syphilis can involve all structures of the eye [3]. In a large series of 115 patients (169 eyes), posterior uveitis (19%) was the most common presentation, followed by anterior uveitis (18%) and panuveitis (16%) [3]. Table 1 summarizes the ocular structures affected in syphilis, their corresponding manifestations, and overlapping rheumatic conditions.

Delayed diagnosis and treatment from symptom onset may compromise the recovery of visual acuity. A retrospective case series by Tsuboi et al., involving 20 men (30 eyes) with ocular syphilis, reported a worse visual prognosis when treatment was initiated more than 28 days after symptom onset [4]. Furthermore, misdiagnosis as non-infectious uveitis and subsequent treatment with immunosuppressive agents or corticosteroids can result in worsening vision or permanent visual loss [5,6]. Long term complications of ocular syphilis include corneal opacity, cataract, glaucoma, epiretinal membrane, macular edema, optic atrophy, chorioretinal scarring, and rarely choroidal neovascularization [7,8]. To help prevent these complications, the American Academy of Ophthalmology recommends including syphilis testing in the initial evaluation of any patient with intraocular inflammation [2].

In 2022, the World Health Organization estimated that 8 million adults aged 15–49 acquired syphilis globally [9]. During the same period, the CDC reported an 80% increase in syphilis cases in the United States between 2018 and 2022 [10], accompanied by a parallel rise in ocular syphilis, particularly in underserved areas [11,12]. Given the recent resurgence of syphilis and the potential for vision-threatening complications, rheumatologists should maintain a low threshold for syphilis testing in patients presenting with unexplained ocular inflammation. The two cases presented highlight the importance of close collaboration between rheumatology, ophthalmology and infectious disease to enable timely diagnosis and treatment, thereby reducing the risk of irreversible vision loss.

Conclusion

Syphilis remains a significant global health challenge with rising incidence worldwide. It can involve any ocular structure and is well known for mimicking rheumatic inflammatory conditions, often leading to misdiagnosis. Given its potential for irreversible vision loss and systemic complications, early recognition is critical. Fortunately, ocular syphilis is treatable, and timely diagnosis not only preserves vision but also mitigates broader systemic risks. Rheumatologists must maintain a high index of suspicion when evaluating intraocular inflammation to ensure prompt, appropriate management.

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