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Case Report

Syphilitic Neuroretinitis with Positive Cytomegalovirus Serology in an Immunocompetent Adolescent: A Case Report

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Keywords
Neuroretinitis · Syphilis · Cytomegalovirus · Optic disc edema · Macular star

Abstract
Introduction: Neuroretinitis is an inflammatory optic neuropathy characterized by optic disc edema followed by macular star formation. It is most commonly caused by *Bartonella henselae*, but other infectious etiologies including syphilis and cytomegalovirus (CMV) should be considered, particularly due to their potential for severe visual morbidity if untreated. ***Case Presentation:*** A 17-year-old immunocompetent female presented with unilateral visual blurring and headache. Ophthalmologic examination revealed optic disc edema, macular star exudates, and peripapillary hemorrhages in the right eye. Dermatologic examination revealed features consistent with secondary syphilis, and the diagnosis was further supported by laboratory investigations confirming syphilis. Serologic testing also demonstrated positive CMV IgM and IgG antibodies. HIV testing was negative. The patient was treated with intravenous ceftriaxone and ganciclovir followed by oral valganciclovir. Complete anatomical and functional recovery was achieved with restoration of visual acuity. ***Conclusion:*** This case highlights the importance of comprehensive infectious evaluation in neuroretinitis, even in immunocompetent individuals. Early diagnosis and appropriate targeted antimicrobial therapy are essential to prevent permanent visual loss.

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Plain Language Summary

Neuroretinitis is an uncommon eye condition that causes swelling of the optic nerve and leakage of fluid into the retina, leading to blurred vision. It is often caused by infections, and early diagnosis and treatment are important to prevent permanent vision loss. In this report, we describe a rare case of syphilitic neuroretinitis in a 17-year-old girl who also had positive blood tests for cytomegalovirus (CMV). Although CMV antibodies were detected, active CMV infection of the eye could not be confirmed. Syphilis is a bacterial infection that can affect many parts of the body, including the eyes, while CMV is a common virus that usually causes serious eye disease only in people with weakened immune systems. The patient developed blurred vision, headache, and characteristic changes affecting the optic nerve and retina. Blood tests confirmed syphilis and showed positive CMV antibodies. She was treated with antibiotics for ocular syphilis and received antiviral medication because CMV eye involvement was initially considered during the diagnostic evaluation. After treatment, her vision returned to normal, and the eye abnormalities resolved completely. This case highlights the importance of a thorough infectious evaluation in patients with neuroretinitis, even if they are otherwise healthy. Positive CMV blood tests should be interpreted cautiously as they do not by themselves confirm CMV eye disease. Early diagnosis and appropriate treatment are essential to achieve complete recovery and prevent permanent vision loss.

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Introduction

Neuroretinitis is a subtype of inflammatory optic neuropathy characterized by optic disc edema followed by the development of a macular star pattern due to lipid exudation along the outer plexiform layer [1]. It represents a distinct clinical entity that must be differentiated from other causes of optic disc swelling such as papilledema, optic neuritis, and ischemic optic neuropathy. The pathophysiology involves inflammation of the optic nerve head and peripapillary retina leading to vascular leakage and exudate deposition [2].

The most common infectious cause of neuroretinitis is *Bartonella henselae*, responsible for cat-scratch disease [3]. However, several other infectious agents including *Treponema pallidum*, cytomegalovirus, tuberculosis, toxoplasmosis, and viral infections have also been implicated [4]. Syphilis has re-emerged globally as an important infectious disease, with increasing incidence over the past decade [5]. Ocular involvement may occur at any stage and can present with diverse manifestations including uveitis, retinitis, optic neuritis, and neuroretinitis [6]. Cytomegalovirus infection is classically associated with immunocompromised individuals, particularly patients with HIV/AIDS, transplant recipients, or those receiving immunosuppressive therapy [7]. However, CMV ocular involvement has been increasingly reported in immunocompetent individuals, although it remains rare [7]. Syphilitic neuroretinitis is an uncommon manifestation of ocular syphilis, and positive CMV serology may further complicate the diagnostic evaluation in immunocompetent patients. We report a rare case of syphilitic neuroretinitis with positive CMV serology in an immunocompetent adolescent, highlighting diagnostic challenges and emphasizing the importance of early recognition and treatment.

This case report was prepared in accordance with the CARE (Case Report) guidelines. The completed CARE checklist is provided as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000553652).

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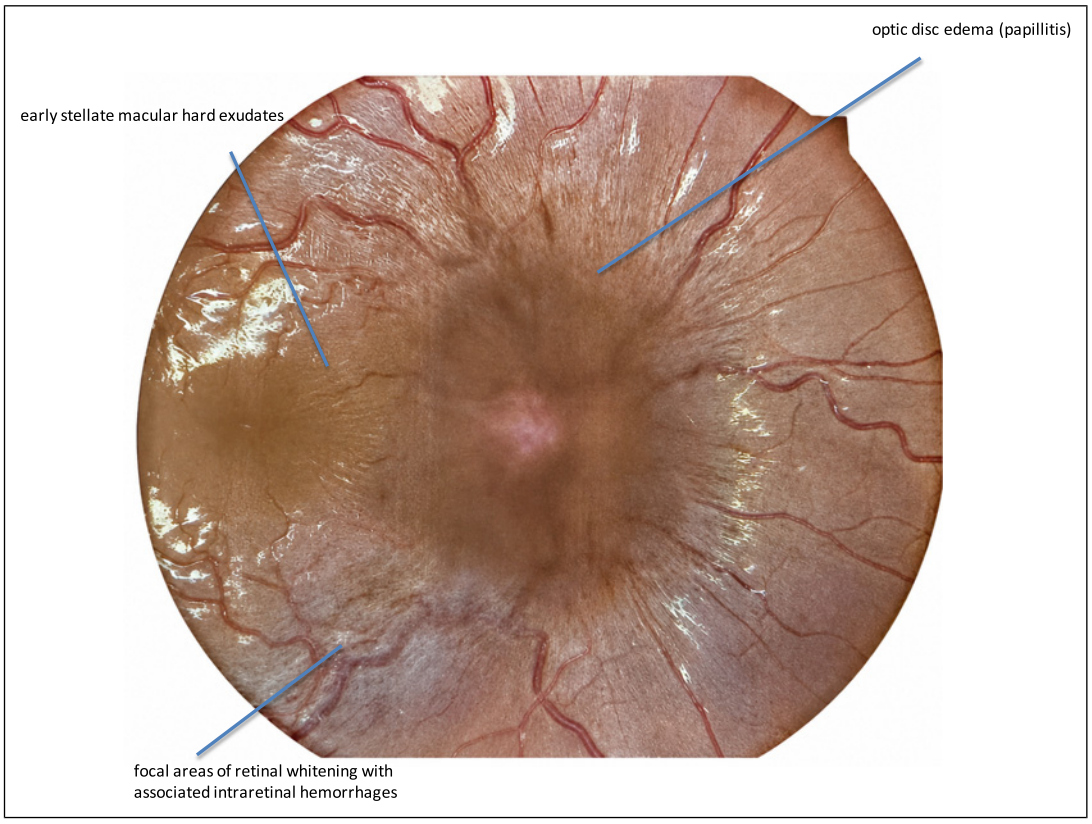


Fig. 1. Color fundus photograph of the right eye at presentation demonstrating marked optic disc edema (papillitis), early stellate macular hard exudates, peripapillary hemorrhages, and focal retinal whitening with associated intraretinal hemorrhages (arrows) along the inferotemporal arcade, consistent with neuroretinitis.

Case Presentation

A 17-year-old girl presented with episodic dizziness for 2 weeks, followed by blurred vision in the right eye and persistent headache for 2 days. Her social history was notable for substance use and multiple unprotected sexual encounters. There was no history of chronic illness or immunosuppression. The associated dizziness raised concern for possible neurological involvement in addition to the ocular manifestations.

On examination, best-corrected visual acuity was 20/30 in the right eye and 20/20 in the left eye. Color vision and contrast sensitivity were normal bilaterally. Intraocular pressure was 18 mm Hg in both eyes, with no relative afferent pupillary defect. Extraocular movements were full. Anterior segment examination was unremarkable. Fundus examination of the right eye revealed marked optic disc edema (papillitis) with early stellate macular hard exudates, peripapillary hemorrhages, and small focal areas of retinal whitening with associated intraretinal hemorrhages along the inferotemporal vessels, suggestive of overlapping neuroretinitis and necrotizing retinitis features (shown in Fig. 1). Optical coherence tomography showed right optic nerve head swelling with preserved foveal architecture (Fig. 2) and visual field analysis showed enlarged blind spot (Fig. 3). The left fundus was normal. Dermatologic examination demonstrated multiple nonpruritic, scaly, reddish-brown macules over the trunk and extremities, including the palms and soles, consistent with secondary syphilis. A detailed neurological examination revealed intact

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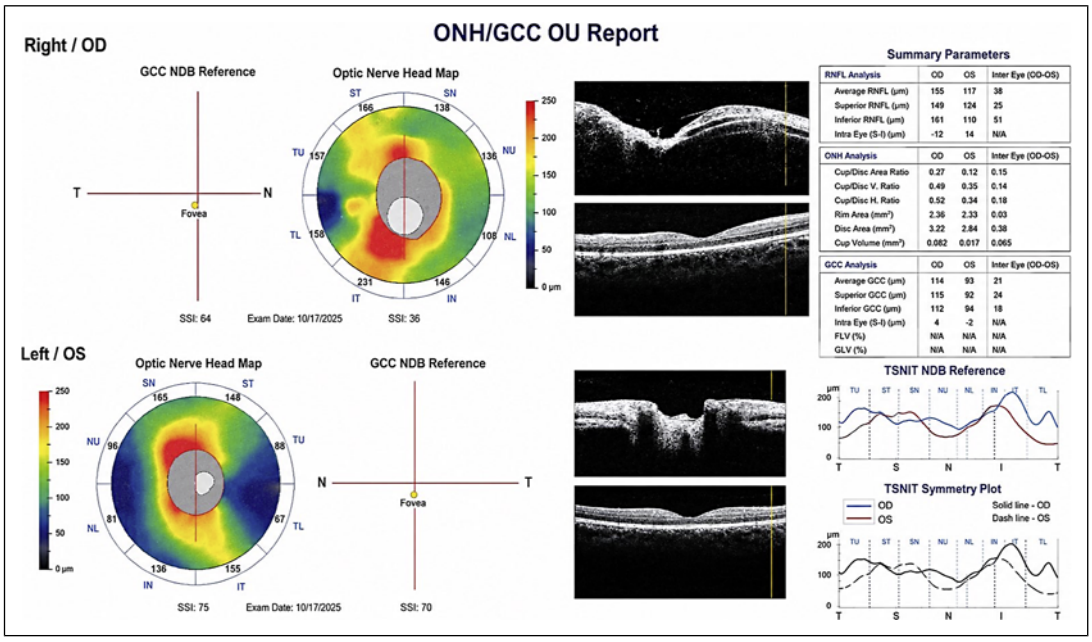


Fig. 2. Optical coherence tomography of both eyes demonstrating marked retinal nerve fiber layer thickening and optic nerve head elevation in the right eye, consistent with inflammatory optic disc edema. The left eye demonstrated normal OCT findings.

cranial nerves, normal motor strength and sensory function in all limbs, symmetrical deep tendon reflexes, normal coordination, and no signs of meningeal irritation. There were no focal neurological deficits. Laboratory investigations showed reactive syphilis serology with a Venereal Disease Research Laboratory (VDRL) titer of 1:64, confirmed by a positive *Treponema pallidum* hemagglutination assay. Cerebrospinal fluid analysis demonstrated reactive *Treponema pallidum* hemagglutination assay (titer 1:16), nonreactive VDRL, and elevated protein levels (150 mg/dL). In conjunction with the normal neurological examination, these findings supported a diagnosis of ocular syphilis treated according to the neurosyphilis regimen, while possible neurological involvement could not be excluded. Serologic testing revealed positive CMV IgM and IgG antibodies. HIV testing was negative, and the CD4 count was within the normal range, with no evidence of significant immunodeficiency. Magnetic resonance imaging of the brain showed no intracranial pathology. Tuberculosis was also considered given its regional prevalence; however, the patient had no constitutional symptoms, and bacteriological investigations were negative. TORCH screening was performed to exclude toxoplasmosis, rubella, and herpes simplex virus infection. *Bartonella* serology was unavailable at our center. Baseline hematological parameters and renal function tests were within normal limits, and urine pregnancy testing was negative prior to initiation of antiviral therapy.

Due to unavailability of aqueous crystalline penicillin G, the patient was treated with intravenous ceftriaxone 2 g daily for 14 days for ocular syphilis. Given the positive CMV serology and the presence of retinal findings raising concern for possible CMV ocular involvement, empiric antiviral therapy was initiated while awaiting clinical response; the patient was treated with intravenous ganciclovir 250 mg twice daily for 14 days, followed by oral valganciclovir 900 mg twice daily for an additional 14 days. The patient weighed approximately 45 kg. Because CMV ocular disease could not be confirmed, antiviral therapy was administered empirically using a lower-intensity regimen based on local clinical practice and

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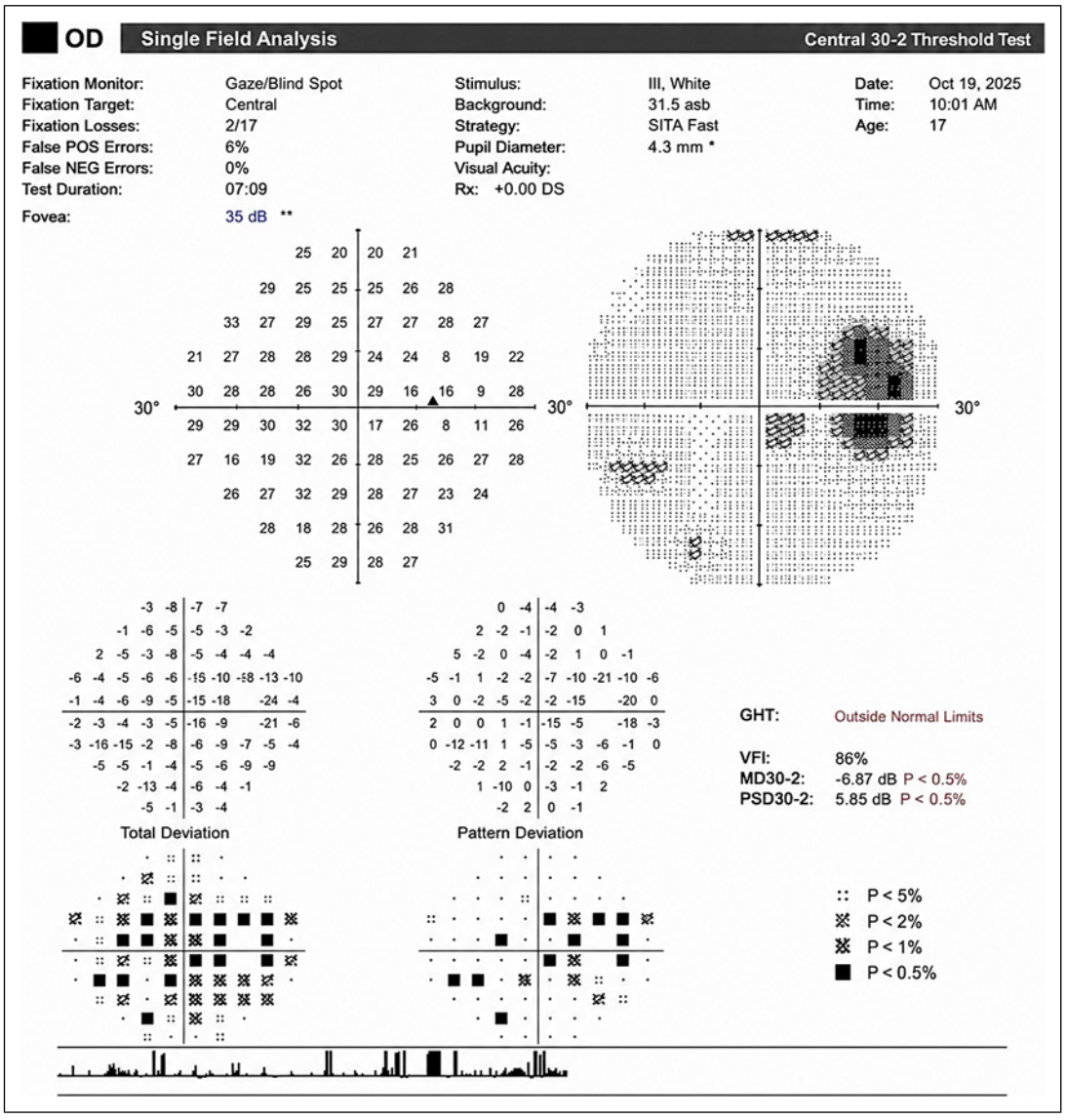


Fig. 3. Humphrey visual field (30-2) of the right eye demonstrating localized visual field defects with generalized depression consistent with optic nerve dysfunction.

body weight. Treatment adherence was assessed during hospitalization and follow-up visits, and the patient completed the prescribed antimicrobial and antiviral therapy without interruption. The medications were well tolerated, with no significant adverse effects observed. At the 1-month follow-up, the patient's best-corrected visual acuity had improved to 20/20 in both eyes. Fundus examination demonstrated complete resolution of optic disc edema, macular star, retinal whitening, and retinal hemorrhages (Fig. 4). At the 6-month follow-up, which was approximately 5 months after completion of valganciclovir therapy, the patient maintained a best-corrected visual acuity of 20/20 in both eyes. Serial VDRL titers continued to decline, consistent with an appropriate serologic response to treatment. Fundus examination was unremarkable, and OCT demonstrated complete resolution of the previously observed retinal and optic nerve changes (Fig. 5). Visual field testing showed no clinically significant defects despite low reliability indices (Fig. 6). These findings, together with the normal clinical examination, indicated complete structural and functional recovery.

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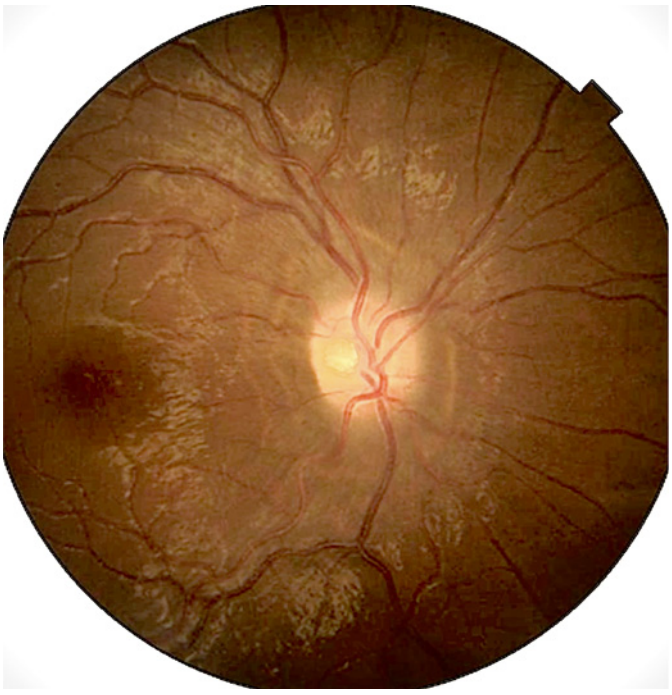


Fig. 4. Follow-up color fundus photograph of the right eye performed at 6 months demonstrating complete resolution of optic disc edema, macular hard exudates, retinal whitening, and retinal hemorrhages following treatment.

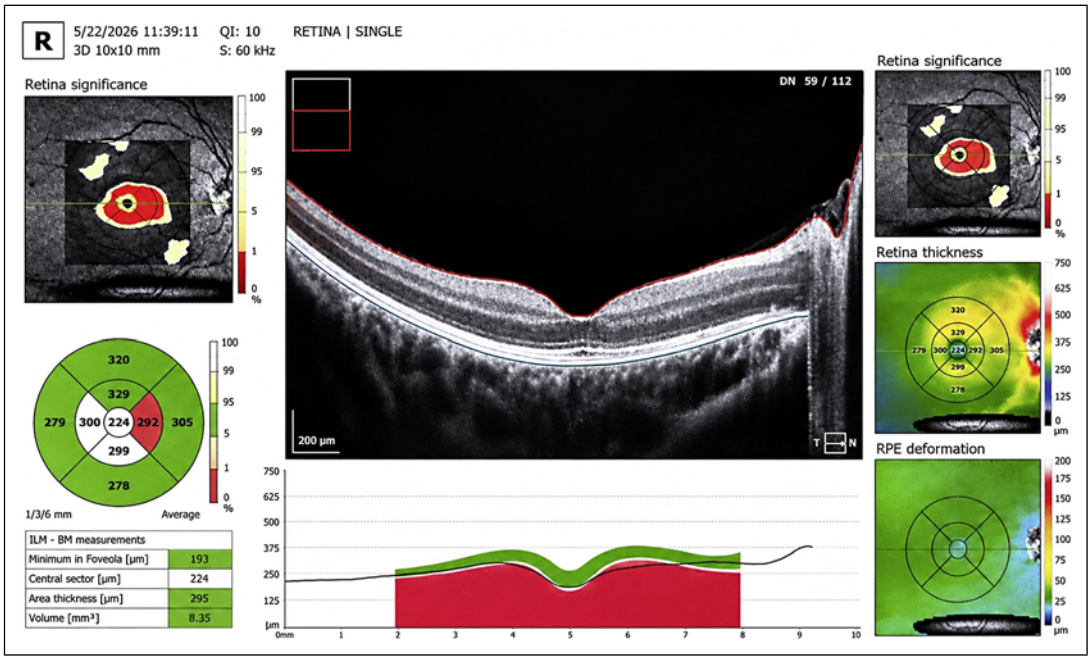


Fig. 5. A follow-up optical coherence tomography scan of the right macula was performed at 6 months, showing a normal foveal contour and well-defined retinal layers. No retinal swelling or fluid was visible.

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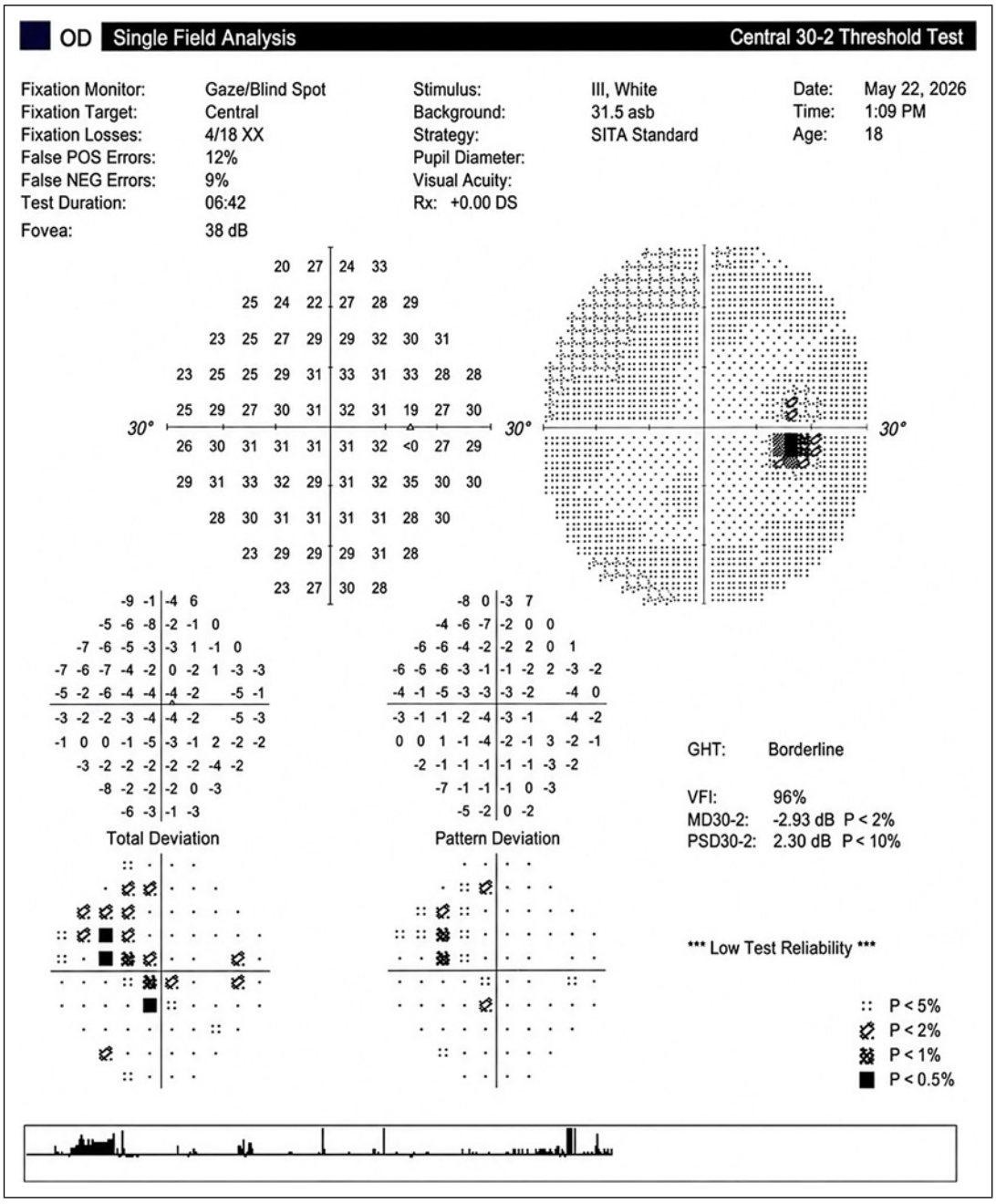


Fig. 6. A follow-up Humphrey visual field (30-2) of the right eye was performed at 6 months. No clinically significant visual field defects were identified; however, interpretation was limited by the low reliability of the examination.

Discussion

Neuroretinitis is a distinct subtype of optic neuropathy characterized by optic disc edema followed by delayed development of macular star exudates resulting from leakage of lipoproteinaceous fluid from inflamed peripapillary capillaries [1]. The macular star typically appears 1 to 2 weeks after the onset of optic disc edema and is considered a hallmark feature of neuroretinitis [2]. Although the condition is often self-limited, identifying the

underlying etiology is critical as infectious causes require prompt treatment to prevent permanent visual loss.

The most common infectious cause of neuroretinitis is *Bartonella henselae*, accounting for the majority of cases associated with cat-scratch disease [3]. However, other infectious etiologies including syphilis, tuberculosis, toxoplasmosis, viral infections, and Lyme disease have also been reported [4]. Syphilis remains an important cause due to its resurgence globally, particularly among young adults. *Treponema pallidum* can affect any ocular structure, including the optic nerve, retina, and choroid, leading to diverse clinical presentations such as optic neuritis, uveitis, and neuroretinitis [6, 8]. Ocular syphilis may occur during any stage of systemic infection and may be the first presenting manifestation, emphasizing the importance of serologic testing in unexplained optic neuropathies [6].

Cytomegalovirus infection is classically associated with immunocompromised patients, particularly those with HIV infection, organ transplantation, or systemic immunosuppression [7]. CMV retinitis typically presents with necrotizing retinitis and hemorrhage in these populations. However, CMV-associated ocular disease has increasingly been reported in immunocompetent individuals, although its pathogenesis remains incompletely understood [7]. Possible mechanisms include transient immune dysfunction, high viral load, or localized viral reactivation. In immunocompetent patients, CMV ocular involvement tends to be less aggressive but may still result in significant visual impairment if untreated.

Syphilis was considered the most likely cause of neuroretinitis in this patient. Positive CMV serology complicated the diagnostic evaluation but did not establish active CMV ocular disease.Intraocular PCR was not performed; therefore, active CMV ocular disease could not be confirmed. The patient's favorable clinical outcome may be attributable to treatment of ocular syphilis, and the contribution of empiric antiviral therapy remains uncertain.

Another important consideration in this case is the systemic manifestation of secondary syphilis, including dermatologic findings, which provided a critical diagnostic clue. Multidisciplinary evaluation involving dermatology and internal medicine was essential for comprehensive management. This highlights the importance of systemic evaluation in patients presenting with neuroretinitis, particularly when infectious causes are suspected.

Early recognition and prompt initiation of appropriate therapy are essential to prevent permanent visual damage. Treatment of ocular syphilis in patients with secondary syphilis requires intravenous antibiotics such as penicillin or ceftriaxone, while CMV infection is treated with antiviral agents including intravenous ganciclovir followed by oral valganciclovir [7]. Timely treatment in this case resulted in complete anatomical resolution and full visual recovery, emphasizing the importance of early diagnosis and intervention.

This case underscores the need for comprehensive infectious evaluation in neuroretinitis. Positive CMV serology should be interpreted cautiously in immunocompetent patients, and the diagnosis of CMV ocular disease should ideally be supported by intraocular PCR or other confirmatory evidence whenever feasible.

Limitations

This report has several limitations. First, the possibility of CMV ocular involvement was considered based on serologic findings and clinical features; however, active CMV ocular disease could not be confirmed because intraocular PCR testing was unavailable. Second, this is a single case report, limiting the generalizability of the findings. Third, the relative contribution of CMV versus syphilis to the neuroretinitis cannot be definitively determined. Further studies are needed to better define the role of CMV in immunocompetent patients with neuroretinitis.

Conclusion

Syphilis should be considered an important cause of neuroretinitis, even in young immunocompetent patients with relevant risk factors. Positive CMV serology may complicate the diagnostic evaluation but should not be interpreted as evidence of active CMV ocular disease without confirmatory testing. Comprehensive infectious evaluation and prompt treatment are essential to prevent permanent visual loss.

The patient and her guardian expressed satisfaction with the treatment outcome, particularly the improvement in vision and the resolution of headache and dizziness following therapy. They also reported good medication tolerability and consistent adherence to follow-up visits.

Statement of Ethics

Written informed consent was obtained from the patient and her legal guardian for publication of this case report and accompanying images. Ethical approval was not required for this study in accordance with institutional policies as this is a single case report and does not involve experimental intervention. All procedures were performed in accordance with the ethical standards of the institutional research committee and with the principles of the Declaration of Helsinki.

Conflict of Interest Statement

The authors declare no conflict of interest.

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Author Contributions

Sundip Dware Chhetri: supervision, interpretation of clinical findings, manuscript drafting, critical revision, manuscript review, and final approval of the manuscript. Meena Kunwar: supervision, manuscript drafting, critical revision, and final approval of the manuscript. Ram Krishna Baral: interpretation of clinical findings, manuscript review, and final approval of the manuscript. Alina Karki and Mohini Thapa: manuscript drafting and final approval of the manuscript. Sabina Maharjan: manuscript review and final approval of the manuscript. Basanta Kumar Bastola: image analysis, manuscript revision, and final approval of the manuscript. Bibek Pun: manuscript revision and final approval of the manuscript. Sudeep Lal Rajbhandari: supervision, critical manuscript revision, and final approval of the manuscript.

Data Availability Statement

All data are included in this article. Further inquiries can be directed to the corresponding author.

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