

# A silent impostor: Neurosyphilis mimicking incomplete oculomotor nerve palsy

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## SUMMARY

Acquired isolated oculomotor nerve palsy (ONP) is a commonly encountered clinical entity in ophthalmology. While most cases are due to microvascular ischemia, the diagnosis of ONP requires careful evaluation for alternate life-threatening etiologies. We share our experience in diagnosing and managing a case of neurosyphilis presenting as unilateral oculomotor nerve palsy with bilateral pupil involvement (Light-Near dissociation) in a healthy 44-year-old man in whom aneurysmal compression was initially suspected. Investigations later revealed the diagnosis of neurosyphilis. Neurosyphilis is an extremely rare cause of isolated ONP and seldom reported in the literature. Timely recognition of this disease by ophthalmologists can help orient patients to the appropriate neurology and infectious disease services.

## INTRODUCTION

Neurosyphilis, a rare complication of *Treponema pallidum* infection, can affect the central nervous system in various ways. While it typically manifests as cognitive decline, meningovascular disease, or tabes dorsalis, isolated third cranial nerve palsy (ONP) is an uncommon presentation that can be mistaken for more prevalent conditions like aneurysmal compression or microvascular ischemia.

Risk factors for neurosyphilis include untreated syphilis, Human Immunodeficiency Virus (HIV) infection, immunosuppression, and high-risk sexual behaviour. Although it is more frequently observed in HIV-positive individuals, its occurrence in immunocompetent patients highlights the importance of considering it in differential diagnoses. The increasing prevalence of syphilis worldwide necessitates awareness of its diverse clinical features.

This case report aims to emphasize the diagnostic challenges associated with neurosyphilis presenting as isolated ONP with bilateral pupil involvement in an HIV- negative patient. Such a presentation is rarely documented, making early recognition and appropriate investigation critical for timely intervention.

What distinguishes this case is the bilateral pupil involvement, a feature seldom reported in neurosyphilis-associated ONP. Additionally, the patient was

immunocompetent and had no significant comorbidities, reinforcing the need to consider neurosyphilis in patients with unexplained cranial neuropathies. Early serological and CSF testing can facilitate prompt diagnosis and treatment, improving patient outcomes.

## CASE PRESENTATION

A 44-year-old healthy male visited the clinic reporting a sudden drooping of the left eyelid accompanied by blurred vision of three days duration. He had no additional neurological symptoms, and his review of neurological systems was normal. He is allergic to paracetamol and otherwise has no notable past medical history, does not smoke, and has not used any prior medications. Both his ocular and family histories were unremarkable. He had history of multiple unprotected sexual encounters with multiple partners many years ago. However, he denied any history of blood transfusions or intravenous drug use.

During the examination, he exhibited exotropia, significant hypotropia, and pronounced deficits in elevation, adduction, and depression of the left eye. These findings were consistent with the Hess chart results (Figure 1 and Figure 2). There was partial blepharoptosis. His uncorrected visual acuity was 6/9 in the right eye and 6/18 in the left. Anisocoria was noted, with the right pupil measuring 5 mm and the left 7 mm, both showing poor reactivity to bright light. Pupil evaluation indicated light-near dissociation. Nuclear cataracts are noted in both eyes, predominantly affecting the left eye. Otherwise, the fundoscopic examination was unremarkable bilaterally.

Based on the patient's clinical symptoms, aneurysmal compression was initially suspected, prompting an urgent computed tomography angiography (CTA) of the brain. However, the results were unremarkable. Blood tests revealed a positive Syphilis Rapid Plasma Reagin (RPR) with a titre of 1:64, while testing for human immunodeficiency virus (HIV) was negative.

The patient was referred to the neurology team, where a lumbar puncture was performed. Cerebrospinal fluid (CSF) analysis confirmed a positive Venereal Disease Research Laboratory (VDRL) test with a titre of 1:1. Magnetic Resonance Imaging (MRI) showed no focal enhancing brain parenchymal lesions or abnormal leptomeningeal

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**Table I: Summary of selected cases of neurosyphilis presenting as oculomotor nerve palsy, supported by magnetic resonance imaging (MRI) findings**

Author	Year	Age	Sex	HIV	Palsy	Pupil Involving	Pupil Involving	Clinical Outcomes
Vogt et al <sup>7</sup>	1993	44	F	-	Incomplete	Yes	Hyperintense lesion in the region of the exit of CN III from the brain stem in T2 (enhancing)	Resolved
Seeley et al <sup>2</sup>	2004	54	M	-	Complete	Yes	Isointense lesion at the base of the midbrain tracing the course of CN III into the cavernous sinus in T1 and T2 (enhancing)	Partially resolved
Corr et al <sup>5</sup>	2004	22	F	+	Complete OD Incomplete OS	Yes (OU)	Marked thickening of both CN III in T2 (enhancing)	Resolved
Hess et al <sup>4</sup>	2013	39	M	+	Complete	Yes	Hyperintense enlargement of CN III in the interpeduncular cistern in T2-FLAIR (enhancing)	Partially resolved
Sung Mo Kang et al <sup>3</sup>	2015	43	M	-	Complete	Yes	Diffuse thickening of CN III in T2 (enhancing)	Partially resolved
Silva et al <sup>6</sup>	2018	29	M	+	Complete	Yes	Diffuse thickening of the cisternal portion of CN III in T2 (enhancing)	Partially resolved
Antaki et al <sup>1</sup>	2020	47	M	-	Complete	Yes	Enlargement of CN III in the interpeduncular and suprasellar cisterns in T2 (enhancing)	Symptomatic improvement
Redzuan et al	2025	44	M	-	Incomplete	Yes	No focal enhancing brain parenchymal lesion or abnormal leptomeningeal enhancement	Partially resolved

Abbreviations: HIV = human immunodeficiency virus; MRI = magnetic resonance imaging; F = female; M = male; Oculomotor nerve = third cranial nerve or CN III; T1 = T1-weighted images; T2 = T2-weighted images; FLAIR = Fluid-attenuated inversion recovery sequence; OD = right eye; OS = left eye; OU = both eyes. Enhancement refers to postgadolinium enhancement in T1-weighted images.

enhancement. A diagnosis of neurosyphilis was established, and treatment was initiated with intravenous penicillin G (4 million units every 4 hours) for two weeks, followed by intramuscular benzathine penicillin (2.4 million units weekly) for three doses.

At the two-month follow-up, the patient's condition showed gradual improvement, though mild blepharoptosis persisted. Eye movement had significantly improved, with only minimal residual deficits in elevation, adduction, and depression. (Figure 3).

## DISCUSSION

In clinical practice, an isolated oculomotor nerve palsy often prompts an evaluation for aneurysmal compression, especially involving the posterior communicating artery. As seen in Antaki et al. and our case, urgent computed tomography angiography (CTA) was performed in such cases but did not reveal any vascular abnormalities.<sup>1</sup> This highlights the limitations of neuroimaging alone in diagnosing neurosyphilis.

Given its ability to mimic other neurological conditions, serological testing for syphilis is crucial when the cause of cranial nerve palsy remains unclear. There have been reported cases where the Rapid Plasma Reagin (RPR) or Venereal Disease Research 1–3 Laboratory (VDRL) tests played a pivotal role in identifying neurosyphilis.<sup>4,5</sup> Furthermore, cerebrospinal fluid (CSF) analysis is essential to confirm active neurosyphilis, particularly in cases where MRI findings are inconclusive.

Neurosyphilis is more frequently reported in HIV-positive individuals likely due to impaired immune response.<sup>4,6</sup> The interplay between HIV and neurosyphilis may contribute to a more aggressive or atypical presentation. However, cases in HIV-negative individuals suggest that neurosyphilis should not be overlooked in immunocompetent patients, as demonstrated in our case.<sup>1,3</sup>

Most reported cases had pupil involvement, reinforcing the classical feature of a “syphilitic pupil”.<sup>4,6,7</sup> However, Sung Mo Kang et al. documented a case of third nerve palsy with bilateral pupil involvement with light near dissociation, which is similar in our case, demonstrating variability in presentation.<sup>3</sup>

Standard treatment with intravenous penicillin G followed by intramuscular benzathine penicillin remains effective.<sup>1,4,6</sup> Improvement is often seen within weeks to months, but some patients have residual deficits, such as persistent mild ptosis or ocular movement limitations.<sup>1,3</sup> The prognosis depends on early diagnosis and treatment initiation; delayed treatment may lead to permanent deficits.

From a public health standpoint, the increasing incidence of syphilis globally including among heterosexual, HIV-negative men highlights the need to broaden screening criteria beyond traditionally defined high-risk groups. Awareness of neurosyphilis as a potential, albeit rare, cause of cranial neuropathies should be heightened among all clinicians, not only those in infectious disease specialties.



Fig. 1: 9 gaze photographs showing left third nerve palsy with ptosis, exotropia, hypotropia, and limitation of adduction, elevation, and depression. (Photo consented by patient).

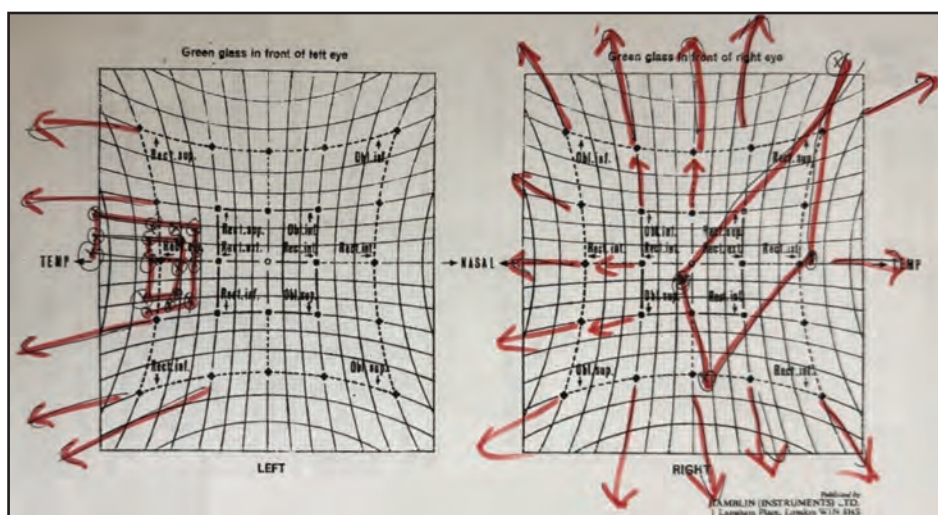


Fig. 2: Hess chart shows marked limitation of left eye adduction, elevation, and depression with compensatory overaction in the right eye, consistent with left third nerve palsy



Fig. 3: 9 gaze photographs showed marked improvement post treatment in ptosis, ocular motility and alignment. (Photo consented by patient)

## CONCLUSIONS

Isolated third cranial nerve palsy caused by neurosyphilis is a rare but important clinical entity that can easily elude diagnosis due to its variable imaging findings and its ability to mimic other neurological conditions, living up to its reputation as the 'great impostor'. This case illustrates that even in immunocompetent, otherwise healthy individuals, neurosyphilis can present with pupil-involving cranial neuropathies that mimic more common aetiologies such as aneurysmal compression or microvascular ischemia.

A high index of suspicion, guided by a careful history including sexual exposure and subtle clinical signs such as light-near dissociation, is crucial. Routine inclusion of syphilis serology in the diagnostic workup for unexplained ONP may prevent misdiagnosis and facilitate early intervention.

Timely cerebrospinal fluid (CSF) analysis and initiation of standard penicillin therapy can lead to substantial clinical recovery, although some residual deficits may persist. This reinforces the importance of early recognition and multidisciplinary management.

Given the ongoing resurgence of syphilis worldwide, healthcare providers across all disciplines should maintain vigilance for its atypical presentations. Future clinical guidelines may benefit from incorporating syphilis testing as a routine component in the evaluation of cranial nerve palsies. Additional research into the clinical and radiological spectrum of neurosyphilis in HIV-negative populations is warranted to better understand its manifestations and optimize outcomes.

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