Isolated Oculomotor Nerve Palsy as the Initial Manifestation of CNS Tuberculoma in an HIV-Positive Adult: A Case Report

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ABSTRACT

Objective: To describe the clinical presentation, management and outcome of a rare case of isolated oculomotor nerve palsy in an immunocompromised adult secondary to a central nervous system (CNS) tuberculoma.

Methods: This is a case report.

Results: A Filipino male in his 30s developed severe throbbing headache followed by binocular diplopia and drooping of the right upper eyelid. Findings were compatible with a neurologically-isolated pupil-involving, complete oculomotor nerve palsy on the right. Brain magnetic resonance imaging demonstrated enlargement and contrast enhancement of the cisternal portion of the right oculomotor nerve. Serologic testing was positive for the human immunodeficiency virus (HIV) and syphilis. Cerebrospinal fluid (CSF) analysis showed lymphocytic pleocytosis and elevated protein. CSF polymerase chain reaction was positive for *Mycobacterium tuberculosis* (TB). The patient was treated with penicillin, quadruple anti-Koch's, and anti-retrovirals. Eyelid position and ocular motility improved after treatment. Aberrant regeneration of the right oculomotor nerve was observed with elevation of the right eyelid on downgaze (pseudo-Graefe sign).

Conclusion: CNS tuberculoma may present as a neurologically-isolated oculomotor nerve palsy, particularly in immunocompromised individuals. In TB-endemic countries, like the Philippines, it should be considered in the differential diagnosis. Early recognition and appropriate antimicrobial therapy can lead to neurologic improvement.

Keywords: Oculomotor nerve palsy, tuberculoma, aberrant regeneration of third nerve, HIV, syphilis, diplopia

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The oculomotor nerve, also known as the third cranial nerve, originates from the midbrain and traverses the subarachnoid space and cavernous sinus before entering the orbit. It innervates the levator palpebrae superioris; the superior, inferior and medial rectus muscles; the inferior oblique muscle; and the pupillary sphincter. Disruption along its course can variably result to ptosis, impaired adduction, elevation and depression, and a mid-dilated pupil. The diagnostic evaluation of the oculomotor nerve palsy often includes neuroimaging, either magnetic resonance imaging (MRI) or computed tomography (CT) of the brain. When clinically indicated, brain angiography may be performed to exclude intracranial aneurysms compressing the nerve.

In this report, we describe a patient with neurologically-isolated, complete, pupil-involving oculomotor nerve palsy in whom subtle but clinically significant abnormalities were detected on MRI — findings that could have been easily overlooked. Diagnostic evaluation revealed multiple infections, including human immunodeficiency virus, *Mycobacterium tuberculosis* (TB) and syphilis, with TB determined to be the most likely, albeit rarely reported, cause of ophthalmologic manifestations.

CASE PRESENTATION

A Filipino male in his 30s experienced a severe throbbing headache followed by binocular diplopia and drooping of the right upper eyelid. He consulted a physician, who requested contrast MRI and MR angiography of the brain, which did not disclose any acute bleed, aneurysm, meningeal enhancement or parenchymal abnormalities on T2-weighted fluid-attenuated inversion recovery (FLAIR) sequences. Recent blood test revealed elevated fasting blood sugar. He was subsequently prescribed a tapering dose of prednisone, starting at 40 mg daily which he took for 3 months, and metformin with no improvement in the external ophthalmoplegia.

The patient reported no history of substance use or high-risk sexual behavior. He had no systemic symptoms.

Neuro-ophthalmologic examination revealed best-corrected visual acuity of 20/20 in each eye. He had a near-complete ptosis of the right upper lid and absent depression, elevation, and adduction of the right eye (**Figure 1**). Abduction and intorsion were intact. Alternate prism cover testing revealed exotropia of the right eye measuring 30 prism diopters on primary gaze. The right pupil was fixed at 5 mm to both light and near stimuli. The left eye exhibited full ocular motility, normal lid position, and a pupil that briskly constricted to light. The anterior and posterior segments of both eyes were normal. The rest of the cranial nerve and neurologic examinations were unremarkable. The examination findings were consistent with a neurologically-isolated, right, complete, pupil-involving oculomotor nerve palsy.

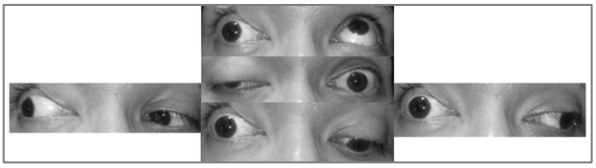

Figure 1. On initial presentation, the patient had near complete ptosis on the right, with the right eye in down-and-out position. Ocular motility exam showed absent adduction, elevation and depression of the right eye. Findings are consistent with a complete oculomotor nerve palsy.

Review of the MR images showed an enlarged and enhancing cisternal portion of the right oculomotor nerve on post-contrast T1-weighted images (**Figure 2**). Further laboratory examination revealed positive serologies for the human immunodeficiency virus (HIV) and syphilis (reactive rapid plasma reagin [RPR] and *Treponema pallidum* particle agglutination assay [TPHA] at 1:8 and 1:180 dilution, respectively). The CD4 cell count was low at 301 cells/ml. Chest X-ray was normal. Lumbar tap and analysis of the cerebrospinal fluid (CSF) showed lymphocytic pleocytosis, elevated protein, and non-reactive CSF RPR. Polymerase chain reaction (PCR) for TB of the CSF came out positive.

He commenced a treatment regimen that included quadruple anti-Koch's, intravenous penicillin for 5 days, and antiretrovirals. Four months later, on follow-up examination, there was improvement of lid position and ocular motility of the right eye. Aberrant regeneration of the right oculomotor nerve was observed, with elevation of the right eyelid on downgaze (pseudo-Graefe sign) (**Figure 3**).

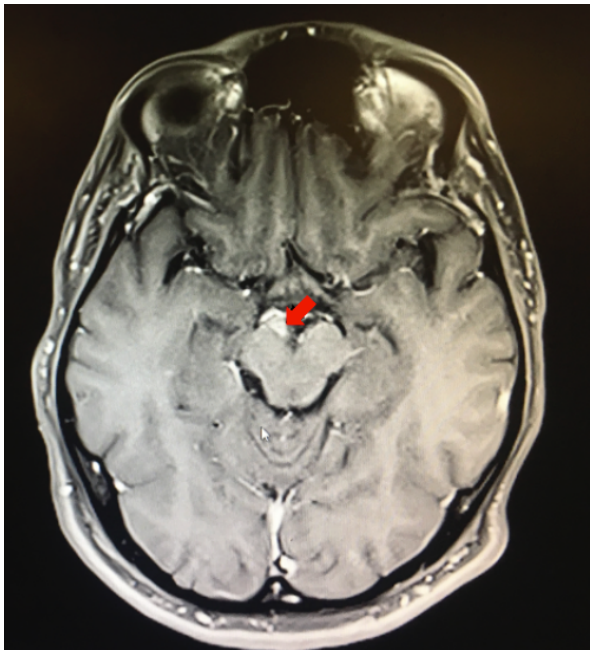

Figure 2. Post-contrast axial T1-weighted MRI shows an enlarged and homogenously enhancing cisternal segment of the right oculomotor nerve (red arrow), indicative of an inflammatory or granulomatous lesion from a presumed noncaseating granuloma.

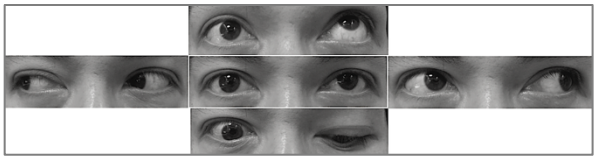

Figure 3. Four months after commencement of treatment, repeat eye exam showed resolution of ptosis, improvement of ocular motility, and development of pseudo-Graefe sign, characterized by lid elevation on downgaze due to aberrant regeneration of the right oculomotor nerve.

DISCUSSION

We report a case of a young adult who developed a neurologically-isolated, unilateral, pupil-involving, complete oculomotor nerve palsy. Brain imaging showed enlargement and contrast-enhancement of the cisternal portion of the ipsilateral oculomotor nerve.

Differential diagnoses for oculomotor nerve palsy with enhancement of the cisternal portion of the nerve on MRI include lymphoma, leukemia, neurofibromatosis, viral meningitis, HIV, coccidioidomycosis, ophthalmoplegic migraine, Tolosa-Hunt syndrome, and diabetes.[1] All these, except for diabetes which has a presumed microvascular mechanism, can potentially cause a pupil-involving oculomotor nerve palsy due to their inflammatory or infiltrative nature. Notably, clinical entities such as ophthalmoplegic migraine and Tolosa-Hunt syndrome are diagnoses of exclusion and should only be considered after more serious causes, such as infection and malignancy, have been ruled out.

Ophthalmoplegic migraine, now termed recurrent painful ophthalmoplegic neuropathy (RPON), is characterized by recurrent episodes of ophthalmoplegia accompanied by ipsilateral headache.[2] It most commonly presents as an oculomotor nerve palsy and may demonstrate focal thickening and enhancement of the cisternal segment of the oculomotor nerve on neuroimaging. CSF analysis may variably show inflammatory changes but should not reveal any evidence of malignancy, infection or thrombosis. Although our patient had oculomotor nerve palsy and headache, RPON was considered less likely because this was the first occurrence of symptoms, and there was central nervous system (CNS) infection.

Tolosa-Hunt syndrome is a rare inflammatory disorder characterized by painful ophthalmoplegia resulting from granulomatous inflammation in the cavernous sinus, superior orbital fissure or orbital apex, in the absence of identifiable infectious or systemic inflammatory etiology.[3] This diagnosis was ruled out in our case due to the isolated involvement of the oculomotor nerve, radiologic and CSF findings, and lack of response to corticosteroid therapy.

Gummatous neurosyphilis has been reported to cause isolated oculomotor nerve palsy with enhancement of the cisternal segment of the oculomotor nerve on imaging.[4-7] In such cases, diagnosis was confirmed by positive CSF syphilis serology, including Venereal Disease Research Laboratory (VDRL) or RPR. [4-7] In the present case, neurosyphilis was initially considered due to positive serologic results; however, the negative CSF RPR and positive CSF TB PCR findings led to the oculomotor nerve palsy being attributed to TB rather than syphilis.

Finally, HIV-related CNS lymphoma should also be considered, as cranial neuropathy, including isolated oculomotor nerve palsy, may represent an early manifestation.[8,9] This diagnosis can be

challenging due to the potential of normal neuroimaging and CSF studies in early disease. However, in this case, HIV-related CNS lymphoma was deemed less likely given the CSF findings suggestive of TB infection and the clinical improvement following initiation of anti-TB therapy.

TB, another common opportunistic infection among HIV-positive individuals, has rarely been reported to cause isolated oculomotor nerve palsy.[10,11] In this population, tuberculous CNS disease most often presents as meningitis, tuberculomas or spinal cord infections.[12] Tuberculomas are inflammatory mass lesions that have variable appearances on MRI. Noncaseating granulomas appear hypointense on T1-weighted MR images and homogenously enhance after gadolinium administration, while caseating granulomas have hypointense centers and rim enhancements.[13,14]

Tuberculomas are mostly located in the cerebral hemispheres and commonly present with neurologic deficits, seizures and altered mental status.[12,15] Published reports of isolated oculomotor nerve palsy from CNS tuberculoma have identified lesions primarily located in the midbrain, typically appearing as ring-enhancing lesions on brain imaging.[10,11] Tuberculomas located in the cavernous sinus may also result in combined ocular motor palsies, including concurrent oculomotor and abducens nerve involvement.[15]

In this report, we describe a presumed noncaseating tuberculoma, based on its radiologic appearance, involving the cisternal segment of the oculomotor nerve, as seen on MRI. The diagnosis was supported by a positive MTB PCR in the CSF, along with inflammatory CSF changes and clinical improvement following anti-TB therapy.

Aberrant regeneration of the oculomotor nerve has been observed in the presence of a compressive lesion and following trauma to the oculomotor nerve. Less commonly, it has been reported in inflammatory lesions such as syphilis, Miller-Fisher syndrome, ophthalmoplegic migraine, and atypical Tolosa-Hunt syndrome.[10,16] This case report demonstrates that aberrant regeneration of the oculomotor nerve can also occur in CNS tuberculoma affecting the oculomotor cranial nerve. Four months after initiation of anti-TB treatment, there was resolution of ptosis and improvement of ocular motility in the right eye. However, eyelid retraction was noted on downgaze, consistent with misdirection of regenerating fibers originally destined for the inferior rectus now innervating the levator palpebrae superioris muscle.

Oculomotor nerve palsy is a rare presentation of CNS tuberculoma in the setting of HIV infection. In a country where TB is endemic and HIV cases are on the rise, a high index of suspicion is necessary to avoid treatment delays. Treatment with anti-tuberculous medicines may result in symptom resolution and clinical improvement.

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