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Pupil involving oculomotor palsy- Examination, Cause and Outcome

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Abstract

BACKGROUND: A patient with a third cranial nerve (CN III) palsy can be a stress inducing event for an optometrist due to the potentially life-threatening etiologies and infrequency of their presentation. The pathogenesis of a CN III palsy can vary from innocuous to life threatening. Palsy of the third cranial nerve results in an impairment of eye movement and / or pupillary response to light depending on the extent of the palsy. CASE REPORT: This case reviews a recent onset of a complete right oculomotor palsy. Literature of similar cases detail the likelihood of variable causes, and while a diagnostic work-up is indicated based on the risk, the etiology of the palsy in this case was determined to be more benign in nature. CONCLUSION: Large scale population studies in the literature reveal the etiology of a CN III palsy from life-threatening conditions is lower than indicated based on published case reports. However, a complete evaluation of a patient including neuro-imagining is still warranted due to the potential life-threatening complications. Further population studies with increased diversity need to be performed to advance knowledge in this area.

Keywords

Cranial nerve 3, oculomotor nerve, oculomotor nerve palsy, microvascular, neuroimaging

INTRODUCTION

Cranial nerve three (CN III), the oculomotor nerve, is partially responsible for extra-ocular movement by innervating four of the six extra-ocular muscles, as well as elevation of the upper lid, constriction of the pupil, and accommodation of the intraocular lens. Presentation of an oculomotor nerve palsy varies but may include a combination of ipsilateral ptosis, dilated pupil and/or down and out appearance of the eye. The infrequent presentation and potential for a life-threatening etiology presents unique challenges for eye care practitioners regarding management of these patients. Potentially life-threatening diagnoses may include brainstem neoplasms or infarctions, intracranial aneurysms or hemorrhages, demyelinating disease, or pituitary apoplexy.[1]

CASE REPORT

A 59-year-old African American male presented with a painless right upper eyelid droop as his chief complaint. His symptoms had been present for about two weeks without a change in severity. He stated that when he raised the eyelid with his fingers his vision was unaffected. He denied any pain or headache and denied any recent eye injuries, surgeries, or illnesses.

The patient's systemic history included hypertension (treated with amlodipine besylate 10 mg one time per day), hypercholesterolemia (treated with atorvastatin 20 mg one time a day), and type 2 diabetes mellitus (treated with Novolog® 100 unit/mL subcutaneous injection). His type 2 diabetes mellitus had been diagnosed about 30 months prior, and he reported his most recent HbA1c as 9.0% measured two months prior. Further history revealed a recent mild cerebrovascular accident (CVA) about 6 weeks prior to this visit, resulting in mildly decreased function and strength in his right foot and leg. He denied experiencing an eyelid droop or diplopia at the time of the CVA.

Objective examination revealed a complete ptosis of the right upper eyelid. With

mechanical elevation of the eyelid, the uncorrected vision was 20/30 in the right eye (pinhole: 20/20) and 20/20 in the left eye. Anterior segment findings of the right eye revealed a fixed and dilated pupil with a diameter of 5 mm. The left pupil was round and reactive to light and accommodation and without an afferent pupillary defect. Mechanical elevation of the right upper lid was necessary for extraocular muscle testing, which revealed that the right eye was in a down and out position and was immobile. The left eye had a full range of motion, and the patient complained of varying diplopia on version testing. The left eye was positioned in primary gaze and had a normal fissure height. Intraocular pressures were 16 mm Hg OD and 14 mm Hg OS by Goldmann applanation tonometry. Except for early nuclear sclerotic cataracts bilaterally, the slit lamp examination did not reveal any further noteworthy findings.

The patient's left eye was pharmacologically dilated in the office with phenylephrine 2.5% and tropicamide 0.5%. No drops were necessary for the right eye due to the extent of physiological dilation present. Examination of the posterior segment revealed a clear vitreous with an optic nerve cup to disc ratio of 0.55 round with clear margins in both eyes. He had dot and blot hemorrhages and scattered cotton wool spots in both eyes and was diagnosed with moderate non-proliferative diabetic retinopathy. The peripheral fundus was flat 360 degrees with no tears or holes in either eye. Peripheral retinal views were limited in the right eye due to the patient's inability to change his position of gaze. Next, causes for the CN III palsy were considered.

Potential causes for an oculomotor nerve palsy include congenital, giant cell arteritis, orbital pseudotumor, subarachnoid hemorrhage, midbrain or cavernous sinus lesion, aneurysm of posterior communicating artery, and microvascular ischemia. The potential causes for this particular clinical case below are listed.

OCULOMOTOR PALSY CAUSES: [2]

1. Congenital

   Congenital oculomotor palsy occurs secondary to abnormal development resulting in restricted innervation of the oculomotor nerve. This often occurs due to abnormalities in the midbrain.[2] This can be ruled out by patient history.

2. Giant cell arteritis (GCA)

   Giant cell arteritis is a common type of vascular inflammation and needs to be considered in older patients presenting with diplopia. Acute vision loss may occur in one or both eyes and is not reversible. The lining of the necessary blood vessels becomes inflamed, reducing the flow of nutrient rich blood to the eye.[2] While this often presents with headache, pain, jaw claudication and change in vision (denied on presentation), erythrocyte sedimentation rate (ESR) and c-reactive protein (CRP) followed by a temporal artery biopsy can be used to confirm or rule this out.[2]

3. Orbital Pseudotumor

   This occurs as a non-infectious inflammation resulting from swollen tissue within the orbit. While the pathogenesis is unknown, the condition is diagnosed more frequently in women and without age predilection. This condition may present with a positive forced duction test.[2,5] This was ruled out because there was no pain or proptosis. Additionally, this diagnosis would not explain pupil or lid findings.

4. Subarachnoid hemorrhage

   Fluid or swelling present within the subarachnoid space can cause compression of the blood supply. Since pupillary fibers surround (on the surface) the oculomotor nerve, they are more susceptible to this type of compression. [2] The patient denied headache or change

in mental state. Despite this, subarachnoid hemorrhage remained a differential diagnosis.

5. Midbrain or cavernous sinus lesion

   Lesions within either the midbrain or cavernous sinus may cause compression to superior colliculus or oculomotor nerves. A lesion within the cavernous sinus may reduce the ability of the oculomotor, trochlear or abducens nerves to communicate with their corresponding ocular muscles. Additionally, a lesion within the cavernous sinus may reduce eye movements by mechanical means, preventing the eye muscles from turning the eye.[2,4] This could not be ruled out and remained as a differential diagnosis. A full cranial nerve screening would be helpful in determining the likelihood of a midbrain or cavernous sinus lesion, but that was not performed.

6. Aneurysm of the posterior communicating artery (PCOM)

   The posterior communicating artery is a part of the circle of Willis and aids in supplying blood to the brain. Although many PCOM aneurysms are asymptomatic, they may increase in size to the point that they apply pressure to the portion of the oculomotor nerve adjacent to the aneurysm. That mechanical pressure can facilitate either an incomplete or (less likely) complete CNIII palsy.[2,6] This could not be ruled out and remained as a differential diagnosis.

7. Microvascular ischemia

   Microvascular ischemia may occur due to any vasculopathy, with both diabetes and hypertension being common causes. This type of event may temporarily or permanently reduce the function of the tissue affected.[2,7] This could not be ruled out and remained as a differential diagnosis.

Due to the severity of the potential diagnoses above, a CT (computed tomography) with and without contrast of the brain and orbits and a CTA (computed tomography angiography) were ordered for later that day. CT results revealed no midbrain, cavernous sinus lesions, or sub-arachnoid hemorrhage. CTA also revealed no aneurysm present. Microvascular infarction was left as a diagnosis of exclusion due to the patient's hypertension and diabetes. Results were provided to the patient via telephone and the patient was educated to potential improvement of symptoms over the next one to two months. He was educated on the effects of the complete ptosis on depth perception.

Visit 2 - 24 days after initial presentation

At the second visit, the patient reported his symptoms had neither worsened nor improved. Exophthalmometry readings were OD 22 mm and OS 22 mm with a base of 105 (which was within normal range). The visit had been scheduled to ensure clinical symptoms had not worsened, warranting further concern. Additionally, an order was placed for a chest X-ray to rule out sarcoidosis, lymphoma, and cancer metastasis as well as magnetic resonance imaging (MRI) with contrast (to obtain higher resolution images) of the brain. A second follow-up 1 month later was scheduled.

Visit 3 - 54 days after initial presentation

The patient returned approximately two months after the initial presentation with an improvement in symptoms. He still had a persistent, but incomplete ptosis of the right upper eyelid, but could see without mechanical elevation of the lid. Visual acuity in the right eye was 20/40 without correction (pinhole OD 20/20). Extraocular motilities were full, and a cover test revealed an intermittent low (~8 prism diopter) exotropia at near without any vertical component. (Previously the right eye was unable to move from the inferior temporal position.) The patient's

chest X-ray was negative. MRI results indicated a subacute small infarct in the right paramedian pons as well as a few chronic right sided lacunar infarcts. The results of the MRI of the brain with contrast revealed multiple small infarctions. These findings served to further support the diagnosis of multifactorial microvascular ischemia to the oculomotor nerve. Unfortunately, the patient was lost to follow up.

DISCUSSION

When concern is present for an ischemic nerve palsy, the following characteristics should be assessed (Table 1). While this is not an exhaustive list, the number of factors present increases the likelihood of an ishchemic etiology.

Table 1 Findings present or absent in an ischemic-related CN III palsy

Finding	**Present or Absent**
Age > 40 years old	Present
Vasculopathy history	Absent
Sudden Onset	Present
Complete ptosis <24 hours	Present
Lack of hemi-facial pain / tingling	Present
Normal Pupil	Absent
Improve in < 3 months	Present
No aberrant regeneration	Present
Normal CN IV and VI	Present
Normal acuity, (-) vitritis, (-) proptosis, (-) redness	Present

Figure 1 shows the diagram of the pathway of innervation CNIII. The oculomotor nerve (CN III) is responsible for innervation of the inferior rectus, superior rectus,

medial rectus, and inferior oblique. The actions of these muscles result in elevation, depression, and adduction of the ipsilateral eye. The nerve is also responsible for innervation of the levator palpebrae which is responsible for raising and maintaining the raised eyelid. Finally, CN III is responsible for providing parasympathetic fibers to the pupillary constrictor and ciliary muscles each responsible for both constriction of the pupil and accommodation of the intraocular lens.[8] Due to the variety of muscles innervated by the oculomotor nerve, the presentation can vary depending on the location and severity of the palsy. While it should be considered a clinical pearl to consider any complete CN III palsy to be an aneurysm until proven otherwise,[9, 10] it is more common for a third nerve palsy to be ischemic and resolve within about 3 months.[8]

Aberrant regeneration may occur following an oculomotor nerve palsy resulting in oculomotor nerve dysfunction, including findings of paradoxical co-constriction from abnormal oculomotor innervation to a muscle not innervated by the oculomotor nerve. Primary oculomotor synkinesis typically presents from slowly developing processes (i.e., intracavernous aneurysm or meningioma). The development of aberrant regeneration occurs within the weeks-to-months timeframe, which is consistent with a secondary oculomotor synkinesis, and presents as the result of trauma, surgery, tumor, or aneurysm of the posterior communicating artery. Studies have shown that aberrant regeneration occurs in about 15% of patients who suffer an acute oculomotor nerve injury.[11] Treatment may not be needed depending on the amount of difficulty it presents to the patient; however, some potential treatment options include the use of patching, prism, or strabismus surgery.

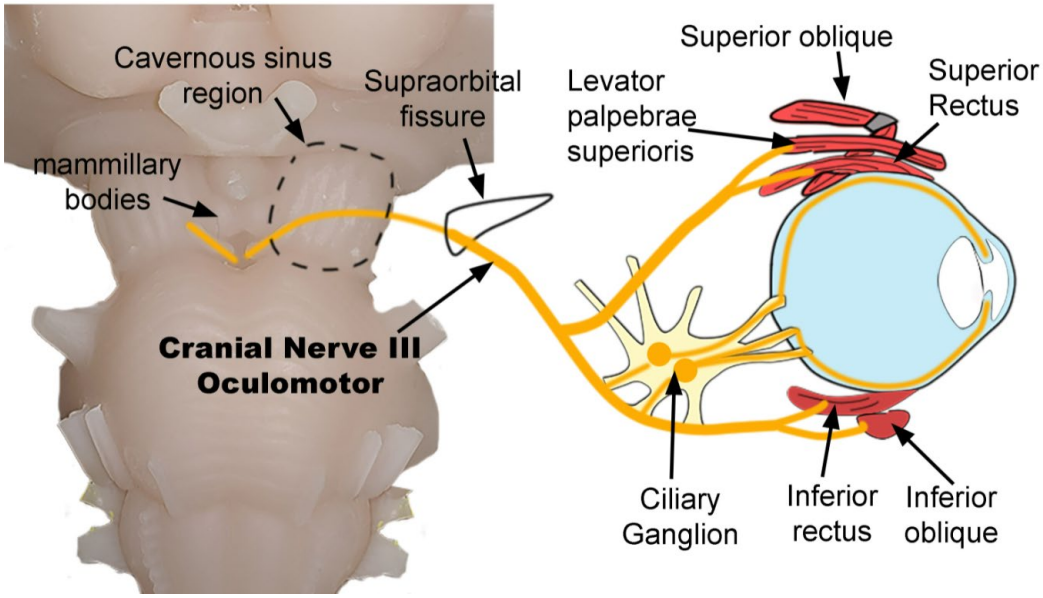

Figure 1 Oculomotor Nerve Pathway from StatPearls[14]

EPIDEMIOLOGY REVISITED

Case studies of acquired CN III palsies often indicate the cause to be due to an aneurysm, however population studies reveal other causes occur at a much higher rate.[12] Due to the severity of an aneurysm, ruling out its presence should be the primary concern of the healthcare practitioner. In a 36-year retrospective analysis, Fang et al. found that the most common cause of third nerve palsy was presumed microvascular (42%). The following causes were less common in their study: compression from neoplasm (11%), post neurosurgery (10%), and compression from aneurysms (6%).[12] The study does have some limitations, most notably that the area sampled, Olmstead County Minnesota, which has a majority (85%) white population.[13] While this information should encourage providers to consider other causes of acquired CN III palsy with greater likelihood, appropriate imaging is still needed. Evaluation of a more diverse population would be helpful to determine frequency of causes in patients of differing demographics.

NEUROIMAGING

The optometrist can and should use characteristics of the presentation to offer guidance concerning location, thus improving the efficacy of the imaging. Additionally, lab testing may be indicated to offer a more complete picture. A complete blood count (CBC), erythrocyte sedimentation rate (ESR) and C- reactive protein should be ordered if giant cell arteritis is being considered.

Neuroimaging is ordered due to the concern about a potential intracranial lesion or aneurysm. Magnetic resonance imaging and / or computerized tomography and magnetic resonance angiography (MRA) or computerized tomography angiography should be ordered (if the patient's kidney function can support it).[10,12] The imaging tests listed have a 90% sensitivity for a 3 mm or greater aneurysm, however the gold standard is still considered to be Digital subtraction angiography (although this is rarely performed).

Improved access to CTs and their cost-effective nature positions CTs as the starting point for neuroimaging to determine the presence of debilitating or life-threatening conditions like hemorrhage, orbital fracture, or intra-orbital abscess. CTs are not without risk, as they deliver large amounts of ionizing radiation. A CT scan uses hundreds of x-rays to construct cross-sectional images by using the tissue density of the anatomy in question.[10,12] The CT scanner, however, does not result in an image in the same way as an x-ray, and the resulting tomographic images must be processed to compute the raw data into a readable image. Multi-slice CTs can obtain scans with a minimum thickness of 0.5-1.2 mm depending on the scanner type and protocol ordered.[10] The use of CT angiography and venography (CTV) allows for the use of contrast opacification of blood vessels. [10]

Magnetic resonance imaging uses non-ionizing radiation to create diagnostic images. An MRI consists of a large magnet and uses an antenna to send radio waves into the patient's body forcing protons to align with the magnetic field. Next, a radiofrequency is pulsed through the patient resulting in protons being spun out of equilibrium. MRI sensors detect time, location, and energy necessary for the

protons to realign with the magnetic field.[10, 16, 17] As discussed previously there are many different sequences that are available: T1, T2, FLAIR, fat suppression, diffusion weighted images (DWI). A complete breakdown of the pros and cons of each type of imaging sequence is beyond the scope of this case report. In general, T1 and T2 are the most common sequences that would be applicable to the optometrist.[10]

Digital subtraction angiography (DSA) is a procedure in which radio-opaque iodine is injected and images are taken as it flows through the patients' blood vessels (much like fluorescein angiography); however, the subtraction as mentioned includes an initial, pre-injection image as well. The post injection image then has the corresponding areas not affected by the dye removed (thus digital subtraction). Currently, this technique is not commonly used due to improved alternate imaging options yet is often noted as the "gold standard" for determining the presence of an intra cranial aneurysm. Additionally, the radio-opaque iodine is difficult to filter through the kidneys and thus is not a good option for diabetic patients or patients with renal insufficiency.[18] As such this would not have been a good option for the patient in question.

CONCLUSION

While a CN III may present as a sign of a more life-threatening condition, it is much more likely to be caused by microvascular ischemia. While this information may put the optometrist somewhat at ease, this does not absolve the optometrist of the responsibility of ensuring coordination of appropriate neuroimaging and laboratory testing. In this case we could not make a definitive diagnosis, but the imaging results and review of retrospective causes of CN III palsy favored a microvascular infarct secondary to hypertension and diabetes.

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