Title: More Than Just the Pupil: An Incomplete Pupil-Sparing Third Nerve Palsy Secondary to a Cavernous Sinus Meningioma

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Abstract: An incomplete pupil-sparing CNIII palsy secondary to a cavernous sinus meningioma can present with variable manifestations. Ancillary testing is crucial for proper diagnosis since the patient can be at a high risk for morbidity/mortality.

I. Case History
   a. 83 year old Hispanic male
   b. Chief Complaint: Periorbital pain and swelling OD x 2 weeks
   c. Ocular history:
      i. 2 weeks prior: Seen by a different provider:
         1. Diagnosed with eyelid swelling OD secondary to allergic conjunctivitis
         2. Mild medial rectus restriction documented but not addressed
         3. Plan: Benadryl PO and ice packs
      ii. 1 week prior: Seen by a different provider:
         1. Findings: Complete ptosis OD, partial 3rd nerve palsy, pupil spared
         2. Documented: restrictions of medial, inferior, and superior rectus; no diplopia secondary to complete ptosis
         3. Plan: Likely vasculopathic etiology. Referral to Neuro-ophthalmology
   d. Medical history:
      i. Dyslipidemia, Hypertension, Thrombocytopenia, Sinusitis, Pneumonia, Prostate Cancer, and Colon cancer
      ii. CT scan 2014 for unknown reason: revealed expansion of right cavernous sinus with a maxillary sinus lesion
      iii. Former smoker. Denies alcohol or drugs.
   e. Medications: Abiraterone, Aspirin, Ergocalciferol, Ferrous Sulfate, Losartan, Nifedipine, Omeprazole, Tamsulosin, Albuterol, Fluticasone

II. Pertinent Findings on Presentation to Neuro-Ophthalmologic clinic:
   a. Clinical:
      i. BCVA 20/30 OD, 20/40 OS
      ii. PERL (-) APD
      iii. Full CVF OD/OS
      iv. Full EOMs OD/OS
      v. IOP in mid-teens OD/OS
      vi. Anterior segment: NSC grade 2+ OD/OS
         1. OD: mild periorbital edema and pain (improvement from previous exam)
         2. Right Alternating Exotropia 35PD 90% fixation OS, (-) diplopia
         3. Ptosis resolved
      vii. Posterior segment: unremarkable, (-) pallor or edema OD/OS
      viii. Color vision with HRR: 3/6 OD, 5/6 OS
   b. Additional Testing
      i. HVF 24-2SS: reliable, non-specific defects OD/OS
      ii. OCT RNFL: WNL OD/OS
   c. Blood work:
      i. ESR/CRP: elevated
      ii. BUN/Creatinine: WNL
      iii. Anti-AChR Antibody Test: WNL
      iv. TSH/Thyroid Antibody Test: WNL
   d. Radiology studies:
i. Head/ Sella Turcica MRI with gadolinium: right side maxillary sinusitis and right cavernous sinus meningioma

III. Differential Diagnosis
   a. Pupil Sparing Third Nerve Palsy secondary to compressive lesion
   b. Evolving third nerve palsy secondary to aneurysm
   c. Pupil Sparing Third Nerve Palsy secondary to vasculopathic factors
   d. Tumor Metastasis
   e. Ocular Myasthenia Gravis

IV. Diagnosis/ Discussion:
   a. Diagnosed with Pupil-Sparing Third Nerve Palsy Secondary to Cavernous Sinus Meningioma
      i. Symptoms of meningiomas may be mild and/or non-progressive for years.¹
      ii. MRI with contrast Head/ Sella Turcica revealed a right cavernous sinus meningioma with the typical “dural tail” differentiating it from other lesions in the cavernous sinus²
      iii. 4-18% of third nerve palsy cases are secondary to neoplasms; meningiomas are among the most common tumors to invade the cavernous sinus³
      iv. Despite the benign and extra-axial nature of meningiomas, the cavernous sinus does house significant structures such as cranial nerve IV, V, VI, posterior communicating artery, and the internal carotid artery, which can potentially be affected.
      v. Signs of third nerve palsies: tropia, ocular motility deficits, spared pupils, and ptosis³
      vi. Symptoms of third nerve palsies: diplopia, periorbital pain, and problems focusing³
         1. Patient had recent/variable restrictions of the medial, inferior, and superior rectus, all of which are innervated by the third nerve
            - Incomplete third nerve palsies are defined as deficits in all of the muscles to only a slight extent or involving only some of the muscles innervated by the third nerve that are subtle yet vary dramatically³
            - Patient’s extraocular limitations were highly variable across all examinations.
         2. Patient had no pupillary involvement from onset through all follow ups
            - 14-20% of pupillary sparing third nerve palsies are associated with neoplasms³
            - Pupillary fibers run along the lateral aspect of the third nerve within the cavernous sinus. Thus, slow growing compressive lesions within the cavernous sinus may spare the pupillary fibers.³
            - Third nerve divides into two divisions prior to entering the superior orbital fissure. The superior division is responsible for the superior rectus and the levator muscles; whereas the inferior division is responsible for the medial rectus, the inferior rectus, the inferior oblique and the pupillary fibers.³ Thus, a compressive lesion that only affects the superior division of the third nerve will spare the pupil as well.
            - The patient’s meningioma most likely did not directly compress the pupillary fibers resulting in spared pupils since the patient did have some restrictions from the inferior division.
         3. Patient did not experience diplopia secondary to complete ptosis
            - Patient would have experienced diplopia if the ptosis was lifted
            - Third nerves are responsible for the levator muscle³
         4. Patient consistently complained about pain with varying severity
            - Pain related to intracavernous sinus third nerve palsy is related to trigeminal nerve involvement³
      vii. OCT retinal nerve fiber layer and visual field examination revealed absence of any compression or compromise along the visual pathway.
   b. Incomplete Pupil-Sparing Third Nerve Palsy Secondary to Aneurysm
      i. 15-20% of third nerve palsies are caused by aneurysms⁴
         1. High incidence of third nerve palsies secondary to aneurysms at the junction between internal carotid artery and the posterior communicating artery⁵
         ii. Aneurysm compression is an acute medical emergency because of the possibility of aneurysm rupture and intracranial hemorrhage⁶
         iii. Clinical presentation: similar to compressive lesions; however, the spared pupil can be evolving into an involved pupil (mydriasis) or be poorly reactive.⁶ Further, there could be oculomotor synkinesis.⁷
1. Oculomotor synkinesis can occur from aberrant regeneration, which presents with an upper eyelid retraction on downward gaze or adduction. Minimal to no ptosis in the primary position. The pupil would also not be reactive light; however, would constrict on adduction and infrauction.

- The patient did not have a retraction in any of the gazes and there was a complete ptosis in one of the exams. Pupils were reactive to light.

2. Pupil presentation
- Pupillary involvement is observed in almost 100% of aneurysmal third nerve palsy cases at some point.
- Aneurysms that reveal incomplete or pupil sparing findings can progress to a complete or pupil involved third nerve palsy in a short period of time. Recommended to initially check patients with spared pupils in the first 24-48 hours for pupil involvement/progression.
  
  o Narrow and long aneurysms can compress at certain locations along the third nerve that don’t involve the parasympathetic fibers, which are responsible for pupillary action.
  
  o “Rule of the pupil” is normally used to distinguish between aneurysms and vasculopathic lesions; however, there is an exception when extraocular muscle restrictions and ptosis are incompletely involved with a spared pupil, which does not entirely rule out an aneurysmal compression and may develop into a pupil-involved third nerve palsy.
    
    ▪ Patient did have a spared pupil, variable partial extraocular muscle restrictions with ptosis and thus, imaging was requested within one week.
    
    ▪ Subsequent exams for frequent monitoring showed continue pupil sparing.

3. Patient’s complaints about pain:
- Up to 64% of patients complain about aneurysmal pain which are related to trigeminal nerve involvement.
- Aneurysmal pain is described as abrupt, severe, and lasting seconds. Other complaints include headache, neck stiffness, and other meningeal signs.
  
  o Although the patient’s pain varied in severity, it was generally mild. The patient had no other meningeal signs.

4. Ancillary Testing
- Whether or not the pupil is involved, an evolving presentation of a third nerve palsy warrants urgent imaging.
  
  o MRI imaging was requested to rule out an aneurysm, which revealed the diagnosis of a meningioma in the cavernous sinus. A prior CT scan also revealed an expansion of the right cavernous sinus with a maxillary sinus lesion giving the impression that this lesion has been present for at least 2 years.
  
  - MRA or CTA are non-invasive testing and are preferred over cerebral arteriography (CA) since CA carry a mild risk of stroke and death in 1-2% of cases. However, CA is the “gold standard” for the diagnosis of aneurysmal compression.
  
  o MRA sensitivity is about 88-97% of lesions greater than 5mm and is lower for smaller aneurysms. About half of aneurysms smaller than 5mm have been missed when using only MRAs.
    
    ▪ Taking the patient’s age (83 years old) and presenting symptoms into consideration, these tests were not administered.
  
  o The MRI done showed the typical “dural tail” with extra-axial enhancement, which are common features of a cavernous sinus meningioma.

  c. Pupil-Sparing Third Nerve Palsy Secondary to Vasculopathic Etiology
  
  i. 20-45% of third nerve palsies are caused by ischemia/microvascular events such as hypertension or diabetes mellitus.
  
  ii. Presentation: Seen as complete paresis: total paralysis of levator muscle leading to complete ptosis with an eye that is “down and out;” however, extraocular muscles can be diffusely incomplete revealing an overall mild deficit in all of the muscles innervated by the third nerve.
iii. Patient’s symptoms resolved and varied in 1 week’s time.
   1. Improvement in symptoms usually occur within 4 weeks in 68%, 8 weeks in 96%, and 100% in 12 weeks with patients who have a third nerve palsy secondary to a vasculopathic etiology.

iv. Patient has a risk factor: hypertension
   1. Given acute variability, ancillary testing was warranted which helped for proper diagnosis.

   d. Tumor Metastasis:
      i. Symptoms of metastatic tumor in the cavernous sinus would be more likely to progress rapidly and explosively, resulting in symptoms such as pain, proptosis, and vision loss in a very short period of time.
         1. Prior CT scan and recent MRI were consistent: showing a lesion in the cavernous sinus that has been present for more than 2 years.

      ii. Patient has history of multiple types of cancer

      iii. Biopsy not preferred due to its location that can result in serious complications: presumptive diagnosis is made based on ancillary testing and onset of the patient’s symptoms.

      iv. MRI revealed the typical, “dural tail” seen in cavernous sinus meningiomas and there was no evidence of metastatic disease was noted.

   e. Ocular Myasthenia Gravis (OMG):
      i. An autoimmune disease affecting the neuro-muscular junction that has the ability to mimic several nerve palsies

      ii. Clinical presentation: variable weakness of extraocular muscles, levator, and orbicularis oculi.

      iii. Negative Acetylcholine receptor (AChR) antibody test
         - Primary blood test for MG. Results are positive in 50-70% of OMG cases.
         - Patient had a negative test. While this does not entirely rule out OMG due to possibility of false negatives, because the results of the MRI showed a meningioma, a tensilon test or ice pack test was not performed.

V. Treatment and Management
   a. Consult with neurosurgery and radiology. Patient is scheduled for a repeat MRI Head/Sella Turcica with and without contrast in 4 months. A MR or CT angiography will be considered at that visit. Serial testing will provide information in regards to any changes or progression.

   b. Consult with otolaryngologist for sinusitis and inflammatory symptoms.

   c. Monitor in a months time for any changes in symptoms, visual acuity, ptosis, extraocular involvement, pain, diplopia, and development of pupillary involvement.

   d. Any changes on subsequent visits warrant further work-ups and referrals.

VI. Conclusion
   a. Optometrist must be able to recognize the variable manifestations of a third nerve. These manifestations can be subtle and/or variable and thus may be disregarded in the exam.

   b. Determining if the palsy is secondary to an aneurysm versus a compressive lesion is critical. Identifying the underlying cause is vital since patients are at a high risk for morbidity and mortality.

   c. Evolving incomplete or pupil sparing third nerve palsies can progress to a complete or pupil involved third nerve palsy in a short period of time and must be monitored closely.

   d. Incomplete third nerve palsies, regardless of pupillary involvement, warrants a neurological work-up with imaging and proper referrals as necessary.

   e. Neuro-imaging is crucial to aid in diagnosis, to determine course of follow up, and to direct treatment and management options.

   f. Co-management with neuro-ophthalmology, neurosurgery, radiology, and possibly oncology is critical in cases of third nerve palsies secondary to cavernous sinus meningiomas.

References


