DISCUSSIONS IN NEURO-OPHTHALMIC DISEASE: RULES, EXCEPTIONS TO THE RULES, AND EXCEPTIONS TO THE EXCEPTIONS TO THE RULES

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THURSTON HOWELL III DOESN'T LIKE NEURO

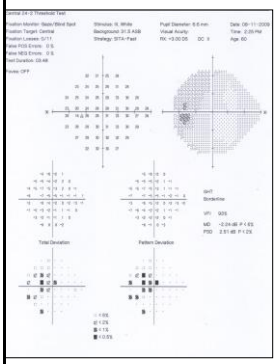
"Neuro equals referral"

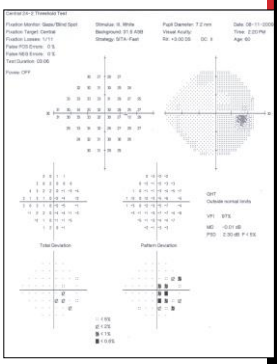
"Diagnose and adios!'

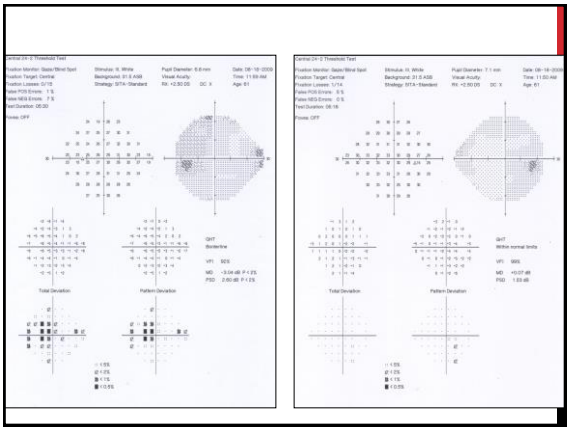
MANAGING PATIENTS WITH NEURO-OPHTHALMIC DISEASE

- **Understanding of anatomy**
- **Following several fundamental principles**
- **Following several simple rules**
- **Developing a network of referral physicians**
  - Neuroradiologist
  - Neurologist
  - Internist
  - Neurosurgeon
  - Rheumatologist

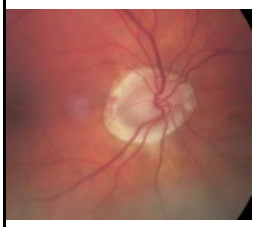
A personal case to prove my point

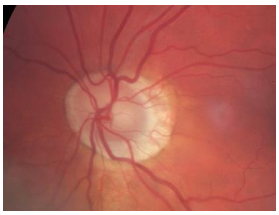


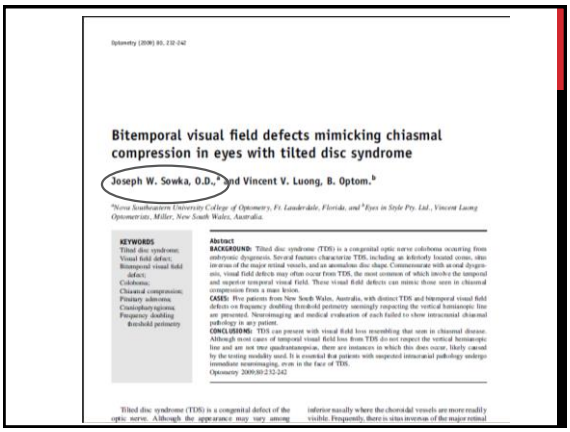




A PERSONAL CASE TO PROVE MY POINT







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Bitemporal visual field defects mimicking chiasmal compression in eyes with tilted disc syndrome

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KEYWORDS
Tilted disc syndrome;
Visual field defect;
Bitemporal visual field defect;
Coloboma;
Chiasmal compression;
Pituitary adenoma;
Craniopharyngioma;
Frequency doubling threshold perimetry

Abstract
BACKGROUND: Tilted disc syndrome (TDS) is a congenital optic nerve coloboma occurring from embryonic dysgenesis. Several features characterize TDS, including an inferotorly located conus, situ inversus of the major retinal vessels, and an anomalous disc shape. Commensurate with ocular dysgenesis, visual field defects may often occur from TDS, the most common of which involve the temporal and superior temporal visual field. These visual field defects can mimic those seen in chiasmal compression from a mass lesion.
CASES: Five patients from New South Wales, Australia, with distinct TDS and bitemporal visual field defects on frequency doubling threshold perimetry seemingly respecting the vertical hemianopic line are presented. Neuroimaging and medical evaluation of each failed to show intracranial chiasmal pathology in any patient.
CONCLUSIONS: TDS can present with visual field loss resembling that seen in chiasmal disease. Although most cases of temporal visual field loss from TDS do not respect the vertical hemianopic line and are not true quadrantanopsias, there are instances in which this does occur, likely caused by the testing modality used. It is essential that patients with suspected intracranial pathology undergo immediate neuroimaging, even in the face of TDS.
Optometry 2009;80:232-242

Tilted disc syndrome (TDS) is a congenital defect of the optic nerve. Although the appearance may vary among

inferior nasally where the choroidal vessels are more readily visible. Frequently, there is situs inversus of the major retinal

You're wife is going to kill you if she finds out!

RULE

Congenital optic nerve anomalies can have (sometimes dramatic) visual field loss

RULE

Don't make diagnosis of immune disease in immunosuppressed patients

RULE

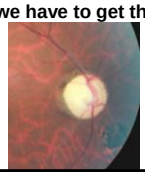
Never diagnose idiopathic anything in a patient with a history of cancer

RULE

Urgency of evaluation is dictated by duration of condition

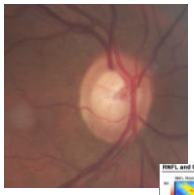
46 YOM

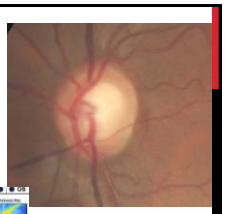
- Reports waking up 3 months ago not being able to see OD
- LP OD, 20/20 OS
- Disc pallor OD- no other concurrent findings
- Last medical exam unknown- no medical hx
- Resident gets nervous- sends to ER immediately
- How long do we have to get this worked up?

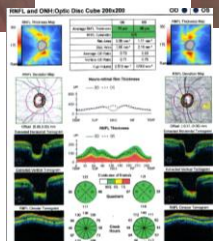


RULES MUST BE OBEYED

- 57 YOF
- Low risk OHTN OU
- GDx, OCT, ONH – perfectly normal OU







Fields are a different story however…

RULE

Chiasmal and retrochiasmal lesions have bilateral involvement.

Unilateral visual field loss reflects anterior visual pathway disease which will show something identifiable in the form of damage to the vision, disc, RNFL, dyschromatopsia or afferent pupil defect.

RULE

A patient can fake a field, but can't fake a retinal nerve fiber layer or pupil defect.

59 YOM

- **Routine exam- c/d 0.5/0.5 OU**
  - IOP 20 mm Hg OU
- **Returns 2 years later- slowly progressive loss of vision OD**
- **RAPD OD; 20/80 OD; 20/20 OS**
- **Superior altitudinal defect splitting fixation OD; mild inferior defect OS**
- **Disc pallor OD**
- **Dx: NAAION**

What is wrong with this picture?

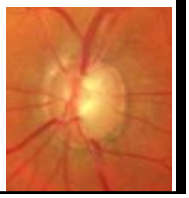
59 YOM

- **Routine exam- c/d 0.5/0.5 OU**
  - IOP 20 mm Hg OU
- **Returns 2 years later- slowly progressive loss of vision OD**
- **RAPD OD; 20/80 OD; 20/20 OS**
- **Superior altitudinal defect splitting fixation OD; mild inferior defect OS**
- **Disc pallor OD**
- **Dx: NAAION**

What is wrong with this picture?

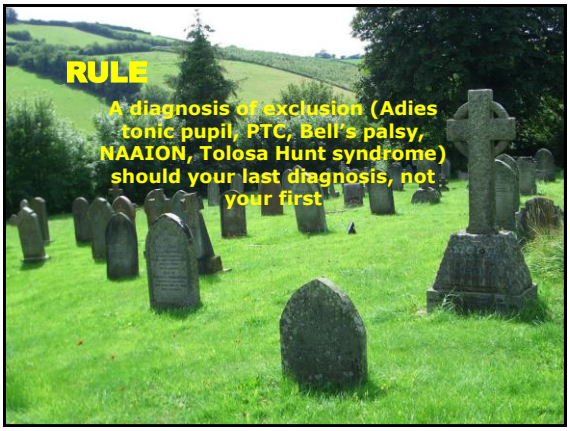
59 YOM

- **IOP 23 mm Hg OD**
- **c/d actually 0.95/0.95 OD and 0.8/0.8 OS**
  - Very shallow cupping
- **Dx: undiagnosed POAG with loss of fixation OD**



RULE

Don't make the diagnosis of NAAION in glaucoma patients

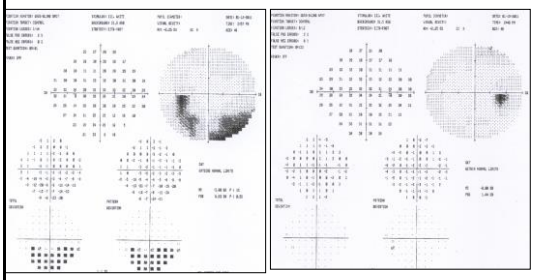


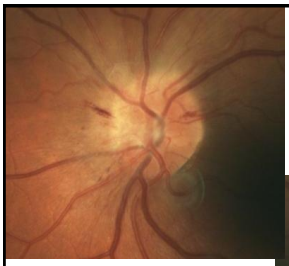
48 YOWM

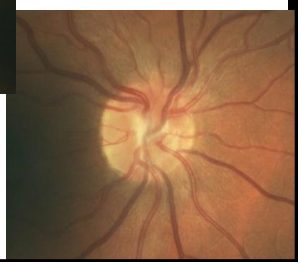
Painless loss of visual field OS

- 20/20 OD, OS
- Noticed upon waking

Med Hx: Unremarkable, except for viral illness 3 weeks before







NAAION OS
Disc at risk OD

Quark NAION study
QRK207

A Phase 2/3, Randomized, Double-Masked, Sham-Controlled Trial of QPI-1007 Delivered By Single or Multi-Dose Intravitreal Injection(s) to Subjects With Acute Nonarteritic Anterior Ischemic Optic Neuropathy (NAION)

Quark Pharmaceuticals

QRK207 NAION

This is a clinical study, sponsored by Quark Pharmaceuticals, working in collaboration with the Neuro-Ophthalmology Research Disease Investigator Consortium (NORDIC).

- *This material is not intended to suggest that any investigational drug discussed is safe or effective for the purposes for which it is under investigation.*

For Health Care Professionals information only

Purpose of the study

- Determine the effect of QPI-1007 on visual function in subjects with recent-onset NAION.
  - Mean change in BCVA score, as measured by ETDRS visual acuity protocol in the study eye from Day 1 to Month 12.
  - Mean change of Visual Fields, as assessed by Humphrey standard automated perimetry using a full-threshold strategy and Size V stimulus testing protocol in the study eye from Day 1 to Month 12.
- Assess the safety and tolerability of intravitreal injections of QPI-1007 in this population.
- Evaluate the structural changes in the retina following administration of QPI-1007.

For Health Care Professionals information only

Key Inclusion Criteria

- Males and females 50-80 years old.
- Positive diagnosis of first episode of NAION in the study eye with symptom onset within **14 days** prior to planned study drug administration/sham procedure (Day 1).
- Best corrected visual acuity score in the study eye is better than or equal to 15 letter score, measured using the ETDRS visual acuity protocol at Day 1 prior to study drug administration/sham procedure.
- Clear ocular media and able to undergo adequate pupil dilation to allow a good fundus examination.

For Health Care Professionals information only

Refer!

- If you suspect your patient has NAION, REFER!
- *Early referral is critical as study enrollment is limited to 14 days from onset of symptoms.*
- Identify and contact a study site
  - Visit www.EyeActNow.com for study information & to locate a study site.
  - May also visit www.ClinicalTrials.gov for current sites.
  - Contact Quark
- Study sites will complete full diagnosis, determine eligibility, and provide all study details.

For Health Care Professionals information only

RULE

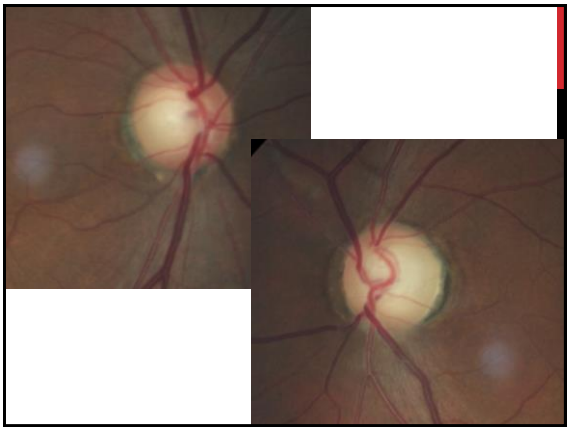
Pallor in excess of cupping indicates something other than, or in addition to, glaucoma

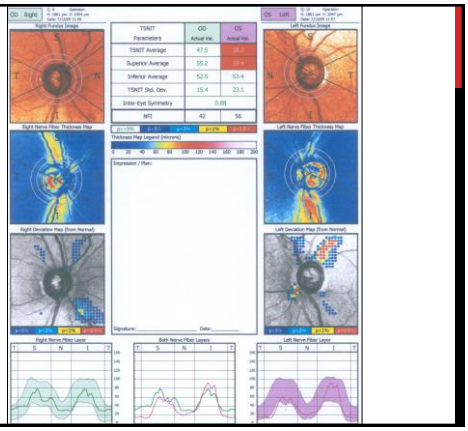
RULE

Nothing notches a nerve like glaucoma

IN THE AGE OF IMAGING, DO WE REALLY NEED FIELDS?

- **54 YO Nigerian man**
- **Referred for glaucoma management**
- **Told he had glaucoma 6 years earlier- no Tx**
- **20/30 OD; HM OS**
  - Vision loss from glaucoma- not coming back
- **30 mm Hg OD; 23 mm Hg OS**
  - Lumigan- 17 mm Hg OD, 15 mm Hg OS

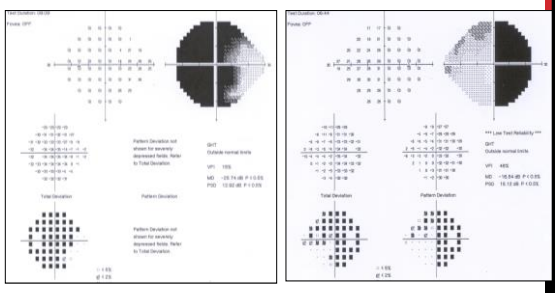




Diagnosis?

Plan?

Do we really need fields in this case?

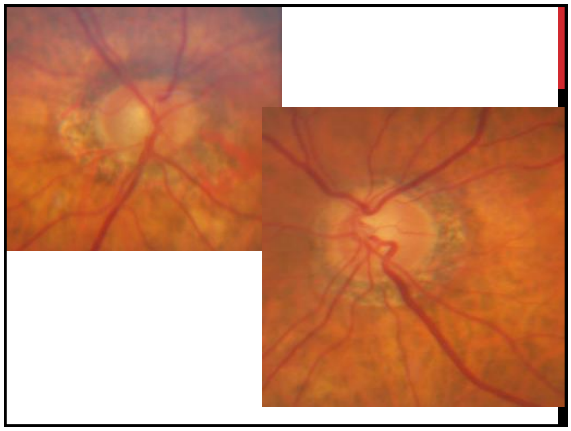


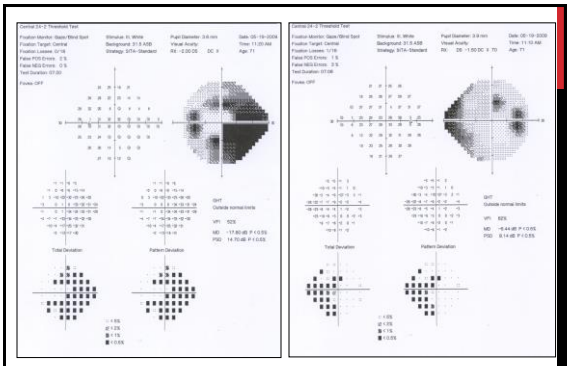
Yes, we still need to do fields in the age of imaging.

Sometimes its not glaucoma

POAG GETS COMPLICATED?

- **70 YOWM**
- **POAG OU**
- **Auto accident with concussion**
- **Develops gaze induced amaurosis fugax**
- **Referred by PCP to neuro-ophthalmologist**
- **Complete evaluation with MRI- negative**
- **Psychological?**





Sometimes it is glaucoma

ODE TO A CUPPED DISC

Oh, to have a cupped disc pink.
That my friend hath a glaucomatous stink.
But to have a cupped disc pale,
Call this glaucoma and you shall fail.
Disc and field damage that is one-sided
Simply cannot be abided.
It might be trauma, infarct or meningioma.
But if the rim is cut always remember,
Nothing notches a nerve like glaucoma

Joseph Sowka, OD

CASE HISTORY 46 WM

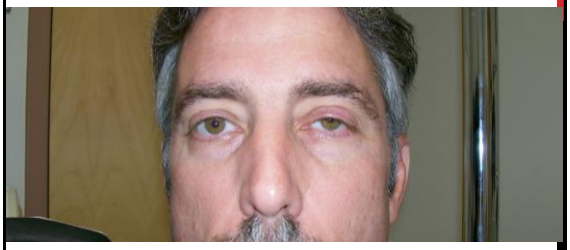
- **CC: Patient reports a "droopy left eye" which began about 6 weeks ago. Headache and numbness ipsilateral; hives**
  - ER diagnosed with "stye". Patient was referred in by a local optometrist.
- **Past Ocular History: unremarkable**
- **Past Medical History: (+) Mitral Valve Prolapse, (+) GERD and recent weight loss of about 20 lbs. over the past 6 months or so.**
  - Medications: Prilosec, Metoprolol Succinate, Xanax, Prednisone, Lipitor, Claritin

PERTINENT FINDINGS

- **BCVA 20/20 OD and 20/20 OS**
- **Pupils : *unequal*, round, reactive to light, No APD**

Bright Illumination	Dim Illumination
OD: 4 mm	OD: 6 mm
OS: 3 mm	OS: 4 mm

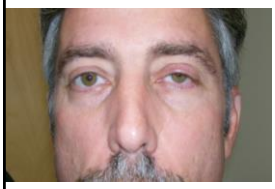
- **Motility and confrontation fields unremarkable**
- **Observation: LUL ptosis, Left miosis**
- **Intraocular pressure: 18 mmHg OD and 19 mmHg OS**
- **Fundoscopy-unremarkable**



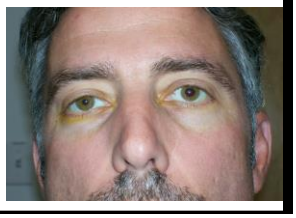
So, what do you think and what do you want to do now?

POST-IOPIDINE

Pre-Iopidine



Post-Iopidine



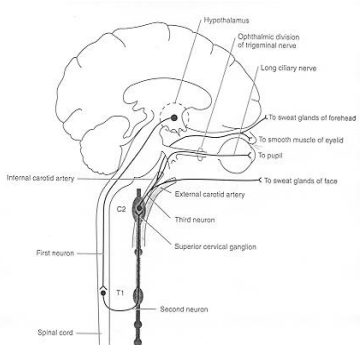
HORNER'S SYNDROME

- **Etiology unclear based upon exam**
- **Headache, neuralgia and 'hives'**
  - Not consistent with cluster migraine
    - Dx of exclusion, not convenience
  - Hives- not consistent with HZO
- **Unexplained weight loss concerning- relationship unclear**
- **Recommend medical eval by PCP**
  - Additional testing dictated by PCP results

DISCUSSION

What is Horner's Syndrome?

- a triad of clinical signs arising from disruption of sympathetic innervation to the eye and ipsilateral face that causes *miosis*, upper lid *ptosis*, mild elevation of the lower lid, and *anhydrosis* of the facial skin.



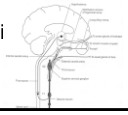
PHARMACOLOGICAL TESTING

- **Cocaine**
  - Horner's pupil doesn't dilate, normal pupil does
- **Hydroxyamphetamine (Paredrine)**
  - Differentiates post- from pre-ganglionic
  - Not available and doesn't matter because bad stuff happens everywhere
- **Apraclonidine 0.5% (Iopidine)**
  - Denervation suprasensitivity
    - 36-72 hours from onset
  - Horner's pupil dilates, normal doesn't
    - Reversal more classic and diagnostic that cocaine

HORNER'S SYNDROME: ETIOLOGIES

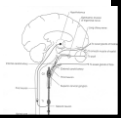
First-order neuron disorder: Stroke (e.g., vertebrobasilar artery insufficiency or infarct); tumor; multiple sclerosis (MS), and, rarely, severe osteoarthritis of the neck with bony spurs.

Second-order neuron disorder: Tumor (e.g., lung carcinoma, metastasis, thyroid adenoma, neurofibroma). Patients with pain in the arm or scapular region should be suspected of having a Pancoast tumor. In children, consider neuroblastoma, lymphoma, or metastasi



HORNER'S SYNDROME: ETIOLOGIES

- **Third-order neuron disorder: Headache syndrome (e.g., cluster, migraine, Raeder paratrigeminal syndrome), internal carotid dissection, herpes zoster virus, otitis media, Tolosa–Hunt syndrome, neck trauma/tumor/inflammation, prolactinoma.**
- **Congenital Horner syndrome: Trauma (e.g., during delivery).**
  - **Facebook tomography**
- **Other rare causes: Cervical paraganglioma, ectopic cervical thymus**

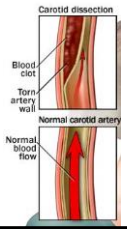


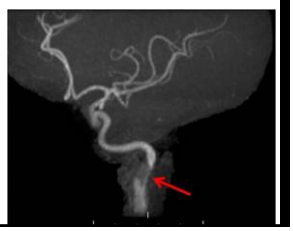
MANAGEMENT

- **Localizable- targeted workup**
  - Neck and facial pain- carotid dissection
  - Facial paraesthesia- middle cranial fossa disease
- **Necessary Work Up (non-localizable):**
  - MRI of brain, orbits and chiasm with and without contrast, attention to middle cranial fossa.
  - MRA of head and neck-rule out carotid dissection
  - MRI of neck and cervical spine, include lung apex and brachial plexus
    - Horner's syndrome patient needs to be imaged from chest to head- 3 scans
    - Horner's protocol
- **All imaging in patient unremarkable**

CAROTID DISSECTION

- ***A 3rd-order Horner's and ipsilateral head, eye, or neck pain of acute onset should be considered diagnostic of internal carotid dissection unless proven otherwise.***





CAROTID DISSECTION

- **Carotid artery dissection presents with the sudden or gradual onset of ipsilateral neck or hemicranial pain, including eye or face pain**
- **Often associated with other neurologic findings including an ipsilateral Horner's syndrome, TIA, stroke, anterior ischemic optic neuropathy, subarachnoid hemorrhage, or lower cranial nerve palsies**
  - 52% with ocular or hemispheric stroke with 6 days
    - 67% within first week; 89% within 2 weeks; none after 31 days
- **Horner's from suspected carotid dissection should go to ER**

HORNER SYNDROME ALGORITHM

1. **Confirm it is Horner syndrome**
   - Apraclonidine; dilation lag
2. **Determine if accidental or surgical trauma as cause**
3. **Urgent imaging**
   - CT/CTA; MRI/MRA head and neck if present< 2 weeks
4. **Image lung apex**

RULE

Diagnosing Horner's syndrome is insufficient. You must try to ascertain a cause and never assume that it is benign.

CASE: 59 BF

- **Long time patient presents for her glaucoma f/u. She reports drooping in the right eye and smaller pupil for about 1 month. Symptoms were noticed at/ about time of dx of lung cancer and subsequent surgery.**
  - `She also reports scapular pain and weakness in the right hand.
- **Past Medical History: (+) Lung Cancer, (+) Pancreatitis, (+) HTN and (+) Acid Reflux**
- **Social History: Smokes 1 pack per day for 45 years, Drinks a 6 pack of beer daily**

CASE: PERTINENT FINDINGS CONTINUED…

- **Pharmacological testing not done**
- **New onset of ptosis and miosis with dx lung cancer and h/o recent lung surgery**
- **Dx=Pancoast Syndrome**

PANCOAST TUMOR

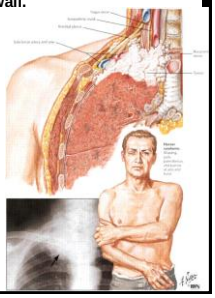
A Pancoast tumor is a lung cancer arising in the apex of the lung that involves structures of the apical chest wall.

Treatment

- Chemotherapy
- Radiation Therapy
- Surgery: lobectomy vs. wedge resection

Prognosis: 5 year survival rate is around 30%

- Not an emergency



ODE TO HORNER'S SYNDROME

When the lid is low and the pupil small,

Check to see the sweat don't fall.

Cocaine is no longer universal,

Iopidine will cause reversal.

You have to scan head to chest,

And remember that MRA is best.

Pain in association, will surely cause commotion.

Send to the ER without correction,

Remember, it might be carotid dissection.

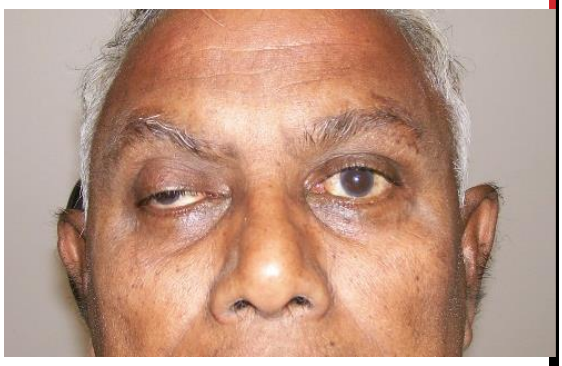
Joseph Sowka, OD

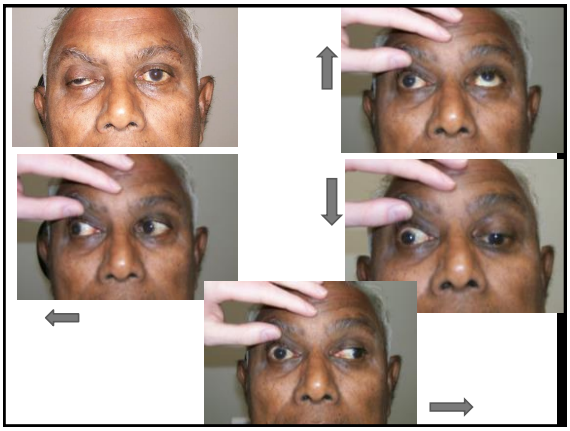
RULE

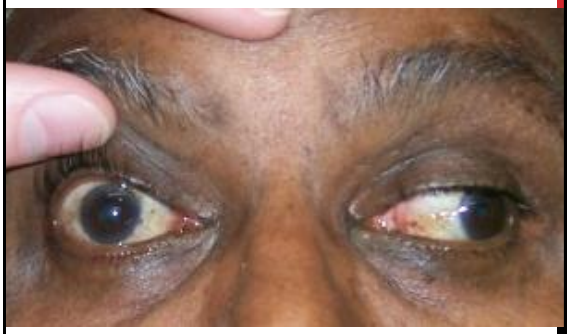
Suspect the worst

63 YOIM

- Long standing glaucoma patient
- Sudden onset of orbital pain x 3 days
- + DM; +HTN
- On coumadin
- Pacemaker
- No vision change
- Presents as walk-in emergency glaucoma eval





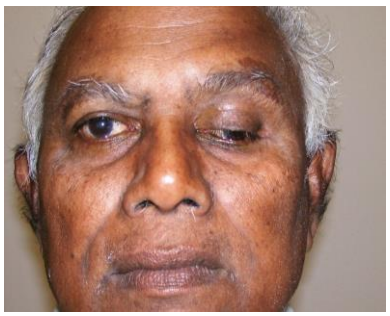


5 mm
unresponsive

2 mm
responsive

63 YOIM

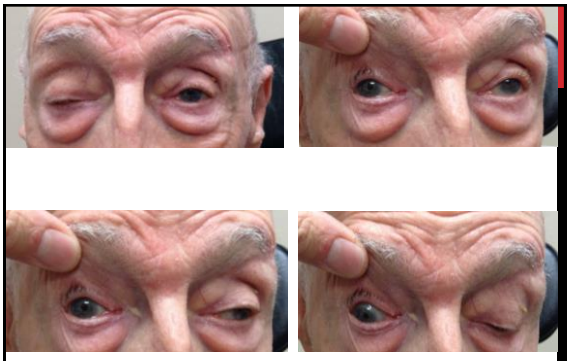
- Pupil involved CN III palsy
- 3 days duration at least
- Most likely cause: intracranial aneurysm
- Sent to ED with detailed notes and recommendations
- Endovascular therapy with coils
- Hospitalized 23 days



Secondary aberrant regeneration

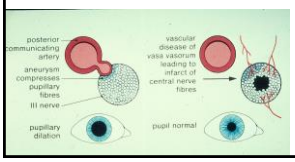
CN III PALSY CLINICAL PICTURE

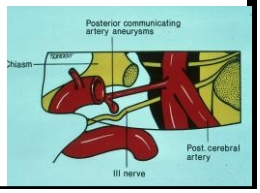
- An eye that is down and out with a ptosis
- Adduction, elevation, depression deficits
- Isocoric or anisocoric



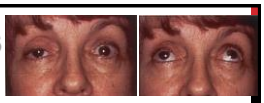
CN III ANATOMY

- Vulnerable to compression from aneurysm in subarachnoid space
  - Posterior communicating artery (PCOM)
  - Junction PCOM and ICA
  - Tip of basilar artery





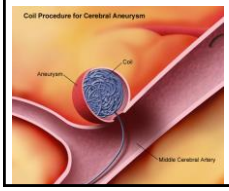
STILL MORE CLUES

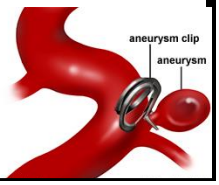


- Pupil involved CN III palsy is PCOM aneurysm until proven otherwise
- Incomplete palsy is PCOM aneurysm until proven otherwise
  - Regardless of pupil
- 30% of CN III palsy are caused by aneurysm
- Pain is pain
  - Only helpful when not present
- Vasculopathic CN III will resolve in time
- Life threatening posterior communicating aneurysm will rupture in time

STILL MORE CLUES

- CN III palsy caused by aneurysm
  - 20% die within 48 hrs from rupture
  - 50% overall die
  - Average time from onset to rupture – 29 days
    - 80% rupture w/i 29 days
  - Many never make it to hospital





RULE

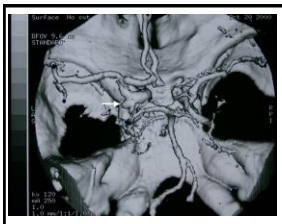
Never dilate a patient with cranial nerve III palsy

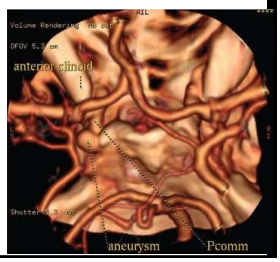
STILL MORE CLUES

- **CN III palsy caused by aneurysm**
  - 20% die within 48 hrs from rupture
  - 50% overall die
  - Average time from onset to rupture – 29 days
    - 80% rupture w/i 29 days
  - Many never make it to hospital
- **Ruptured aneurysms**
  - 5% surgical mortality
  - 60% functional impairment post-op
- **Unruptured aneurysms**
  - No mortality; 75% with normal outcomes; 50% with CN III recovery

RULES FOR CN III PALSY IMAGING

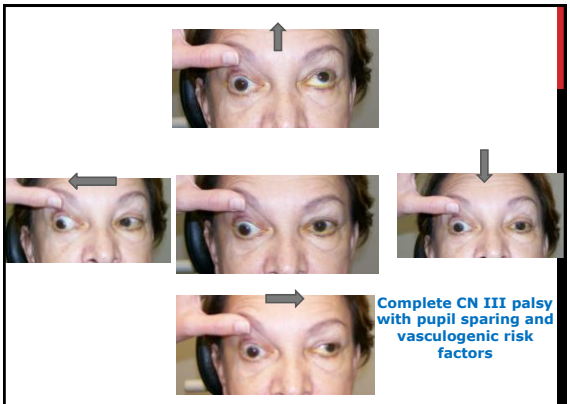
- High suspicion of aneurysm: DSA (gold standard)
- **CT/CTA is preferred non-invasive imaging for CN III palsy**
  - CT for SAH
- **CTA requires contrast- renal impairment prefers MRI/MRA**
- **CTA superior to MRI when patient can't have MRI**
  - Pacemaker, claustrophobia
- **MRI superior for non-aneurysmal causes (tumor)**
  - MRA adds very little time to scan





A DIFFERENT PATIENT AND PROGNOSIS

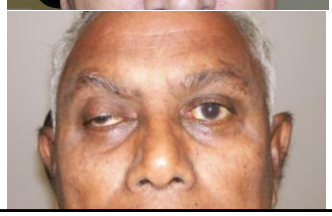
- **63 YOF**
- **Diabetes and HTN**
- **Sudden onset retro-orbital pain**



Complete CN III palsy with pupil sparing and vasculogenic risk factors

WHICH IS BETTER? ONE OR TWO?

Resolves over several weeks



Hospitalized 23 days with 2 neurosurgical procedures

SUSPECT THE WORST

- Optometrist sees patient with CN III palsy
- Referred to ophthalmologist next day
- Pt dies from SAH before consult

DOES PRESENCE OF VASCULOPATHIC RISK FACTORS HELP?

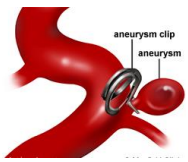
- Arteriosclerotic risk factors in elderly favors microvascular etiology but does not rule out aneurysm
- HTN, DM, atherosclerosis, hyercholesterol all common and don't protect against aneurysm
- Answer: no, but makes me very nervous when NOT present

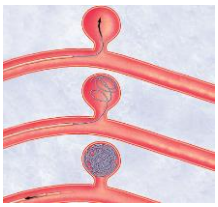
DOES ACUTENESS OF PRESENTATION HELP?

- Ans: Yes and No
- Aneurysm expansion usually produces acute manifestations, but chronic and evolving cases well known
- Acute is more worrisome
- Chronic and improving less worrisome but does not rule out aneurysm
- Resolved without recurrence reassuring

ANEURYSM RISK ASSESSMENT: ISOLATED CN 3 PALSY

Isolated dilated pupil	none
Complete CN3-normal pupil	low
Partial CN3 – normal pupil	high
Pupil involved CN3	emergency





NEVER OUT OF THE WOODS

- Pt develops CN III palsy from aneurysm
- Successfully treated with aneurysm clip
  - All coils are inert and MRI safe; not all clips are MRI safe
- Radiologic tech doesn't verify type of clip
- Pt undergoes F/U MRI with non-MRI safe clip in major medical center
- Clip displaces during MRI
- Patient has fatal hemorrhage during procedure
- Patient survived disease…killed by follow up

ODE TO A THIRD NERVE

When the eye is down and out with ptosis,

You better hope for miosis.

If the palsy is total with pupil sparing,

In an Oldie it's vascular and not too daring.

A partial palsy calls for double duty,

Because it's probably an aneurysm going through puberty.

But if the pupil is dilated,

An aneurysm has violated.

No time for deferral and no time for referral.

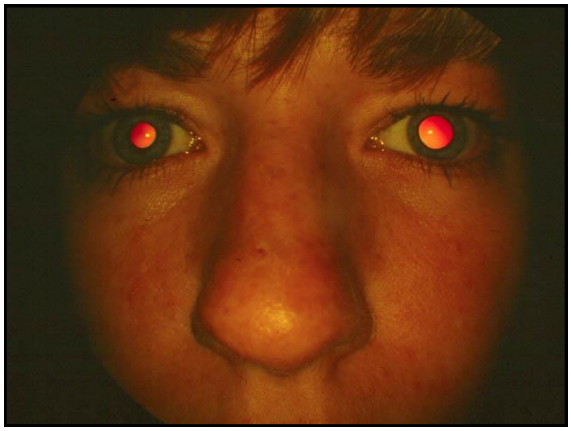
Send to the ER without debate.

Remember, twenty percent will die within the first forty-eight

Joseph Sowka, OD

CASE: 23 YEAR OLD WHITE FEMALE

- **CC: Sudden onset pupil dilation with ipsilateral headache**
- **Medical Hx: normal**
- **BVA: 20/20 OD, OS**
- **Pupils:**
  - 3 mm anisocoria, OS larger, anisocoria greater in bright illumination. Previously isocoric. (-) RAPD, (+) Accom
- **Remainder of exam normal**
- **Similar incident 2 days antecedent, resolved within hours**
- **What does she look like?**



CASE: 23 YEAR OLD WHITE FEMALE

What questions do you want to ask?

What tests do you want to order?

CASE: 23 YEAR OLD WHITE FEMALE

Additional questions to ask:

- ***Any double vision?*** **No!**
- ***Any use of ophthalmic pharmaceuticals?*** **No!**
- ***Any history of migraine headaches?*** **Maybe…**

Differential diagnosis?

Aneurysmal compression on CN III? **No**

Pharmacological misadventure? **No**

BENIGN EPISODIC PUPILLARY MYDRIASIS

Episodic unilateral mydriasis

- Lasts minutes to weeks

Accompanied by blurred vision and headache

Young, healthy females (*may have migraine history*)

Peculiar sensations about affected eye

- Often progresses to headache
- Not typical migraine

Defective accommodation

Lid and motility defects not present

Extensive medical testing unremarkable

BENIGN EPISODIC PUPILLARY MYDRIASIS

Increased sympathetic activity?
- Reverse Horner's syndrome – not likely

Pupil paralysis following migraine?
- Tends to last longer – not likely
- No ophthalmoplegia

Spasm of segment(s) of iris dilator muscle?
- Round pupil, so not likely

Pharmacologically dilated?
- Parasympatholytic – no light or near reactivity
- Sympathomimetic – can mimic and must R/O

BENIGN EPISODIC PUPILLARY MYDRIASIS

- **Anisocoria greater in bright than dim**
  - Parasympathetic dysfunction
    - Not an aneurysm
    - Edinger-Westphall lesion?
- **Migraine variant – most likely etiology**
- **Treatment – none except to avoid unnecessary testing**

PUPIL RULES

- **Anisocoria greater in dim = sympathetic dysfunction**
  - Horner's syndrome- look for dilation lag
  - Miotic use
- **Anisocoria greater in light = parasympathetic dysfunction**
  - CN 3 palsy
  - Tonic pupil
  - Pharmacologic or traumatic pupil
    - No reactivity?

PUPIL RULES

- **Fixed and dilated and unresponsive to light or near = pharmacologic or iris trauma**

RULE: ISOLATED DILATED PUPIL IS ALMOST NEVER AN ANEURYSM

Ambulatory patients with isolated dilated pupil more likely to harbor iris or ganglion (Adie's) lesion or medication misadventure than CN 3 palsy

Comatose patient is a different story

Risk of angiography is much higher than risk of aneurysm in this setting

No imaging needed for isolated dilated pupil