The “I’s” in Neuro-Optometry

Iatrogenic #1: Medication Related Conditions
- Optic Disc Edema
  - Amiodarone
  - Chloramphenicol
  - Tetracycline
  - Interferon
  - Cyclosporine
  - PDE-5 Inhibitors
  - Isotretinoin

Iatrogenic #2: Perioperative Vision Loss
- Tacrolimus
- Oral contraceptives
- Radiation therapy

Inflammatory Orbitopathy
- Ethambutol
- Methotrexate

Autoimmune Conditions

Abnormal Intracranial Pressures

OBJECTIVES

- Review what medications, chemotherapeutic agents and radiation therapies may affect the optic nerve
- Review how medications, chemotherapeutic agents and radiation therapies may affect the optic nerve
- Discuss the management of neuro-ophthalmic implications of these medications and other agents
**AMIODARONE**
- Commonly used for arrhythmias
- Optic disc edema
  - Bilateral > unilateral
  - Large range of onset
  - Mean: 6-9 months; 88% within 1 yr
- MOA: Obstructed axonal transport/reduced axoplasmic flow

**AMIODARONE**
- Similar features and risk factors to NAION
- Vascular conditions (DM, HTN, OSA), age

<table>
<thead>
<tr>
<th>Condition</th>
<th>AMIODARONE optic neuropathy</th>
<th>NAION</th>
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<tbody>
<tr>
<td>M=W</td>
<td>M=W</td>
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</tr>
<tr>
<td>Insidious onset</td>
<td>Acute onset</td>
<td></td>
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<tr>
<td>Bilateral</td>
<td>Unilateral</td>
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</tr>
<tr>
<td>Slow resolution (3-mo)</td>
<td>Shorter (6-8 wks)</td>
<td></td>
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<tr>
<td>Any c/d ratio</td>
<td>“Disk at risk”</td>
<td></td>
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<tr>
<td>More mild vision loss</td>
<td>Worse vision loss</td>
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</tbody>
</table>

**ANTI-INFECTIVES**

**ETHAMBUTOL**
- First line tx of tuberculosis
- Retrobulbar optic neuropathy
- Optic nerves may look normal initially
- Bilateral, painless, generally symmetric vision loss
  - Insidious, mild
  - Typically present by 9 months
  - Range: mild – NLP
- Color vision deficiencies
- Central/cceo-central or bitemporal scotomas
- Pallor in later stages = poor visual prognosis

**ETHAMBUTOL**
- Dose dependent, overall incidence 2-6%
- Risk factors: dose >15 mg/kg, age, concurrent HTN, renal disease and vitamin deficiencies
- MOA: Zinc and copper deficiencies affecting myelin and glial cell proliferation
**ETHAMBUTOL**
- Baseline eye exam and 10-2 visual field
- Monthly visual screenings in high-risk groups
- Pocket acuity chart and Amsler grid
- Contrast sensitivity may pick up subclinical toxicity
- RNFL OCT for subclinical neuropathy is being explored
- Prompt cessation is necessary for preventing further vision loss
- Visual recovery (avg 2 lines) in 30-60%

**CHLORAMPHENICOL**
- Broad spectrum antibiotic
- Diminishing popularity after 1960’s
- Toxic optic neuropathy
- Bilateral disc swelling in early stages
- Vision loss, color vision deficits
- Visual field deficits: central or ceco-central scotoma
- May effect Vitamin B12 metabolism

**CHLORAMPHENICOL**
- Duration and dose dependent
  - > 6 weeks
  - >100 mg cumulative dose
- Accompanying limb paresthesia
- Reversible within weeks
- Vit B12 supplements

**TETRACYCLINES**
- Pseudotumor cerebri
- MOA: Decreased CSF absorption
- Bilateral disc edema
- Blurred vision, headache, diplopia, nausea

**INTERFERON THERAPY**
- Glycoproteins: Interferon alpha, beta, gamma
- Hepatitis C, MS, leukemia, lymphoma
- Anterior ischemic optic neuropathy and optic neuritis with ischemic retinopathies
- Underlying condition being treated may also affect the optic nerve
INTERFERON THERAPY
- MOA: Deposition of immune complexes, inflammation, systemic hypotension
- Onset: minutes to months, avg 3 months
- 50% some degree of vision loss

IMMUNOMODULATORY
- Cyclosporine
- Tacrolimus
- Methotrexate

CYCLOSPORINE
- Immunosuppressive, antirheumatic
- High rate of neurological side effects (5-40%)
  - HA, seizure, cortical blindness, tremor, peripheral neuropathy
- Ophthalmic: Restasis = NOT a risk

CYCLOSPORINE
- Bilateral disc edema
  - With and without intracranial hypertension
  - MOA: Modifies mitochondrial structure and function; may have direct toxicity
  - Workup including MRI, LP
  - Many resolve completely

TACROLIMUS
- Immunosuppressant
- Post organ transplant
- Severe eczema and psoriasis
- Fun fact: Treats dry eye in pets
- Many ocular side effects, including optic neuritis and optic neuropathy
- MOA: Direct toxicity to myelin causing axonal swelling, inflammation causing ischemia

TACROLIMUS
- Optic neuropathy
- Bilateral optic nerve pallor, progressive vision loss
- Optic disc edema
- Variable vision loss, large range of onset
- Variable visual field and color deficits
- Can occur at subtherapeutic levels
- Reluctancy to discontinue
**Methotrexate**

- First line antineoplastic/chemotherapy and immunosuppressive agent
- Leukemia, lymphoma, other neoplasms, RA, psoriasis, Chron’s disease

- Many anterior segment effects, also linked to optic neuropathy
- Mainly posterior optic neuropathies
- Symptoms of scotomas, color vision deficits and worsening vision with normal dilated exam appearance
- MOA: Interferes with folic acid metabolism
- Generally, many recover after discontinuing

**Other**

- Oral Contraceptives
- PDE-5 Inhibitors
- Isotretinoin

**Oral Contraceptives**

- CDC (2019): 14% women age 15-49
- Can affect almost any part of the eye
- Well documented cases of PTC, optic neuritis, ischemic optic neuropathies
- MOA: Thrombotic properties
- Variable VA reduction and recovery

- Cerebral venous sinus thrombosis
  - Risk within 3-12 mo
  - Ophthalmic signs in 70%, presenting symptom in 21%
  - Blur, diplopia, disc edema, proptosis, visual field defects
  - Disc edema in 25-63%
  - STAT Head Imaging

**PDE-5 Inhibitors**

- ED, Pulmonary Hypertension and BPH
- Frequently prescribed (>2% men over age 65)
- One of the largest selling Rx drug in the world
- Well-documented visual side effects
- Possible link to NAION
PDE-5 INHIBITORS

• Link to NAION?
• Blurred vision, disc edema, altitudinal field defects
• Common risk factors: age, vascular conditions, risk of nocturnal hypotension
• MOA: Altering NO → Perfusion of ONH; Nocturnal hypotension
• No large-scale studies with significant evidence
• May be worth warning those at risk

ISOTRETINOIN

• Retinoid and Vitamin A derivative
• Indication: Severe acne; skin, head and neck cancers
• Pseudotumor cerebri
• Vitamin A well-documented cause of PTC
• MOA: Possible alterations in CSF absorption

ISOTRETINOIN

• 1.3% of those with ocular side effects involved the optic nerve
• 67% women, mean age 25
• Avg 2 months after initiating
• May also be treated with tetracyclines, increasing risks

RADIATION-INDUCED OPTIC NEUROPATHY

• Radiation therapy for head and neck tumors – intracranial, sinus, nasopharyngeal, intraocular and intra-orbital tumors
• Any tumors close to the optic nerve, chiasm or optic tract
• MOA: Vascular occlusion and damage causing demyelination, free radical injury

RADIATION-INDUCED OPTIC NEUROPATHY

• Initial stages: Exudative Retinopathy with
  • Disc edema OR
  • Normal appearance if retrobulbar/chiasm affected
• Later stages: Optic nerve atrophy, disc pallor
• Abrupt, progressive, irreversible vision loss, poor prognosis
• Variable visual field loss

RADIATION-INDUCED OPTIC NEUROPATHY

• Proximity, dose, frequency, age, concurrent DM, MS, concurrent chemotherapy, and compressive lesions may influence severity
• Typically occurs 10-20 mos after tx
• No proven treatment
• Anti-VEGF, Hyperbaric oxygen therapy, Intravitreal triamcinolone
**DIFFERENTIALS**

- Compressive, infectious, infiltrative, inflammatory, ischemic, hereditary, nutritional and traumatic optic neuropathies, meningitis, hypertensive emergency, pseudo-papilledema

**MANAGEMENT**

- Careful history
- In office testing
  - Pupils, acuity, color vision
  - Dilated fundus exam
  - Visual fields
  - Blood Pressure
  - OCT RNFL and GC
  - VEP

**ADDITIONAL TESTING**

- MRI with and without contrast
- MRV
- Lumbar puncture with CSF analysis
- Lab testing: CBC, ESR, CRP, tests for infectious etiologies

**INTERDISCIPLINARY CARE**

- Prompt communication
- Primary care
- Specialty prescribing providers
- Referral to ophthalmology
- Recommendation for Screenings
- Low vision

**SUMMARY**

- While rare, many medications can affect the optic nerve by causing optic disc edema and optic neuropathies
- Diagnosis of exclusion
- Careful review of medications
- Many recover some degree of vision if the offending agent is stopped
- Prompt communication with prescribing provider is crucial
References

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Thank You!
The “I’s” in Neuro-Optometry

Iatrogenic #1: Medication Related Conditions
Iatrogenic #2: Perioperative Vision Loss
Inflammatory Thyroid Orbitopathy
Auto-Immune Conditions
Abnormal Intracranial Pressures

EPIDEMIOLOGY OF PERIOPERATIVE VISION LOSS (POVL)
• New-onset visual loss that occurs during or in the period just after non-ocular surgery
• RARE, ~1/60,000 to 1/125,000; may see an ominous increase in incidence
• More common following spine and cardiac surgeries
• American Society of Anesthesiologists (ASA) developed a POVL practice advisory for clinicians

ASA PRACTICE ADVISORY SUMMARY

Table 1: Summary recommendations of the American Society of Anesthesiologists Task Force on perioperative blindness

<table>
<thead>
<tr>
<th>Perioperative Vision Loss (POVL)</th>
<th>Ischemic Optic Neuropathy</th>
<th>Retinal Arterial Occlusion</th>
<th>CRAO</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Risk factors for POVL include:</td>
<td>- Anterior ION</td>
<td>- Posterior ION</td>
<td>- CRAO</td>
</tr>
<tr>
<td>1. Recent cardiac surgery</td>
<td>1. External Ocular Injury</td>
<td>2. Cardiac Mismatch</td>
<td>3. Anterior Angiitis Chiasm Glaucoma</td>
</tr>
<tr>
<td>2. Cortical blindness</td>
<td>2. Cerebral Ischemia</td>
<td>3. Posterior Ocular Injury</td>
<td>4. CRAO</td>
</tr>
<tr>
<td>3. Acute Angle Closure Glaucoma</td>
<td>3. Cerebral Ischemia</td>
<td>4. CRAO</td>
<td>5. BRAO</td>
</tr>
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</table>

ETIOLOGY OF POVL

<table>
<thead>
<tr>
<th>Distribution of Cases from the ASA POVL Registry</th>
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DISCLOSURES
No financial relationship with any company or products mentioned in this presentation
ETIOLOGY OF POVL

Perioperative Vision Loss (POVL)

Ischemic Optic Neuropathy

a. Anterior ION
b. Posterior ION

Retinal Arterial Occlusion

c. CRAO
d. BRAO

EXTERNAL OCULAR INJURY: ANTERIOR SEGMENT

- MOST COMMON: corneal abrasion, irritation secondary to exposure, and/or laceration
- Self-limiting conditions
- Application of lubricants and taping the eyes shut prior to positioning

EXTERNAL OCULAR INJURY: ACUTE ANGLE CLOSURE GLAUCOMA

- RARE after general anesthesia
- Bilateral presentation
- EMERGENCY!!
- Tx: Standard IOP reduction protocol

EXTERNAL OCULAR INJURY: CORTICAL BLINDNESS

- RARE; Higher risk associated with cardiothoracic surgery
- Almost always ischemic in origin
- Most common mechanism is embolic cerebral infarction, usually to the posterior cerebral arteries

RISK FACTORS

<table>
<thead>
<tr>
<th>PRE-Operative</th>
<th>INTRA-Operative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia</td>
<td>Long Duration in the Prone Position</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Decreased Oxygen Perfusion Pressure</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>Excessive Blood Loss &amp; Anemia</td>
</tr>
<tr>
<td>Carotid Artery Disease</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Smoking</td>
<td>Hypoosmotic</td>
</tr>
<tr>
<td>Obesity</td>
<td>Excessive Fluid Replacement</td>
</tr>
<tr>
<td>DM</td>
<td>Elevated Venous Pressure</td>
</tr>
<tr>
<td></td>
<td>Head Positioning</td>
</tr>
</tbody>
</table>
MECHANISMS OF RAO

- 3 main mechanisms:
  1. External ocular compression
     - Improper head positioning or unintended movement of the head
  2. Decreased retinal arterial supply
     - Often related to cardiopulmonary bypass surgery, especially left sided cardiac valve surgery
     - Impaired retinal venous drainage

RETINAL ARTERY OCCLUSION: CLINICAL FINDINGS

- Unilateral painless vision loss
- Retinal whitening may not be initially apparent AND resolves as the retina atrophies

PROGNOSIS, TREATMENT & PREVENTION

- Poor prognosis and available treatment is unsatisfactory
- Proper prone position for surgery
  - Ensure eyes are checked intermittently by palpation or visualization every 20 mins
  - Head/orbit should be place at or above level of the heart
  - Ocular massage to decrease intraocular pressure and dislodge emboli
  - IV acetazolamide or IV thrombolysis
  - Intra-arterial fibrinolysis via a catheter in the ophthalmic artery

ISCHEMIC OPTIC NEUROPATHY (ION)
ISCHEMIC OPTIC NEUROPATHY (ION)

MECHANISM OF AION
- **Arteritic** (inflammatory) vs **Non-arteritic** (occlusive disease or other non-inflammatory disorders)
- Non-arteritic is more common
- NAION usually affects those with a morphologically small or crowded optic nerve head, the “disc-at-risk”
- ION in cardiac surgery has been anterior, in contrast to ION associated with spine surgery which is predominantly posterior

MECHANISM OF PION
- NOT WELL UNDERSTOOD
- PION results from infarction of the intraorbital optic nerve
- Infarction results from hemodynamic or blood flow abnormalities
- Causes for hemodynamic disruption: anemia, hypotension, increased venous pressure, head-down operative position, increased cerebrospinal fluid pressure, direct ocular compression, and embolism
- Infarction may result from a combination of factors
**CLINICAL FINDINGS**

- Painless visual loss in one or both eyes
- Dx typically within 24-48 hrs after surgery, but can be delayed in sedated pts
- Associated APD with unilateral presentation, sluggish pupils, non-reactive pupil
- Severe vision loss with central and peripheral visual deficits
- Color vision decreased or absent

**Characterized according to the segment of the optic nerve involved**

**Anterior ION:**
- ONH is swollen acutely
- Hemorrhaging and CWS
- Late pallor
- RAPD

**Posterior ION:**
- ONH appears normal initially
- Optic atrophy develops over time, late pallor (6-8 weeks)
- RAPD

**PROGNOSIS, TREATMENT & PREVENTION**

- Prognosis is poor and no definitive treatment for PION
- Be aware of external compression to the eye
- Acetazolamide and diuretics reduce IOP and disc edema
- Steroids has not yet been proven
- Hypotension and anemia should be corrected both intra- and post-operatively
  - Careful monitoring of blood pressure during surgery
  - Head-up position if increased ocular venous pressure is suspected
- Hyperbaric oxygen or other drugs to lower IOP
CASE REPORT

- 73 YOM, Annual comprehensive eye exam
- H/o optic atrophy OD>OS secondary to intraoperative ischemic event during heart surgery in 2005
- BCVA:
  - OD: 20/HM @ 3'
  - OS: 20/25+
- Entrance Tests:
  - Equal, Round, Reactive OU, (+)APD OD
  - CVF: complete restriction OD, FTFC OS
  - IOP 27/29 with known h/o ocular HTN OU

ONH PHOTOS & OCT RNFL (OD)

ONH PHOTOS & OCT RNFL (OS)

HVF 30-2
OS ONLY
1. H/o diffuse optic atrophy OD and superior sectorial optic atrophy OS

- Intraoperative ischemic event (CRAO/BRAO vs. bilateral NAION) during heart surgery (quadruple bypass) in 2005
- Severe secondary vision loss OD and inferior altitudinal vision loss OS
- (+)APD OD; OCT RNFL stable OU
- Discussed re-evaluation in low vision clinic to further assess pt's specific needs

ASSESSMENT & PLAN

2. Ocular Hypertension OU

- Consistently elevated IOPs with h/o ischemic optic atrophy: New Tmax OU today
- OCT RNFL OU and last HVF 24-2 OS stable
- Prophylactic treatment vs. observation
- Pt elected to start treatment

OPTOMETRIC MANAGEMENT

- Advise monocular precautions such as safety eye wear and good contact lens hygiene
- Recommend appropriate safety lens materials like Polycarbonate or Trivex
- Preserve remaining vision by treating secondary ocular conditions
- **Low Vision Services

SUMMARY OF PERIOPERATIVE VISION LOSS

- Rare, but among the most devastating complications
- May see an ominous increase in incidence
- Patients undergoing spine surgery are the largest group affected
- Residual effects of anesthetic agents may mask the initial signs and symptoms
- In most cases, the diagnosis is ischemic
- Most commonly: Posterior Ischemic Optic Neuropathy
- Followed by Retinal Artery Occlusion
- Most patients will benefit from low vision services

REFERENCES


THANK YOU!

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QUESTIONS??

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