Diagnostic Dilemmas in Optic Nerve Disease

Peter W. DeBry, M.D.
NV Eye Surgery
Reintroducing Myself

• 10 years in practice in Las Vegas
• Had great experiences moving around the country with medical training (oldest daughter went to 5 elementary schools)
  – Utah
  – Wisconsin
  – Albuquerque
  – Miami (Glaucoma and anterior segment fellowship)
  – Kansas City
What I like to take care of

• Interesting patients who need surgery or medical management of their eye condition
  – Glaucoma
  – Cataract
  – Cornea (DSEK, PKP)
  – Neuro (optic nerve, pupils, visual fields)
  – Pterygium
  – ICL
What I take pride in

• Taking patient care to a higher level than any other practice
• 1st 10 years in practice = focus on technical aspects of surgery and disease management
• New focus = creating programs focused on delivery of care and engaging patients in the treatment of chronic eye diseases
Examples

Common Approach
• What is the diagnosis?
• Which drop is the most effective?
• Which surgery has the lowest side effects?
• Is the field progressing?

Higher Level (trumps common)
• Who puts your eye drops in?
• How much do they cost and can you afford your drops?
• Do you understand why you are supposed to take these medications?
• How can we help you take care of your condition?
How to accomplish this

• Detailed patient education materials
  – Glaucoma
  – Cataract

• Patient care program including workshops
  – Glaucoma
  – IOL Selection

• Clinic visits focused around the social work aspects of patient care
General Information

• NEW Main office located in Henderson
• Satellite clinic on West Sahara and Ft. Apache near Summerlin
• Yes, I still see Lions Club and other indigent patients (Saturday clinics to restart in January)
• No patient will ever get turned away for financial issues!
• But – I do appreciate regular referrals too
Tools for you and your patients

- Web site – www.nveyesurgery.com
- Referral pads
- Business cards

- Available after hours and on weekends to help with patient care
- Put this number in your contacts
  - 702-219-8770
INTRODUCTION
Question – What program suffered a major setback after a 2.2 micron error required a 630 million dollar repair?
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• A) Star Wars Missile Defense System
• B) B-2 Stealth Bomber
• C) Hubble Space Telescope
• D) U.S. Mint printing process for new $100 bill
What program suffered a major setback after a 2.2 micron error required a 630 million dollar repair?

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History of a space telescope

• German rocket scientist Herman Oberth was a pioneering thinker of his time and suggested a space bound telescope as early as 1923

• The American Lyman Spitzer proposed a more realistic plan for a space telescope in 1946 and lobbied for his idea for almost 30 years
History of a space telescope

• In the 1970s NASA and the European Space Agency took up the idea and proposed a 3 meter space telescope

• It was decided to name the telescope after Edwin Powell Hubble who had discovered the expansion of the Universe in the 1920s
An Expensive Endeavor

• Congress eventually approved funding of $36,000,000 for 1978, aiming for a launch date of 1983

• Construction of the mirror began in 1979, starting with a blank manufactured by Corning from their ultra-low expansion glass. Mirror polishing continued until May 1981. NASA was forced to postpone the launch date until March and then September 1986. By this time, the total project budget had risen to $1.175 billion.

• Hubble was finally launched in 1990
Initial Photos

• Best image quality obtained was drastically lower than expected. Images of point sources spread out over a radius of more than one arcsecond, instead of having a point spread function (PSF) concentrated within a circle 0.1 arcsec in diameter as had been specified in the design criteria (ping pong ball at 50 miles)

• Factor of 10 difference in focusing precision
Point Spread Function

- The degree of spreading (blurring) of the point object is a measure for the quality of an imaging system
What had gone wrong?
Options

a) 2.2 micron impurities in the glass were causing an irregular surface to the mirror
b) Heating of the mirror from the sun caused 2.2 micron warping of the mirror
c) The mirror was ground incorrectly with a 2.2 micron thickness error at the periphery
d) A 2.2 micron meteor struck the mirror causing a permanent defect
Amazing Accuracy

• Optical telescopes typically have mirrors polished to an accuracy of about a tenth of the wavelength of visible light

• The Space Telescope was to be used for observations from the visible through the ultraviolet (shorter wavelengths) and was specified to be diffraction limited to take full advantage of the space environment

• Its mirror needed to be polished to an accuracy of 10 nanometers, or about 1/65 of the wavelength of red light
The Flaws of Men

• Mirror grinding was flawed
• At the perimeter the mirror was too flat by about 2,200 nanometers (2.2 microns)
• Error related to minor flaw in the design of the instrumentation required to guide the mirror polishing
• This resulted in induced spherical aberration
Negative Spherical Aberration, Peripheral rays are bent too little

Positive Spherical Aberration, Peripheral rays are bent too much
How do you measure accuracy within the space of a wavelength of light?
Figure 7-4. Displacement due to the interferometer focusing on the field cap instead of the metering rod.
The Fix

• New mirrors needed to be placed further down the image pathway with negative spherical aberration to overcome the induced positive spherical aberration of the first mirror

• Similar concept to Tecnis aspheric IOL with negative 0.27 spherical aberration to balance cornea +0.27 spherical aberration
### Residual Spherical Aberration of Monofocal Lenses (4 mm pupil)

<table>
<thead>
<tr>
<th>Lens</th>
<th>TECNIS® IOL</th>
<th>AcrySof® IQ IOL</th>
<th>B&amp;L LI61A0 IOL</th>
<th>Spherical IOL</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Point Spread Function</strong></td>
<td><img src="image1" alt="Image" /></td>
<td><img src="image2" alt="Image" /></td>
<td><img src="image3" alt="Image" /></td>
<td><img src="image4" alt="Image" /></td>
</tr>
<tr>
<td><strong>20/20</strong></td>
<td>E</td>
<td>E</td>
<td>E</td>
<td>E</td>
</tr>
<tr>
<td>Average Corneal SA</td>
<td>+.27</td>
<td>+.27</td>
<td>+.27</td>
<td>+.27</td>
</tr>
<tr>
<td>Lens SA</td>
<td>-.27</td>
<td>-.17</td>
<td>0.0</td>
<td>+.15</td>
</tr>
<tr>
<td>Total Residual SA</td>
<td>0.0</td>
<td>+0.10</td>
<td>+0.27</td>
<td>+0.42</td>
</tr>
</tbody>
</table>

*Image simulated using ZernikeTool, created by George Dai, PhD.*
Result = sharper photos
Case Presentation

- 68 year-old male presents for a second opinion
- Unhappy with results of cataract surgery done by doctor in St. George, UT this summer
- Patient chose Restor Multifocal IOL
- Has had a film over his vision since the surgery
- Now s/p YAG capsulotomy and on Restasis
Case Continued

• Visual Acuity 20/40 OD, 20/50 OS

• Anterior Segment
  – Mild blepharitis
  – Clear cornea
  – Multifocal IOL in good position
Visual Field
Summary

• Patient has optic atrophy as cause of his visual symptoms rather than a problem with the multifocal IOL
• Nerve ignored by surgeon who gave the patient Restasis and a YAG Capsulotomy trying to improve his acuity
• Pallor can be easily missed if taking a quick glance at a nerve in a pseudophakic patient
• May also have optic nerve issues OS.
Major Nerve Categories

Nerve Edema
- One Nerve
- Both Nerves
- With normal vision
- With decreased vision

Nerve Pallor
- One Nerve
- Both Nerves
- With normal vision
- With decreased vision

Third Category = normal appearance with visual symptoms and VF findings and history suggestive of optic nerve disease
Work-up for this patient

- Category = unilateral optic neuropathy which is subacute and no observed edema
- Requires radiology work-up to rule out compressive lesion
- If MRI normal requires blood testing to rule out treatable causes
Important History Elements

• What could cause nerve damage?
• You get to be the detective
• One situation where the history really can make a difference (compared to cataract)
  – Eye or head trauma
  – Severe hypotension, shock, anemia
  – Family history of eye disease
  – Systemic symptoms
  – Lived outside of US
Systemic Symptoms

- Focal neurological defects (balance, paresthesias, weakness, gait problem)
- Fever, night sweats, fatigue
- Skin rashes, arthralgia
- Cough, shortness of breath
Systemic Symptoms

- Focal neurological defects (balance, paresthesias, weakness, gait problem) MS
- Fever, night sweats, fatigue (GCA, TB)
- Skin rashes, arthralgia (Sarcoidosis, Lupus, Syphilis)
- Cough, shortness of breath (TB, Sarcoidosis)
Next Case

• 37 year-old male with recent decline in visual acuity in the left eye
• No past eye conditions
• No family history of eye disease
What history questions?

- Do you have recent contact with a cat or kitten?
- Recent travel to the East Coast?
- High risk sexual activity?
- Recent fever, fatigue, malaise
Etiology

- Cat Scratch Disease (Bartonella Henselae)
- Lyme Disease
- Syphilis
- Non-specific viral syndrome
- Toxoplasmosis
- histoplasmosis
Neuroretinitis

- Optic nerve edema
- Macular star (hard exudate)
- OCT with subretinal fluid, leaking from nerve
- Minor visual decline
- Generally self limited but may improve faster with appropriate treatment
Case Presentation

• 17 year old girl
• Generally asymptomatic
• With questioning some mild issues discovered (what might you ask)
  – Headache
  – Diplopia
  – Transient visual obscurations
  – Permanent blurred vision
Papilledema

• Both optic nerves swollen from increased intracranial pressure
  – Except Foster-Kennedy Syndrome

• Visual function is normal or near normal
Differential Diagnosis

- Space occupying lesion
- Anatomical pathology (Hydrocephalus)
- Idiopathic Intracranial Hypertension
  - Pseudotumor Cerebri
- Venous Sinus Thrombosis
- Meningitis
IIH Most Commonly

• Young to middle aged female
• Mild to moderate obesity
• Normal MRI
• Normal CSF
• Fortunately most common cause of papilledema
Abnormal morphology

• Causes of a visual field defect
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Last Case

• 56 year old female with sudden onset of a visual field defect
• Medical history significant for diabetes for 25 years
• Acuity 20/20 in each eye
• VF with mild patchy peripheral defects OD
Diagnosis Options

• AION
• Optic Neuritis
• Common problem is that diseases don’t always present in the classic way
# Types of Optic Neuritis

<table>
<thead>
<tr>
<th>Retrobulbar Neuritis</th>
<th>Inflammation of the optic nerve behind the eye, is the form most commonly associated with MS</th>
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</thead>
<tbody>
<tr>
<td>Papillitis</td>
<td>Inflammation of the optic disc, can also be associated with MS.</td>
</tr>
</tbody>
</table>
| Perineuritis         | Inflammation of the optic nerve sheath, sparing the optic nerve itself.  
                      - Patients are older, and vision loss is mild to moderate.  
                      - Due to infectious or inflammation ex: syphilis or sarcoidosis. |
| Neuroretinitis       | Concomitant swelling of the ON & macula. Exudates that form around the macula give the appearance of a star. |
Anterior Ischemic Optic Neuropathy

- Most common acute optic neuropathy in pts > 50 y/o reflecting ischemic damage to the optic nerve head.
- Presenting signs: Painless monocular vision loss developing over hours to days with an RAPD unless bilateral involvement.
- 2 Types: Arteritic & Non-Arteritic
# Anterior Ischemic Optic Neuropathy

<table>
<thead>
<tr>
<th>Arteritic AION</th>
<th>inflammatory &amp; thrombotic occlusion of the short posterior ciliary arteries causing severe Va loss with pale disc edema.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Arteritic AION</td>
<td>Compromise of the optic disc microcirculation in the setting of a ‘crowded’ disc causing hyperemic or pale optic disc edema with less severe vision loss compared to AAION.</td>
</tr>
</tbody>
</table>
Epidemiology-Optic Neuritis in MS

• Most common optic neuropathy in 20-45 years old
• Atypical cases in the elderly
• Uncommon in children < 10 y/o
• 3:2-female:male ratio
• Prodromal flu like illness
• (+) Family Hx of MS (20x greater risk with 1st-degree relatives)
• Caucasian (rare in Asian/African Decent)
• Strong association with HLA-DRB1 antigen
• More common in people who live farther from the equator
Pathophysiology - Optic Neuritis in MS

- Immune-mediated inflammatory demyelination of ON
- Myelin destruction → mononuclear cell infiltration → myelin removal by macrophages
- Astrocytes proliferate → deposition of glial tissue where axons were before
- Gliotic (sclerotic) areas throughout brain & spinal cord → “multiple sclerosis”
Pathophysiology - Optic Neuritis in MS

- Axons now poorly conduct impulses
- Retinal ganglion cell axons starts to degenerate
- Recurrences → more damage to retinal ganglion cells → Irreparable
- Axonal loss ~ ‘black holes’ on MRI
- Inflammation of Optic Nerve + ➖ Va + optic nerve dysfunction
Ophthalmic Presenting Signs - Optic Neuritis in MS

- acute unilateral Va loss
- Periorbital pain with eye movement
- Dyschromatosisia - \(\downarrow\) color vision particularly for red
- \(\downarrow\) peripheral vision
- \(\downarrow\) contrast/brightness sensitivity
- (+) RAPD
- VF defect (50% diffuse, 20% central, rare altitudinal)
- Optic nerve normal or edematous \(\rightarrow\) pallor late in course
- Diplopia
Presenting Signs (continued)

- **Uhthoff’s Phenomenon** – transient deterioration of vision brought on by exercise/ elevation of body temperature

- **Pulfrich Phenomenon** – motion of pendulum appears elliptical due to altered depth perception from delayed conduction in demyelinated nerve

- **Phosphenes** – bright flashes of light with movement of affected eye

- **Photisms** – light induced by noise, smell, taste, touch
Diagnosis-Optic Neuritis in MS

• Clinical diagnosis based on ocular & systemic symptoms and findings
  – Complete Ophthalmic exam & neuro exam
  – Pupillary assessment
  – Color plates
  – Dilated fundoscopic exam

• 1\textsuperscript{st} episode & atypical cases – order MRI of Brain/Orbits with gadolinium + FLAIR (fluid-attenuated inversion recovery)

• Atypical presentations – consider ordering CBC, RPR, FTA-Abs ESR, CRP
Optic Neuritis Treatment Trial (O.N.T.T.)

• Multi-centered, randomized, prospective, controlled clinical trial

• Designed to evaluate the efficacy & safety of oral prednisone vs. IV methylprednisolone followed by oral prednisone compared with oral placebo for treatment of acute optic neuritis

• 15-year f/u on pts with acute unilateral optic neuritis
O.N.T.T. Results

• Va recovery with or without treatment!

• 250 mg IV methylprednisolone QID x 3 days followed by PO prednisone of 1mg/kg/day x 11 days
  – More rapid recovery of Va @ 2 weeks
  – NO improvement of endpoint Va recovery
  – No reduction of risk of subsequent attacks
  – Decreased incidence of MS @ 2 years, but no difference @ 3 years

• PO Prednisone ➔ increased rate of new attacks @ 1 year
  – PO Prednisone alone CONTRAINDICATED!

• Pts with optic neuritis should undergo MRI to r/o demyelinating lesions consistent with MS

• Additional lab tests not necessary for typical optic neuritis, consider for atypical cases
MRI = Prognosis for development of MS

- MRI Brain with (+) T2 hyper intensity lesions = higher MS risk
  - 5 years = 50%
  - 10 years = 60%
  - 15 years = 72%

- Normal Brain MRI = low MS risk
  - 5 years = 15% risk
  - 10 years = 20% risk
  - 15 years = 25% risk
  - Overall Visual acuity was 20/20 or better in 72%, 20/25 – 20/40 in 20% and worse then 20/200 in 3%

- No MS @ 15 years in pts with:
  - painless optic neuritis, no light perception vision at onset, severe disc edema or disc hemorrhage, or macular star figure exudate
Treatment

In Pts with no prior Hx MS or Optic Neuritis:
• 250 mg IV methylprednisolone QID x 3 days followed by PO prednisone of 1mg/kg/day x 11 days
  – Speeds up recovery by 1-2 weeks
  – Taper prednisone over 4 days (20 mg day 1, 10 mg days 2 and 4)
  – Anti-ulcer meds for GI prophylaxis (ex: ranitidine)

• In cases where rapid return of vision is essential (ex: monocular pt or occupational need) IV methylprednisolone on outpt basis considered
  – Otherwise, treatment for visual recovery is not indicated.

In Pts with diagnosis of MS or Optic neuritis previously
• Observation
  Re-examine pt in 4-6 weeks after presentation & then q 3-6 months
Epidemiology – Arteritic AION

• Arteritic AION
  – Usually occurs in older patients with a mean age of 70.
  – Signs/Symptoms temporal arteritis typically present
    • Headache, temporal tenderness, jaw claudication, malaise, anorexia, weight loss, fever, joint & muscle pain, ear pain
Diagnosis—Arteritic AION

• Definitive Diagnosis: Temporal Artery Biopsy
  – 2 cm bx – minimum length
  – Do not delay treatment to wait for bx
  – Bx able to be performed up to 2 weeks after the start of steroid treatment
Epidemiology – Non-Arteritic AION

- NA-AION
  - Mean age of 60 years (younger than AAION)
  - F=M

- Increased risk in pts with:
  - HTN
  - DM
  - Smokers
  - Hyperlipidemia
  - Use of phosphodiesterase inhibitors

- Unproven risk factors:
  - Sleep apnea, hyperhomocysteinemia, platelet polymorphisms, nocturnal hypotension
Diagnosis—Non-Arteritic AION

• No definitive diagnosis, diagnosis primarily clinical

• Typical history includes:
  – Acute, painless, unilateral vision loss
  – Classic findings on examination including a hyperemic and swollen optic nerve with peripapillary splinter hemorrhages
  – Fellow eye with a small cup to disc ratio ‘disk at risk’
Treatment– Arteritic AION

• IV Methylprednisolone @ 1 gram/day for first 3-5 days

• PO Prednisone (up to 100mg/day) tapered slowly over the following 3-12 months
  – Alternate day treatment = inadequate
  – Medrol dose pack = inadequate
Treatment— Non-Arteritic AION

• No proven treatment for NA-AION
• Ischemic Optic Neuropathy Decompression Trial (IONDT)
  – No benefit of surgery
• No proven prophylaxis, however pts typically placed on a daily 81mg ASA.
# Anterior Ischemic Optic Neuropathy

<table>
<thead>
<tr>
<th></th>
<th>Arteritic (A-AION)</th>
<th>Non-Arteritic (N-AION)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Avg ~ 70 years</td>
<td>Avg ! 60 years</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>F &gt; M</td>
<td>F = M</td>
</tr>
<tr>
<td><strong>Associated Symptoms</strong></td>
<td>HA, Scalp tenderness, jaw claudication, transient Va loss</td>
<td>Usually None</td>
</tr>
<tr>
<td><strong>Va</strong></td>
<td>&lt;20/200 in &gt; 60% pts</td>
<td>&gt;20/200 in &gt; 60% pts</td>
</tr>
<tr>
<td><strong>Disc/Fundus</strong></td>
<td>Pallid disc edema, cup normal, CWS</td>
<td>Hyperemic disc edema, fellow eye with small C:D ‘disc at risk’</td>
</tr>
<tr>
<td><strong>ESR</strong></td>
<td>~70 mm/hr</td>
<td>20-40 mm/hr</td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td>Elevated</td>
<td>Normal</td>
</tr>
<tr>
<td><strong>FA</strong></td>
<td>Disc delay &amp; Choroid delay</td>
<td>Disc delay</td>
</tr>
<tr>
<td><strong>Clinical Course</strong></td>
<td>Rarely Improves</td>
<td>31% cases improve</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Systemic Steroids</td>
<td>None Proven</td>
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