Glaucoma Clinical Conundrums
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Abstract: During the course of caring for patients with glaucoma, clinicians will undoubtedly encounter clinical issues that are challenging and controversial. This lecture will examine several clinical conundrums such as to what to do when a patient develops a disc hemorrhage, what to do when patients can’t or won’t use medications, whether or not to judge progression based upon structural or functional changes, and whether or not the patient has glaucoma or some other disease. This course will discuss these and other clinical conundrums and, combined with evidence based medicine, suggest options and approaches for each situation.

Conundrum: Is this really glaucoma?
• Optic nerve anomalies: ONH hypoplasia, coloboma, buried drusen, optic pits, tilted disc, obliquely inserted disc, etc. These are misdiagnoses.
• Neurological diseases: optic atrophy, chiasmal syndromes, compressive lesions of the anterior visual tract. These are misdiagnoses.
  • Arteritic anterior ischemic optic neuropathy does have enlargement and deepening of the optic cup, but has other features including devastating sudden vision loss and disc pallor that are not found in glaucoma

Not All –Omas are Glaucoma: “-Omas”
• Pituitary adenoma
• Craniopharyngioma
• Meningioma
• Glioma
• Metastatic carcinoma
• “Ischemioma”
• Anterior ischemic optic neuropathy (AION)
  • Both arteritic and non-arteritic
• Congenitaloma
• Coincidentaloma
• Prolonged compression results in optic atrophy, which may present with pallor and/or cupping of the nerve head.
• Optociliary collateral vessels may be noted at the disc margin.
• There will frequently be increased progressive cupping of the optic nerve head somewhat similar to that seen in glaucoma.
  • The main differentiating factor from glaucomatous optic atrophy is the pallor of the remaining neuroretinal rim in compressive neuropathy.
• Additionally, there is more significant neuroretinal rim compromise in the form of notching that occurs in glaucoma but not in compressive lesions where cup increase is more symmetrical with pallor.
• Associated field defects include central scotomas, arcuate or altitudinal defects, paracentral scotomas, field constriction, and defects respecting the vertical hemianopic line.

**Conundrum: Help, my patient can’t/won’t afford/use medications. What do I do?**

• Resources for patient assistance
  o RXHOPE
  o Drug company patient assistance programs

• Generic medications
  o Issues, safety, effectiveness of generics for glaucoma
  o Laser Trabeculoplasty: SLT and Efficacy
  o SLT & ALT are equivalent in their capacity to decrease the IOP in glaucoma patients
  o Produces different effects at the treatment site
  o ALT induces mechanical alterations, due to collateral thermal effects
  o SLT induces no apparent tissue alterations, due to the lack of such thermal effects
  o It is believed that SLT can be performed more than once, but this is unproven. Most will only repeat one time.
  o Lack of coagulative necrosis produced by SLT is related to the nanosecond duration of each pulse and the selective targeting of melanin chromophores
  o Application of SLT obliterated macrophages, leaving the non-pigmented lining TM cells intact
  o An acceptable if ephemeral initial therapy option

• Trabeculectomy vs. Minimally Invasive Glaucoma Surgery (MIGS):
  o Appear to have improved safety profile over trabeculectomy, but reduced efficacy
  o Procedures:
    o Canaloplasty
    o Trabectome
    o Glaukos iStent
    o ECP

**Conundrum: The medications are hurting the ocular surface. What are my options?**

• Tafluprost
  o Preservative free PGA in unit dose vials

• Cosopt PF
  o Preservative free combo med in unit dose vials
  o Safety, tolerability and efficacy?

• Travatan Z
  o Sofzia, not BAK

• Simbrinza
  o Very low concentration of BAK

**Conundrum: Should I look at structure or function when trying to judge progression?**

• Progression can be categorized as event analysis or trend analysis
  ▪ Event analysis- compares baseline to most recent data; change as dictated by criteria has occurred or not
Trend analysis looks at the significance of rate of change over time.
  • Identifies progression by looking at patient behavior over time.
  • Uses all data points and a linear regression formula
  • Main weakness: progression is not necessarily linear
Glaucoma progression rate is the most important determinant of therapy and future visual impairment
Past progression rate is the most influential determiner of future progression rate
Measuring rate of progression is difficult as it is hard to differentiate true change from variation in testing.
Progression may be measured by
  • Functional change as indicated by visual field deterioration
  • Structural change in the optic disc or retinal nerve fiber layer
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In reality, there are patients that show structural changes first in glaucoma (likely the majority) and others that show functional changes first
The combination of a functional test (visual field analysis) and a structural measurement (disc photograph or imaging device) allows for most accurate diagnosis as one alone is likely not enough.
Importance and limitations of clinical assessment
  • Wide diversity of normal appearance
  • Potential overlap of non-glaucomatous and glaucomatous
Clinical application of imaging
  • Diagnosis
    • Normal vs. abnormal
  • Determination of progression or stability
Limitations of Functional Measurement
  • Reliability and reproducibility biggest limiting factor
    • In the OHTS, an attempt was made to identify the occurrence of normal visual field test results following 2 vs. 3 consecutive, abnormal, reliable test results in the OHTS study
Limitations of Structural Measurement
  • Artifact in acquisition
    • Motion, media, placement of measurement, operator skill
  • Anatomy not consistent with normative database to which patient is being compared
- severely tilted discs, extreme variations in disc size, high myopia
- Very early damage
  - acquired change has occurred but does not exceed the range of normal values
- Advanced damage
  - little value obtained from images from clearly end extensively abnormal optic nerves and retinal nerve fiber layer
  - dynamic range of device is exceeded, abnormality is clear, values too low to be able to determine progression
- Subjective interpretation of results

**Conundrum: Help! My patient has a disc hemorrhage and the pressure is 12 mm. Now what?**
- Disc hemorrhages
  - Patients with normal tension glaucoma, primary open angle glaucoma, ocular hypertension
    - Anemia, posterior vitreous detachment, vascular occlusion can cause hemorrhages of the disc that are mistaken for glaucomatous disc hemorrhages
  - Ischemic or mechanical
  - Probable infarction of the blood supply to the ONH
  - Inferior, inferior temporal, superior, superior temporal regions of the disc most susceptible and account for virtually all true disc hemorrhages
    - Hemorrhages at other areas of the disc (nasal and temporal) tend to not be associated with glaucoma
  - Typically occurs where notches occur
  - Resides in the retinal nerve fiber layer
    - Not in the cup!
  - Small and contiguous with the neuroretinal rim
  - Can be recurrent and, if it recurs, it typically is in the same place on the disc each time
  - Precedes notching, NFL defect, field loss. Perhaps the earliest change in glaucoma (if it happens)
  - More common in patients with large IOP variations
  - Meaning is unclear – possibly indicates poor control of IOP?
    - EMGT study showed that lowering IOP cannot prevent disc hemorrhages from occurring
  - Disc hemorrhages do not constitute a diagnosis of glaucoma nor a progression or conversion to glaucoma or an endpoint for any major glaucoma studies

**Conundrum: Should I look at the ganglion cell complex or nerve fiber layer to diagnose glaucoma?**
- Ganglion Cell Complex (GCC)
  - Measures thickness for the sum of the ganglion cell layer and inner plexiform layer (GCL + IPL layers) using data from the Macular 200 x 200 or 512 x 128 cube scan patterns.
RNFL distribution in the macula depends on individual anatomy, while the GCL+IPL appear regular and elliptical for most normals. Thus, deviations from normal are more easily appreciated in the thickness map by the practitioner, and arcuate defects seen in the deviation map may be less likely to be due to anatomical variations.

Conundrum: The diagnostic imaging doesn’t agree with my diagnosis? Now what?
- Issue of ‘red disease’
- Understanding imaging interpretation and role in glaucoma diagnosis