When Retina Meets Vitreous

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Course Goal

- To provide useful clinical information in the diagnosis and treatment of vitreous and vitreo-retinal interface disorders.

Introduction

Anatomy and Physiology of the Posterior Segment

The Vitreous Humor

- Composition of the vitreous humor
  - Water
  - Hyaluronic acid
    - Provides elasticity, viscous quality
  - Protein
    - Type II Collagen
      - supports shape

The Vitreous

- Anterior Vitreous Base
  - Pars Plana
- Posterior Vitreous Base
  - Ora Serrata
- Vitreous-lens interface
- Posterior Retina and Optic N.
Vitreous

- Functional Anatomy of the Anterior Vitreous
- Anterior Vitreous Base
  - Pars Plana
- Posterior Vitreous Base
  - Ora Serrata
- Vitreous-lens interface

Functional Anatomy: The Vitreous

- Vitreous cavity ~4 ml in volume
  - 80% of globe’s total volume
- Composed of water, proteins, and mucopolysaccharides (MPS).
  - Protein
    - Type II
    - Type 9
      - Helps support shape
  - MPS
    - Hyaluronic acid
      - Gives vitreous elastic and viscid qualities

Vitreous Basics

- Position – located between the lens and retina and fills the center of the eye
- The largest tissue of the eye
- Comprised of ~99% H2O

Vitreous Basics

- Function:
  - Acts as a storage area for metabolites for retina and lens
  - Provides an avenue for the movement of these metabolites within the eye
  - Acts as a "shock absorber" (due to its viscoelastic properties) protecting fragile retinal tissue during rapid eye movements or strenuous activity
  - Transmits and refracts light; absorbs UV
  - Source of ascorbic acid (Vitamin C)

Cloquet’s Canal

Cortical Vitreous – Posterior Hyaloid

- Posterior Hyaloid
  - Vitreous posterior to the vitreous base
  - Attachment of vitreous to retina is tenuous (except at ON & macular region)
Two-Zone Classification

- Clinical view
  - Cortical Vitreous
  - Central Vitreous

• Cortical Vitreous (Cortex)
  - Outer rim of vitreal cavity
  - Firmer than central vitreous
  - 100-200 μm thick
  - Makes up 2% of vitreous volume
  - Contains both anterior & posterior hyaloid
  - Randomly arranged fibrils
  - Metabolic centre
    - Contains vitreous cells - Hylotytes

Persistent Hyperplastic Primary Vitreous or Persistent Fetal Vasculature

Physiologic Changes

- With age, liquification due to reduction in hyaluronic acid causes loss of support.
  - This process is referred to as synchesis.
- Vitreous shrinkage and collapse (syneresis) can cause traction.

The Vitreoretinal Interface

Complete PVD
Anomalous PVD

• May damage the cells of the trabecular meshwork
• May also induce apoptotic neuronal cell death
• Oxidation of lens nuclear proteins causes nuclear sclerosis

Oxidative Stress

- Ascorbate

Vitrectomy surgery offers highly suggestive evidence that an intact vitreous gel protects against POAG.

When the gel is removed surgically, a substantial % of eyes show evidence of POAG if followed long term.

Chang estimated the risk to be 15 -20% of eyes with long term follow-up.

Vitreous loss during cataract surgery in glaucoma pts. affects long term control of IOP.

The crystalline lens and intact vitreous gel is protective against POAG.

Evaluate the entire vitreous routinely.

Evaluating the Vitreous
Examine the Vitreous Routinely

- Anterior
- Intermediate
- Posterior
- V/R Interface

Ominous Clinical Signs

- Pigment
- Heme
- Inflammatory cells

Rhegmatogenous Retinal Detachment

Vitreoretinal Interface

Evaluate the vitreoretinal interface routinely.

Watzke-Allen Test

- Subjective
- Purpose: identify full-thickness v. lamellar
- Fundus lens at SL
- Vertical beam
- Central break indicates full-thickness
- Maddox rod, direct scope
Lamellar Macular Defects

ERM with Macular Pucker
Epiretinal membrane with macular pucker, pseudohole

Hole eventually forms in the posterior vitreous which allows liquefied vitreous to rush into the retrovitreal space, rapidly separating the posterior hyaloid from the retina

Posterior Vitreous Detachment
Foss, et. Al:
• 10% < 50 years old
• 27% 60-69 years old
• 63% > 70 years old
Evaluate PVD on day of event:
• Then 1 week?
• Then 2 months
Case: 58 y/o WM  
Gradual blur, VA 20/60

Posterior Segment Applications of OCT
- Vitreous/Vitreoretinal Interface
- Neurosensory retina, RPE
- Choriocapillaris
- Optic Nerve/NFLA

The Vitreous

Persistent Vitreomacular Adhesions

Vitreoretinal interface without PVD
PVD initially occurs in the perifovea with a predilection for superior quadrant.
Detachment extends widely in the perifovea with persistent attachment to fovea, optic nerve head.
Detachment occurs in the fovea, persistent attachment of the posterior vitreous face to the optic nerve head.
Detachment is complete with release of the vitreo-papillary adhesion.

Liquefaction w/out vitre-o-retinal dehiscence

Anomalous PVD
Partial Thickness = vitreoschisis  Full-Thickness with partial PVD
Premacular Membrane  Peripheral Separation Post. Traction
Centrifugal outward contraction  Centripetal inward contraction  VMTS  Exudative ARMD
Macular Hole  Macular Pucker  Vitreo-Papillopathies

Retinal-Tears/BD
VMA-related Diseases by Mechanism

Vitreomacular Adhesion
- May hasten the AMD process.

Additional Reading
Emerging nonsurgical methods for the treatment of vitreomacular adhesion: a review

Asteroid Hyalosis
Reports exist that suggest an association between asteroid hyalosis and diabetes mellitus. Other investigators dispute such an association.

Yu and Blumenthal proposed that asteroid hyalosis results from aging collagen, whereas other studies suggested that asteroid formation is preceded by depolymerization of hyaluronan.

Questions and Comments?
Case: 72 y/o WF
Gradual central blur OS
VA = 20/100
**Patient OR**

- 78 yo female
- Vision has been decreasing lately
- 20/50 OD and 20/40 OS
- Pupils normal
- 2+ cataracts (hazy view)
- Matrix VFs show some defects OU
Line Scan of Macular OCT OS

Retinal Thickness OU OCT

Amsler grid OS

Line Scan of Macular OCT OS 1 wk later
- It was measured to be 172u
Line Scan of Macular OCT OS 1 mon later

Vitreous traction RD

Serous RD PVD OCT

Patient Z
- 57 yo male
- Complains of distortion in the vision of the OS for the past month which is worse on reading or looking down. Started in 4'-06
- 20/20 OD/OS
- Pupils normal

Parafoveal Traction OD

V-F Traction OS 5-11-06
V-F Traction OS 5-11-06

V-F Traction OS pre accommodation 12-8-06

V-F Traction OS during accommodation 12-8-06

V-F Traction OS post accommodation 12-8-06

Amsler Grid post accommodation 12-8-06

V-F Traction OS 4-18-07
Pharmacologic Vitreolysis - Microplasmin

Pharmacologic Vitreolysis Based on Biochemical Prop.

<table>
<thead>
<tr>
<th>Enzymatic</th>
<th>Non-Enzymatic</th>
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<tr>
<td>• Non-Specific</td>
<td>Urea/Vitreosolve</td>
</tr>
<tr>
<td>• Tissue plasminogen</td>
<td>RGD peptides</td>
</tr>
<tr>
<td>• Microplasmin</td>
<td></td>
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<td>• Nattokinase</td>
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Substrate Specific

• Chondroitinase
• Dipase
• Hyaluronidase

MIVI-TRUST Program

• Microplasmin for IntraVitreous Injection-Traction Release without Surgical Treatment
• Two randomized, placebo controlled, double-masked, multi-center trials (Phase III)
  – single-dose 125-μg intravitreal Ocriplasmin (ThromboGenics) v. placebo for symptomatic VMA.
• Primary endpoint of both trials was resolution of VMA one month after injection.
• Over 650 patients were enrolled
• 90 centers in 7 countries.
Results

- At 28 days, VMA resolved in 29.8% of 464 eyes treated with Ocriplasmin and 7.7% of 188 eyes given placebo.
- Total posterior detachment occurred in 17% of treated eyes.
- Moreover, 25.5% of treated eyes gained two or more lines of acuity at 6 months.
- At 6 months, 40.6% of treated eyes achieved full-thickness macular hole closure, compared with only 17% of placebo eyes.

Status of Ocriplasmin
Pharmacologic Vitreolysis

- ThromboGenics gained FDA approval and will bring Ocriplasmin to market in the U.S. in January 2013.
- New unique ICD-9-CM disease code approved specifically for vitreomacular adhesion (VMA).
- ICD-9 = 379.27

Epiretinal Membrane
ERM
Patient ARN

- 58 yo female
- Fell down steps while texting
- Floater appears almost immediately OS
- 20/50 OD and 20/20 OS
- Nuclear sclerotic cataract OD

ERM P200C OS 2-20-10

3-D OD 2-20-10

ERM Mac Thickness OS 2-20-10
Vitrectomy for PDR

Anomalous PVD

- May hasten the Wet AMD process.

The Posterior Hyaloid in AMD

- If microplasmin can successfully produce a PVD, there may be some future therapeutic benefit in the prevention of progression to wet AMD.

> Sebag J, Binder S. Posterior hyaloid adhesion is significantly increased in NV AMD. Program and abstracts of the 40th Annual Scientific Meeting of the Retina Society; September 27-30, 2007; Boston, Massachusetts.

Extracellular matrix “glue” = fibronectin, laminin, opitcin, chondroitin sulfate, heparan sulfate

BIO with Scleral Depression

- Brings the peripheral retina into better view
- Does not induce further detachment

Retinal Breaks and Detachments
Retinal Breaks

Retinal breaks in symptomatic eyes should be treated.

Types of RD

- Rhegmatogenous
  - Secondary to breaks
- Tractional
  - Fibrosis, Neovascularization
- Exudative/Serous
  - Tumor, Inflammation, Acute HTN

RRD Treatment Strategy

- Find and treat all breaks
- Relieve traction
- Drain/remove sub-retinal fluid

~95 % Success rate with Vitrectomy and …

- Scleral buckle
- Gas bubble
- Silicone Oil

Scleral Buckle
Review of Key Points

- The vitreous has long been an under-examined tissue.
- The vitreous has been an under-recognized cause of macular pathology.
- OCT has led to an increased recognition of the role of the posterior vitreous.

Conclusions

- Despite some success in clinical trials, rates of spontaneous PVD using microplasmin are relatively low.
- The future of pharmacogenic vitreolysis will likely involve simultaneous administration of different agents.
  - Liquefactants
  - Weakening of V/R adhesion

Thank you!

Bill and Joe