Morning Report
04/27/2011

Brad Gustave MD
Patient Presentation

• 24 day old infant
• CC: “Spot” in both eyes
• HPI:
  • Father has noted “spot” on right eye since birth.
  • Noted by primary care physician approximately 1 week prior to presentation
  • Close examination revealed a similar spot in patient’s left eye as well
  • Father feels child is able to track and seems to see
  • No other problems developmentally or physically
  • Patient was term with no complications pre/peri/post-partum
Patient Presentation

- Birth History: Uncomplicated
- PMHx: No documented medical problems
- Meds: None
- ALL: NKDA
- Social Hx: Lives at home with family, no abuse, no trauma
- Family Hx: glasses, glaucoma, ARMD, adult-onset cataracts
- ROS: As per HPI
Exam

- **Va**: BTL
- **IOP**: 15
- **Pupils**: Normal

**RE**  
**LE**

**BTL**  
**BTL**

**8**  
**Normal**
<table>
<thead>
<tr>
<th></th>
<th>RE</th>
<th>LE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial Structures:</td>
<td>No abnormalities</td>
<td></td>
</tr>
<tr>
<td>Lids/Lashes:</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Conj/Sclera:</td>
<td>W&amp;UI</td>
<td>W&amp;UI</td>
</tr>
<tr>
<td>Cornea:</td>
<td>Clear</td>
<td>Clear</td>
</tr>
<tr>
<td>AC:</td>
<td>D &amp; Q</td>
<td>D &amp; Q</td>
</tr>
<tr>
<td>Iris:</td>
<td>Iris Lens Adh</td>
<td>Normal</td>
</tr>
<tr>
<td>Lens:</td>
<td>dim RR Both, 3 mm, Cataract R &gt; L</td>
<td></td>
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</tbody>
</table>
### Fundus

<table>
<thead>
<tr>
<th></th>
<th>RE</th>
<th>LE</th>
</tr>
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<tbody>
<tr>
<td>Disc:</td>
<td>0.1, rms hlthy</td>
<td>0.1, rms hlthy</td>
</tr>
<tr>
<td>Macula:</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Vessels:</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Periphery:</td>
<td>Normal</td>
<td>Normal</td>
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Differential Diagnosis
Congenital Cataracts

• **Bilateral**
  - Idiopathic (30%)
  - Autosomal Dominant (30%)
  - Identifiable (30%)
    - TORCHS
    - Metabolic
      - Galactosemia
      - Hypocalcemia
    - Oculorenal Disease
      - Lowe
      - Alport

• **Identifiable (Cont)**
  - Craniofacial Syndromes
    - Hallerman-Streiff
  - MSK
    - Myotonic dystrophy
  - Aniridia
  - Trisomy 21/13/18
  - Iatrogenic: Steroids/Radiation
Bilateral

• Metabolic workup required
  – RBC galactokinase, Urine reducing substances, Calcium, Phosphorus, TORCHES titers, Urine amino acids

• CE recommended around 6 weeks

• > 3 mm are often visually significant

• Surgery in better seeing eye 1st, then 2nd eye closely thereafter

Our Patient

- TORCH titer
  - Negative
- RBC Galactokinase
  - Negative
- Ca/Phos
  - Normal
- Urine Reducing Substances
  - Initially positive, retest negative
- Urine Amino Acids
  - Normal
- Urinalysis
  - Normal
Associations

• Lowe: X-linked recessive
  – Renal tubulopathy: aminoaciduria, proteinuria, rickets
  – Hypotony and mental retardation
  – Cataract type: Posterior lenticonus

• Alport: X-linked
  – Basement membrane disorder
  – Renal failure with HTN, deafness, renal cysts
  – Cataract: Anterior lenticonus
Associations

– Galactosemia: Autosomal recessive
  • Mental retardation, hepatomegaly, jaundice and malnutrition
  • Cataract: Oil droplet cataract

– TORCH: Rubella
  • Glaucoma, microphthalmos, necrotizing iridocyclitis, retinopathy, corneal clouding
  • Cataract: Nuclear
Associations

- Hypocalcemia: Sporadic
  - Symptoms of hypocalcemia
  - Cataract: Punctate iridescent opacities in anterior/posterior cortex
Anterior Polar Cataract

- Alport’s Syndrome
- Characteristics:
  - <3mm in diameter
  - Non-progressive
  - Not visually significant
  - Anisometropia is common
Posterior Subcapsular

- Hypocalcemia
- Characteristics
  - Bilateral
  - Progressive
Nuclear

- Rubella
- Idiopathic
- Characteristics
  - 3 mm in diameter
  - Irregularity extends peripherally
  - Density variable
  - May enlarge
Lamellar

- Idiopathic
- Characteristics
  - 5 mm or more
  - Onset usually after birth
  - Better fixation
  - Visual prognosis comparatively better after surgery
Posterior Lenticiconus/Lentiglobus

• Galactosemia
• Lowe
• Characteristics:
  – Thinning of central posterior capsule
  – “Oil Droplet” appearance
Visual Assessment

• Younger than 2 months
  – Fixation not developed
  – > 3 mm are typically significant
  – Red reflex
  – Strabismus in unilateral
  – Nystagmus in bilateral

• Older than 2 months
  – Fixation behavior: Fixation preference, objection to occlusion
Surgery

• Timing
  – Younger children: early to prevent amblyopia
  – Older children: when interference with visual need
  – Recommended: < 20/40

• IOL placement
  – Infants
    • Rapid shift in refractive error during first 1-2 years of life
    • High complication rate
  – Improved success rates after 1-2 years of life
Surgery

• Technique
  – Vitreorhexis
  – Removal of lens material
  – Posterior Capsulotomy
    • Prevents inevitable posterior opacification
  – Anterior vitrectomy
Amblyopia

- Treat as quickly as possible with correction
- Contact lenses or glasses
- Treat to produce myopia as most visual activity is at near
- Monocular aphakia: contact lenses optimal if tolerated
- Part time occlusion in unilateral/assym bilateral cases
- Later: placement of IOL
Complications

• Major: Aphakic and pseudophakic glaucoma
• Rare:
  – Retinal detachments
  – Macular Edema
  – Corneal abnormalities
Aphakic Glaucoma

• Incidence after removal of congenital cataract 15-50%
• Typically occurs several years after lensectomy
  – Can occur weeks to months after
• Lifelong risk
• Mechanisms
  – Outflow compromise
    • Abnormal angle, early surgery/inflammation, loss of lens support
The Infant Aphakia Treatment Study

Design and Clinical Measures at Enrollment

The Infant Aphakia Treatment Study Group

- Randomized clinical trial
- 114 infants, unilateral cataracts 4 wks - 7 mo (28 to 210 days)
- CE + CL, CE + IOL/Spectacles.
- Compare visual outcomes contact lenses and IOLs for infantile aphakia
The Infant Aphakia Treatment Study

Design and Clinical Measures at Enrollment

The Infant Aphakia Treatment Study Group


<table>
<thead>
<tr>
<th>Table 1. IATS Inclusion/Exclusion Criteria</th>
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<tr>
<td><strong>Inclusion Criteria</strong></td>
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<tr>
<td>1. Visually significant congenital cataract (≥3 mm central opacity) in 1 eye</td>
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<td>2. Aged 28 d to &lt;7 mo (&lt;210 d) at time of cataract surgery</td>
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<td>3. At least 41 postconceptional weeks at time of cataract surgery</td>
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<td>4. Written informed consent provided by parent or legal guardian agreeing that patient could be randomized in operating room if EUA confirmed that patient was eligible for study</td>
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<tr>
<td><strong>Exclusion Criteria</strong></td>
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<tr>
<td>1. Cataract was known to be due to trauma or acquired as adverse effect of treatment administered postnatally</td>
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<td>2. Corneal diameter &lt;9 mm</td>
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<td>3. Intracocular pressure ≥26 mm Hg</td>
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<td>4. PFV causing stretching of the ciliary processes or tractional detachment of retina</td>
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<td>5. Active uveitis or signs suggestive of previous episode of uveitis</td>
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<td>6. Child was product of preterm pregnancy (&lt;36-wk gestational age)</td>
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<td>7. Retinal disease that may limit visual potential of eye</td>
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<td>8. Previous intracocular surgery</td>
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<td>9. Optic nerve disease that may limit visual potential of eye</td>
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<td>10. Fellow eye had ocular disease that might reduce its visual potential</td>
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<tr>
<td>11. Child had medical condition that might interfere with visual acuity testing at age 12 mo or 4½ y</td>
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<tr>
<td>12. Child was not able to return to IATS clinical center for regular follow-up examinations</td>
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Abbreviations: EUA, examination under anesthesia; IATS, Infant Aphakia Treatment Study; PFV, persistent fetal vasculature.
The Infant Aphakia Treatment Study

Design and Clinical Measures at Enrollment

The Infant Aphakia Treatment Study Group

- Ψ: IOL with posterior capsulectomy and anterior vitrectomy through pars plicata
- Aphakic: CE, posterior capsulectomy, ant vit
- Patching to phakic eyes in all pts until 8 mo of age
- Follow-up: 1 day/wk/mo, 3 mos then Q3-month (±2 wk), then 4, 4 1/4, 4 1/2, and 5 yrs
- Primary Outcome: Acuity @ 12 mo and 4 1/2 yrs
• Results: Median logMAR Va not significantly different
  – (contact lens group, 0.80; IOL group, 0.97; P=.19).
• IOL group: more surgery, more complications
  – (63% vs 12%; P.001).
• Conclusions: Caution performing IOL implantation in children aged 6 months or younger given the higher incidence of adverse events and the absence of an improved short-term visual outcome compared with contact lens use.
Infantile Aphakic Glaucoma: A Proposed Etiologic Role of IL-4 and VEGF

- Normal Human TM cells and Fetal Lens Epithelium Cells were grown in culture (48 hours)
- LECs and TM cells then combined in culture
- RayBio Human Cytokine Antibody Array
  – IL-4, VEGF, TGFBeta2,
  – LEC + TM, and in isolation
- TM with cytokines
- TM with LECs +/- inhibitors
Infantile Aphakic Glaucoma: A Proposed Etiologic Role of IL-4 and VEGF

Inbal Michael, PhD; David S. Walton, MD; Shulamit Levenberg, PhD


• Results:
• LECs exclusively demonstrated IL-4 and TGFB2
• TM with IL-4 +/- VGEF
  – TM cell enlargement/abnormality
• TM with VEGF alone
  – No significant TM cell enlargement/abnormality
• TM with TGFBeta2 alone
  – Normal size, greater number
Infantile Aphakic Glaucoma: A Proposed Etiologic Role of IL-4 and VEGF

Inbal Michael, PhD; David S. Walton, MD; Shulamit Levenberg, PhD

- TM + LECs
  - Larger number of cytokines
  - Abnormal TM structure
- TM + LECs + Inhibitors
  - Return to normal structures
Infantile Aphakic Glaucoma: A Proposed Etiologic Role of IL-4 and VEGF

Inbal Michael, PhD; David S. Walton, MD; Shulamit Levenberg, PhD

Figure 4. Proposed mechanism of infantile aphakic glaucoma development. Residual lens epithelial cells secrete vascular endothelial growth factor (VEGF) and interleukin-4 (IL4) to the aqueous humor, which drains into the trabecular meshwork (TM) tissue. VEGF and IL4 bind to receptors on TM cells, and activate biological processes, resulting in altered TM cells, leading to development of aphakic glaucoma. This mechanism should be further validated in vivo. IOL = intraocular lens.