LONG TERM RESULTS OF PLANNED PRETERM DELIVERY AND TREATMENT OF NORRIE DISEASE

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DISCLOSURES

• Robert Sisk, MD
  • Leica (C)
  • Gyroscope (C)
  • AGTC (A, C)
• Virginia Utz, MD – Retrophin (R)
• Terry Schwartz, MD - None
SUMMARY

- There were no late sequelae or developmental delay after planned preterm delivery and ablative laser treatment for Norrie disease.
- The retinas remained attached and no further treatment was required beyond the first year of life.
- Despite no neurovascular development of the fovea at birth, visual function gradually improved over the first few years of life.
REVIEW OF PAST HISTORY

- +FamHx Norrie disease (Older brother and maternal uncle blind at birth from TRD OU) and +NDP, +LRP5 by amniocentesis
- Delivered at 34 weeks GA with EUA; 2 days later, laser ablation of avascular retina, and intravitreal bevacizumab (IVA) OS
- Zone 1 ROP/PFV phenotype OU with severe FEVR-like capillary abnormalities and preretinal neovascularization
REVIEW OF PAST HISTORY

• At 20 weeks postnatal, limited vitreous hemorrhage OU from hyaloid artery regression was treated with repeat IVA OU

• OCT demonstrated no foveal architecture at birth or during first year of life
NDP/NORRIN FUNCTIONS TO:

• Stimulate retinal angiogenesis and capillary development from the superficial vascular plexus from the astrocytic framework
• Regress hyaloid vascular system
• Promote retinal ganglion cell survival
WITHOUT NORRIN:

• Angiogenesis beyond vasculogenesis does not occur, including lack of deep retinal vessels
• Creates relative ischemia, even in portions of the retina with larger vessels coursing through them
• Hypoxia upregulates VEGF-A, HIF-1α, and Angiopoietin 2, which promote retinal neovascularization
• Fibrosis, tractional retinal detachment, and pseudoglioma formation with secondary microphthalmia from RD/tethering by hyaloid system that failed to regress
# FUNCTIONAL OUTCOMES: FIRST YEAR OF LIFE

<table>
<thead>
<tr>
<th>Age</th>
<th>Binocular Visual Acuity (Teller)</th>
<th>Refractive Error</th>
<th>Other Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 mos</td>
<td>20/540 (38 cm)</td>
<td>-9.50+1.00x100 -8.00+3.75x097</td>
<td>-Horizontal right jerk nystagmus - Alternating XT</td>
</tr>
<tr>
<td>5 mos</td>
<td>20/360 (38 cm)</td>
<td>-8.50+3.00x080 -8.00+5.00×100</td>
<td>Horizontal right jerk nystagmus - Alternating XT</td>
</tr>
<tr>
<td>9 mos</td>
<td>20/360 (38 cm)</td>
<td>-8.50+3.00x080 -8.00+5.00×100</td>
<td>Horizontal right jerk nystagmus (improved) X(T)</td>
</tr>
<tr>
<td>12 mos</td>
<td>20/190 (38 cm)</td>
<td>-8.50+3.00x080 -8.00+4.75x100</td>
<td>Horizontal right jerk nystagmus (improved) X(T) (well-controlled)</td>
</tr>
</tbody>
</table>
5 YEARS LATER:

Near = 20/40 with +4.00
Nystagmus – intermittent, dampens with convergence, and small left face turn
Green = normal VF
Red = Patient’s VF

1cm round stimulus, 100% contrast against white background
DISCUSSION

• Patient has functional real-world vision - drives dirt bikes, plays baseball, and attends regular school with help from low vision aids.

• Foveal vascularization never progressed beyond pattern observed at birth, even in eye not initially treated with bevacizumab.

• Visual acuity improvement over time may relate to foveal differentiation or cortical development (visual maturation).

• Recurrent retinal neovascularization or secondary vitreo-retinal traction was not observed beyond the first year of life.
CONCLUSIONS

• The onset of RD in Norrie disease is unknown. Prenatal genetic confirmation and preterm delivery affords the opportunity to prevent lifelong blindness by ablative laser and intravitreal bevacizumab

• Visual acuity improved despite foveal hypoplasia and incomplete retinal vascular development, and the patient achieved a highly functional visual outcome