Intra-Arterial Chemotherapy for Treatment of Retinoblastoma:
Keeping an Eye on Therapeutic Advancements in Interventional Radiology

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Disclosures

• I am not a Physician, topics discussed in this presentation is from my perspective and experiences at Seattle Children’s Hospital.

• I do not have any affiliation to any products, equipment or pharmaceuticals discussed in this presentation.

• Some devices are considered OFF label use and may not be FDA approved for pediatric use.
Retinoblastoma Background
Retinoblastoma – malignant tumor of the retina that typically present before 5 years of age.

- Non Hereditary Retinoblastoma
  - RB1 genes in a single retinoblast (immature cell) undergo the mutation sometime after conception or birth
  - Typically develops in only one eye (unilateral)
  - Does not have an increased risk of developing other cancers, and their offspring have the same risk of developing retinoblastoma as other children in the population
Background

• Genetic Retinoblastoma
  • Test positive for the RB1 Gene deletion or duplication
  • Increase risk of Bilateral disease
  • The increase risk of tumor in the offspring of a child with the genetic form of retinoblastoma is about 50%.
  • Increase the risk of developing other cancers later in life
  • Radiation concerns!!
<table>
<thead>
<tr>
<th>Group</th>
<th>Subgroup</th>
<th>Quick reference</th>
<th>Specific features</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>Small tumor</td>
<td>Retinoblastoma ≤3 mm in size*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Larger tumor</td>
<td>Retinoblastoma &gt;3 mm in size* or</td>
</tr>
<tr>
<td>B</td>
<td>B</td>
<td>Macula</td>
<td>Macular retinoblastoma location (≤3 mm to foveola)</td>
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<tr>
<td></td>
<td></td>
<td>Juxtapapillary</td>
<td>Juxtapapillary retinoblastoma location (≤1.5 mm to disc)</td>
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<td></td>
<td></td>
<td>Subretinal fluid</td>
<td>Clear subretinal fluid ≤3 mm from margin</td>
</tr>
<tr>
<td>C</td>
<td>C1</td>
<td>Focal seeds</td>
<td>Retinoblastoma with</td>
</tr>
<tr>
<td></td>
<td>C2</td>
<td></td>
<td>Subretinal seeds ≤3 mm from retinoblastoma</td>
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<td></td>
<td>C3</td>
<td></td>
<td>Vitreous seeds ≤3 mm from retinoblastoma</td>
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<td></td>
<td></td>
<td></td>
<td>Both subretinal and vitreous seeds ≤3 mm from retinoblastoma</td>
</tr>
<tr>
<td>D</td>
<td>D1</td>
<td>Diffuse seeds</td>
<td>Retinoblastoma with</td>
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<td>D2</td>
<td></td>
<td>Subretinal seeds &gt;3 mm from retinoblastoma</td>
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<td></td>
<td>D3</td>
<td></td>
<td>Vitreous seeds &gt;3 mm from retinoblastoma</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Both subretinal and vitreous seeds &gt;3 mm from retinoblastoma</td>
</tr>
<tr>
<td>E</td>
<td>E</td>
<td>Extensive</td>
<td>Extensive retinoblastoma occupying &gt;50 percent globe or</td>
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<tr>
<td></td>
<td></td>
<td>retinoblastoma</td>
<td>Neovascular glaucoma</td>
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<td></td>
<td>Opaque media from hemorrhage in anterior chamber, vitreous, or subretinal space</td>
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<td></td>
<td>Invasion of postlaminar optic nerve, choroid (&gt;2 mm), sclera, orbit, anterior chamber</td>
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* Refers to 3 mm in basal dimension or thickness.

Treatment Options

• 1800’s – Early 1900’s Enucleation was the only option

• Development of External Beam Radiation Therapy, Advance chemotherapy treatments, Local Cryotherapy, Vitreal Chemo Injections

• 2004 Japanese Yamane & Kaneko introduced IA chemo with the use of micro occlusion balloons placed just distal to the orifice of the OA then infusing chemo indirectly in the OA.

• 2006 Abramson & Gobin (NY Memorial Sloan-Kettering) advancing the Japanese technique by performing super selective catheterization of the OA
WORKUP OF RETINOBLASTOMA PATIENT

Referral to:
- Ophthalmology
- Oncology

Preliminary Eye Exam by Ophthalmology

DIAGNOSTIC WORKUP

Arrange for:
- MRI (CT if <3mo) of orbit and brain
- CBC, BUN, Cr, AST, ALT, Alk Phos, bili u/c
- RB1 deletion/duplication analysis – peripheral blood + tumor, if available

Examination under anesthesia (EUA) by experienced Ophthalmologist

Staging using international classification

Decision on definitive therapy

Possibility for useful vision

Disease in orbit, brain, nodes or marrow → RB BAT for Metastatic Disease

Group E - No useful vision present or likely

- Enucleation of eye
- Follow-up exams

Optic nerve positive beyond Lamina cribrosa but not to cut end of nerve

- Start on RB BAT for Nerve Positive
  - Line placement
  - VCE chemotherapy x 6 cycles
  - MRI before 4th and after 6th cycles
- Follow-up exams

Small tumors (Group A & Some Group B) amenable to local therapy

- Local therapy to eye (laser, cryotherapy) – q6wk EUA until disease control
- Follow-up exams

Vitreous seeding or tumor too large for local therapy – Groups C, D, and some E

- VCE chemotherapy x 4 cycles – EUAs before 3 & 4, MRI after 4 cycles
- Until response or max 6 cycles given - Incomplete by cycle 4, add Carboplatin and Topotecan for 4, 5, & 6
- Enucleation
- Follow-up exams

Intra-arterial Melphalan x 3 courses

Complete response

Incomplete response

Start on RB BAT for Nerve Positive

- Line placement
- VCE chemotherapy x 6 cycles
- MRI before 4th and after 6th cycles
- Follow-up exams
Leukocoria Diagnosis

Symptoms:

• A pupil that looks white or red instead of black
• Strabismus (crossed eye)
• Poor vision
• A red, painful eye
• An enlarged pupil
• Differently colored irises
Diagnostic Evaluation
Retinal Photographs

Pre

Post IA Chemo
Diagnostic Evaluation
MRI Axial T2 Imaging

Pre

Post IA Chemo
Procedure
### Medication Safety

#### IR Arteriogram Cerebral Plan - RADIOLOGY USE ONLY (Pending/Review)

<table>
<thead>
<tr>
<th>Component</th>
<th>Status</th>
<th>Details</th>
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<tbody>
<tr>
<td><strong>Medications</strong></td>
<td></td>
<td></td>
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<tr>
<td>1. Amobertil</td>
<td></td>
<td>500 mg intramuscular ONE TIME (Unscheduled), send visit to IR for procedure, to be mixed by radiologist and radiologist at the time of procedure.</td>
</tr>
<tr>
<td>2. Lidocaine (lidocone 1% injectable for IR USE ONLY)</td>
<td></td>
<td>10 mL by injection ONE TIME (Unscheduled), for IR procedure.</td>
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<tr>
<td>3. Iverol (iv. 60 mg/ml) (Optrynt-320)</td>
<td></td>
<td>6 mL/kg intravenous IR ONE TIME (Unscheduled), Max dose 200 mL, for IR procedure.</td>
</tr>
<tr>
<td>4. Heparin (heparin 1 unit/mL in NS for IR USE ONLY)</td>
<td></td>
<td>500 mL (route is not applicable) ONE TIME (Unscheduled), for IR procedure.</td>
</tr>
<tr>
<td>5. Nitroglycerin (Nitroglycerin 2% topical ointment)</td>
<td></td>
<td>Apply 0.1 inch strip on chest topically ONE TIME (Unscheduled), for chest vasospasm, for IR procedure, 9 to 5 years of age.</td>
</tr>
<tr>
<td>6. Phenylephrine ophthalmic (phenylephrine 2.5% ophthalmic solution)</td>
<td></td>
<td>2 drops topically ONE TIME (Unscheduled), routine for ophthalmic artery myelphlum injection, for IR procedure, Apply 2 drops to the skin of the for...</td>
</tr>
<tr>
<td>7. Verapamil (Verapamil 0.5 mg/mL in NS for IR USE ONLY)</td>
<td></td>
<td>2.5 mg intramuscular ONE TIME (Unscheduled), Initial Dose 0.1 mg/kg. Will order as 0.5 mg in 3 mL of NS. Actual dose used is determined during an...</td>
</tr>
<tr>
<td><strong>Radiology</strong></td>
<td></td>
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<tr>
<td>8. IR Arteriogram Cerebral</td>
<td></td>
<td>Radiological examination, not elsewhere classified.</td>
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Chemotherapy

- Chemo Roadmap/Orders are placed by HemOnc with set doses based on age/weight of patient

- Chemo double check

- Treatment options
  - **Single drug therapy** – 3-5mg of Melphalan
    - 20mL NS volume with a 1mL per minute injection
  - **Triple drug therapy** – Topotecan, Carboplatin, and Melphalan
    - 10mL NS volume each with a 1mL per minute injection

- Medication Transfer Risk
  - Staff Exposure/ Disposal
  - Bubbles
Procedure Supplies

- 4fr Terumo Pinnacle Vascular Sheath

- 4fr Cordis Vert Catheter 0.038” acts as a guiding catheter

- Medtronic 1.5fr (0.5mm) Marathon Micro-catheter with Mirage 0.008” wire

- Stryker 1.7fr Excelsior SL10 with Synchro 2 soft 0.014” wire

- MicroVention 1.3fr or 1.6fr Duo Headway Micro-catheter
Normal Anatomy
Micro-catheter Placement
Carotid Loop

AP

Lateral
Menigolacrimal Arterial Supply
Persistent Dorsal Ophthalmic Artery
Persistent Dorsal Ophthalmic Artery
Closing

• Challenges
  • Pediatric anatomy
    • OA Catheterization in a patient less than 6 years of age
      • Femoral sheath vessel occlusion
      • Micro Catheter vessel occlusion
    • Spasm
      • Verapamil
  • Melphalan has a life span of 60 minutes
    • Potency
  • Reconstitution of the chemo agent with the timing of the catheterization
  • Delivery and verification of the medication
  • Administration in 15-20 minutes prior to Melphalan expiration

• GOAL of SAVING the GLOBE
Questions?

Thank You!

Contact Information
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