Intra-Arterial Chemosurgery for Advanced Intraocular Retinoblastoma: 9-year experience

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Retinoblastoma
- Cancer of the retina
- Children < 3-year-old
- Rb1 Gene mutation 40%
- Presenting signs:
  - leukocoria: 60%
  - Strabismus: 25%
  - painful glaucoma: 10%
- Late diagnosis: leukocoria tumor visible through an undilated pupil is already large.

May 2006: selective ophthalmic artery infusion of chemotherapy: Chemosurgery
MSKCC
Cornell- NYPH

Inclusion/Exclusion criteria
- Intra-ocular tumors
- Local ophthalmic treatment by laser or cryotherapy impossible or would compromise vision
- First line treatment
- Age ≥ 3-month and weight > 6 Kg

Chemosurgery protocol
- EUA +/- chemo surgery at 4 weeks interval
- General anesthesia
- Alternate femoral puncture
- Heparin IV 80 mg/kg
- 5 hour recovery
Current drug dosage

<table>
<thead>
<tr>
<th>Age/Drug</th>
<th>3-6 month</th>
<th>6-12 month</th>
<th>1-3 year</th>
<th>&gt; 3 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melphalan</td>
<td>2.5-3 mg</td>
<td>3 mg</td>
<td>4 mg</td>
<td>5 mg</td>
</tr>
<tr>
<td>Topotecan</td>
<td>0</td>
<td>0.5 mg</td>
<td>1 mg</td>
<td>1 mg</td>
</tr>
<tr>
<td>Carboplatin</td>
<td>30 mg</td>
<td>30 mg</td>
<td>40 mg</td>
<td>50 mg</td>
</tr>
</tbody>
</table>

Increase dose:  
- OA has large extra ocular branches  
- Insufficient result from previous cycle  
- Balloon and MMA

Decrease dose:  
- Recent IV chemo/EBR  
- Wedge flow  
- ERG decrease previous cycle  
- Inflammatory reaction previous cycle  
- Total dose would be > 0.5 mg/kg

Before After
**Patient population**  
(May 30 2006 to June 10 2015)

- 381 eyes treated in 305 patients
  - Sex: 165 females, 140 males
  - Age: 1 month to 21 years (median: 15 months, mean: 21 months)

- Previous treatments:
  - IV chemotherapy: 127 (42%)
  - Bridge: 21 (7%)
  - EBR: 15 (5%)
  - IAC (other center): 34 (11%)
  - Contralateral enucleation: 27 (9%)

**Complications of 1112 procedures in 305 patients**  
(extra ocular)

- Cerebral:
  - 1 mild hemiparesis 2 weeks (normal MRI)

- Bronchospam reaction: 25%
  - 2nd and later 1st but can be present at first injection
  - More frequent in youngest children
  - Watch Tidal Volume
  - Epinephrine (0.5 to 1 mcg/Kg)

- Epistaxis: 3

- Allergy:
  - Iodine: 3
  - Carboplatin: 1

- Systemic toxicity:
  - Neutropenia (ANC<1000): 23% patients
    - Recently: 3%
  - Symptomatic (8.5%): 13 required GCSF, 6 transfusions, 7 admissions for neutropenic fever

**Complications of 1298 infusions in 381 eyes**  
(ocular)

- Toxic retinopathy: 5 avascular retinopathy, all in the first 100 infusions
  - All had previous treatment
  - All had high dose IA and ≥ 5 treatments
  - Dose predictor of toxicity
- Inflammatory reaction: 9%
- Periocular blush (melphalan only)
  - Transient discoloration: 20% melphalan injection
  - Permanent sequelae: 3 (2 small scars, 1 permanent pigmentation)
  - Phenylephrine (AK dilate) cutaneous: 2 erythema desquamation

- Temporary loss of eye lashes: 7% (1 frontal alopecia)
- Temporary ptosis + ONP: 5%
- CRAO:
  - 2 (same patient, one side recovered)
  - 1 hemGRAO
- CRVO: 1
- Purtscher retinopathy: 1
- ON swelling, transient: 4
Prevention:
- Catheterization:
  - 3F (1mm) femoral sheath
  - no guide catheter
  - Catheterization of ostium OA (1.5F - 0.5mm - catheter)
  - No wedge flow (no flow arrest) in the OA
- Anticoagulation
- Epinephrin
- Dose of chemotherapy adapted to age and anatomy (decided by INR)
- Steroids IV then oral
- Nasal vasoconstrictor + Skin vasoconstrictor

Eye survival (no enucleation)

Kaplan-Meier estimate of ocular survival:
- 88% at 2 years
- 77% at 5 years
- 71% at 7 years

Conclusion
- In eyes with advanced retinoblastoma
  IA chemotherapy: cure > 70% eyes
- Minimal complication and predictable ocular toxicity

For advanced Retinoblastoma, Chemosurgery has become the first line treatment, before IV chemotherapy and Radiation

Thank you