Treatment of Transient Peripheral Neuropathy During Chimeric 14.18 Antibody Therapy in Children with Neuroblastoma: A Case Series

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Introduction

- Ch14.18: human-mouse chimeric antibody against GD2 ganglioside
- Causes tumor cell lysis through complement activation or ADCC (antibody dependent cellular cytotoxicity) reactions
- Treatment for children with high-risk neuroblastoma
- Daily 10 hour infusion x 4 days
- MOST COMMON side effect: PAIN - transient, located in extremities, abdomen, and back
- Transient pain syndrome compared to neuropathic pain
- Other expected toxicities: fever, tachycardia, tachypnea, hives and thrombocytopenia
- Our current practice: morphine nurse controlled analgesia (NCA), 2h prior to infusion until 1h post infusion

Methods

- Retrospective chart review of 8 patients
- Treated at Children’s National Medical Center 2009-2012
- Morphine NCA during first chimeric antibody infusion
- Recorded effectiveness (FLACC), morphine requirements, side effects and adverse events

Results

- Morphine NCA: demand dose 0.02 to 0.04mg·kg⁻¹, lockout interval 8-20 minutes, basal rate 0.02 mg·kg⁻¹·h⁻¹
- Dosing increased and time interval decreased in 2 of 8 patients during their 4-day infusion
- One patient on continuous morphine infusion (0.02 mg·kg⁻¹·h⁻¹) with once per hour as needed morphine bolus (0.25 mg·kg⁻¹) instead of NCA (mean FLACC 3.5)
- No serious or life-threatening adverse effects

Table 1: Characteristics of Study Patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>4.5 (2-8)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>15.4 (11.9-22)</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>4/4</td>
</tr>
<tr>
<td>FLACC</td>
<td>1.75 (0-5)</td>
</tr>
<tr>
<td>Morphine (mg/kg/d)</td>
<td>0.5 (range 0.29-1.15)</td>
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<tr>
<td>Pain medications upon discharge</td>
<td>0 (0)</td>
</tr>
</tbody>
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Discussion

- Major side effects: intense pain and allodynia during antibody infusion
- Associated with increased heart rate and hypertension
- Pain syndrome similar to neuropathic pain
- Described as opioid-resistant
- Compared to adults, GD-2 induced pain less severe and less opioid-resistant in children
- Recent studies with IV lidocaine to control anti-GD2 antibody induced pain: no significant difference in morphine requirements and a significant increase in emesis on infusion day 4
- Morphine NCA appears safe and effective in treating Ch14.18 induced transient peripheral neuropathy
- Methods for this pain syndrome are still developing, warranting future studies

References