Outcomes of children with opsoclonus myoclonus syndrome and neuroblastoma: the MSK experience 2000-2018

Patel A1; Basu EM2, MD; Kushner B2, MD; De Braganca KC2,3, MD; Khakoo Y2,3,4, MD

1 Medical Student, NYU School of Medicine, New York, NY, USA
2 Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA
3 Department of Neurology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
4 Department of Pediatrics, Weill Medical College of Cornell University, New York, NY USA
Disclosures

- Naevus International: Board Member
- Nevus Outreach Inc.: Board Member
- Child Neurology Society: Scientific Advisory Committee
- MSK: Information Technology Committee
- Amgen: Brother is head of oncology clinical trials
The successful person is the one who had the chance and took it.

– Roger W. Babson
My journey to OMS

- 1982-1986: Barnard College, Columbia Univ, BA, Chemistry
- 1986-1990: Medical School at Columbia University College of Physicians and Surgeons
- 1990-1993: Pediatric internship and residency: UCSF
- Maybe neurology is a good choice for me?

- 1993: Adult neurology rotation at the VA
- Paraneoplastic syndromes project UCSF plus Memorial Sloan Kettering Cancer Center
- MSKCC for Fellowship
- Large NB population
Incidence: Adults vs. children
Paraneoplastic Syndromes (PNS)

- Tumor-associated, immune-mediated syndromes

- Neurologic PNS
  - Antibody against a tumor antigen cross-reacts with antigen in the nervous system
  - Occurs in 0.01% of all cancer patients
  - Symptoms precede diagnosis of cancer in 50% of patients
  - E.g.: Lambert-Eaton Syndrome, OMS, sensory neuronopathy, cerebellar degeneration, etc.
  - Pediatric: OMS, NMDAR encephalitis
Opsoclonus Myoclonus Syndrome (OMS)

- Incidence: 1 in 10 million; 2-3% of all neuroblastoma patients
  - Up to 50% of children with OMS also have a neuroblastoma

- Clinical features: abnormal eye movements, jerking of the arms and legs, and incoordination
  - Behavior problems/irritability; sleep disturbances

- OMS and neuroblastoma (NB)
  - Lower stage/risk grouping of NB
  - MYCN amplification typically not seen
  - Better overall survival with respect to NB than patients with non-OMS associated NB

- Treatment: tumor resection and immunomodulation
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¹ Medical Student, NYU School of Medicine, New York, NY, USA
² Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, NY, USA
³ Department of Neurology, Memorial Sloan Kettering Cancer Center, New York, NY, USA
⁴ Department of Pediatrics, Weill Medical College of Cornell University, New York, NY USA
Hypotheses

1. Early initiation of IVIg, ACTH, and rituximab combination therapy may improve outcomes, as determined by treatment duration and OMS relapse.

2. Beginning 2 years post treatment completion, childhood immunizations can resume without complications, including no recurrence of OMS.
Methods

- IRB approval was obtained prior to data collection.

- Reviewed the records of 15 patients with NB-associated OMS who received care at MSK from 2000-2016.

- Variables including clinical presentation, treatment, outcomes, and long-term sequelae were collected.

- A univariate descriptive analysis was conducted.
Results

Patient characteristics and clinical presentation

- Median age at diagnosis = 16 months (range: 4-21 months)
- Twelve of 15 patients presented with stage 1 NB
  - The remaining patients: stage 2B (1), intermediate risk stage 4 (1), and stage 4S (1)
- Favorable tumor histology in 80% of the patients
- No patients had MYCN amplification
• Mean treatment duration: 47 months (range: 1 – 96 months)

- I = IVIg
- A = ACTH
- R = Rituximab
- D = Dexamethasone
- C = Low dose chemotherapy

### Results cont.

#### Treatment

<table>
<thead>
<tr>
<th>Number</th>
<th>OMS Treatment</th>
<th>Treatment duration</th>
<th>OMS Relapse</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>I, A, D, R, C</td>
<td>48 months</td>
<td>Y</td>
</tr>
<tr>
<td>2</td>
<td>I, A, R, C</td>
<td>Transfer</td>
<td>N</td>
</tr>
<tr>
<td>3</td>
<td>I, A</td>
<td>Ongoing</td>
<td>N</td>
</tr>
<tr>
<td>4</td>
<td>I, A, R, C</td>
<td>72 months</td>
<td>Y</td>
</tr>
<tr>
<td>5</td>
<td>I, A, R</td>
<td>72 months</td>
<td>Y</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>1 month</td>
<td>N</td>
</tr>
<tr>
<td>7</td>
<td>I, A, R</td>
<td>36 months</td>
<td>N</td>
</tr>
<tr>
<td>8</td>
<td>I, A, D, R</td>
<td>Transfer</td>
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<tr>
<td>9</td>
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<td>10</td>
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<tr>
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</tr>
<tr>
<td>15</td>
<td>I, A, R</td>
<td>96 months</td>
<td>Y</td>
</tr>
</tbody>
</table>
Results cont.

- Seven patients received rituximab within 3 months of diagnosis.
  - Only 1 patient in this group had OMS relapse, which occurred during ACTH taper.

- Six patients received rituximab 4 or more months after diagnosis.
  - Five of these patients had OMS relapse. One patient has active therapy 10 months since diagnosis.
Outcomes

- Overall survival is 100% at 1-15 years (median: 9) from diagnosis
- One patient has had relapse of NB: very unusual
- Neurologic sequelae

![Bar chart showing neurologic outcomes]
- Behavior problems
- Motor deficits
- Cognitive deficits
- Speech delay

No. of patients
Revaccination

- 5 patients resumed childhood immunizations without complications, including no recurrence of OMS
- Reinitiating vaccinations 2 years after treatment completion with no interim OMS recurrence
- Pre-vaccination evaluation:
  - Reconstitution of immune system (lymphocyte panels normalized)
  - No need to check vaccine titers prior to revaccination (we did this initially but no evidence that this is helpful)
  - No need to check titers after revaccination
- Live vaccines are last
- Patients may receive vaccine at primary care providers
Other pearls

• One of the risks of rituximab is reactivation of hepatitis B
  – In addition to IgA levels we have also begun to check hepatitis serum panel on all children prior to IVIG initiation (as well as IgA levels)
• No child developed PML after rituximab treatment
Future directions

• Collecting clinical data for patients regarding relapse
  – Neuropsychologic testing for all our patients
• Working to better understand OMS pathophysiology
• COLLABORATIONS in US and International
Conclusion

• Patients with NB-associated OMS had excellent overall survival.

• Early initiation of rituximab, in combination with IVIg and ACTH, may be associated with lower risk of OMS relapse and shorter treatment duration.

• Vaccinations can be resumed without exacerbations of OMS symptoms, following a 2-year period of no recurrence.
Acknowledgements

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