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

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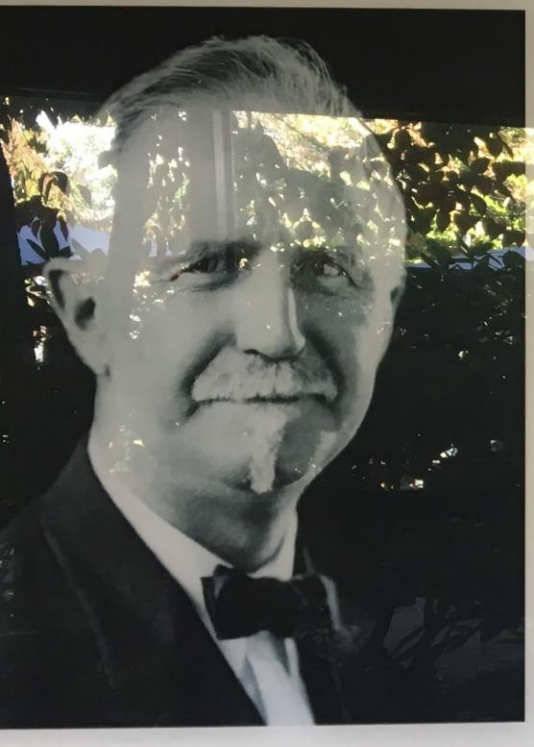
Disclosures

- 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



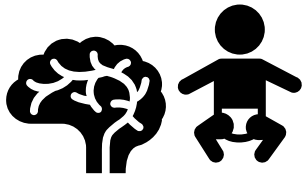
The successful person is the one who had the chance and took it.

– 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?
- 1993-1996: Child Neurology residency: UCSF

- 1993: Adult neurology rotation at the VA
- Paraneoplastic syndromes project UCSF plus Memorial Sloan Kettering Cancer Center
- MSKCC for Fellowship
- Large NB population

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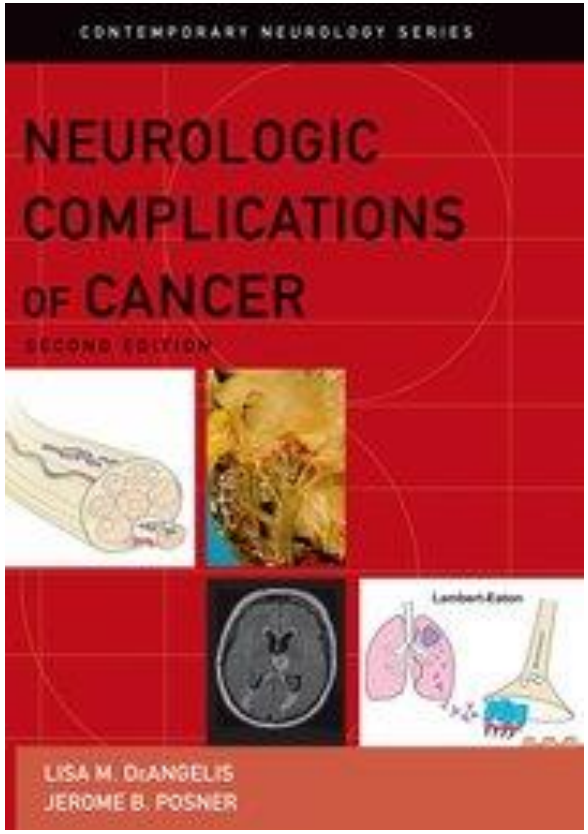
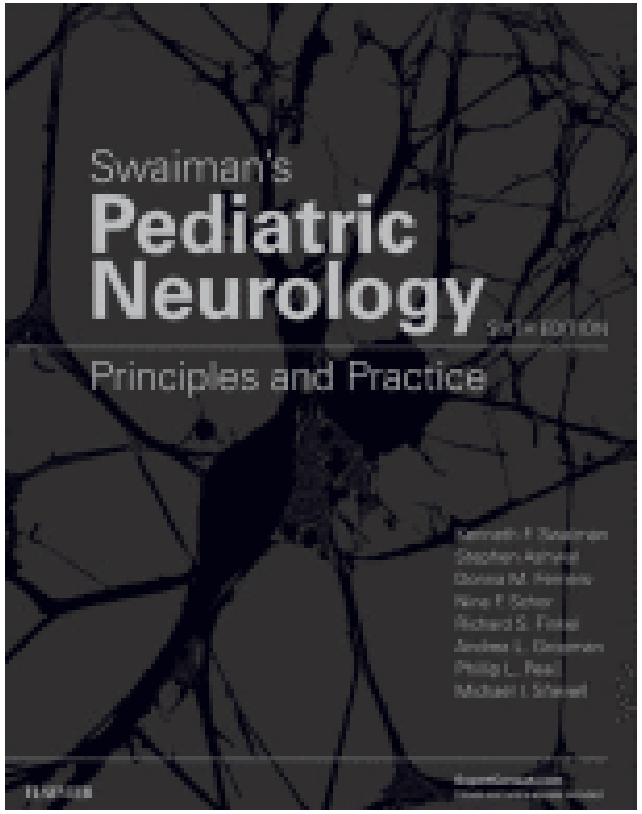
Incidence: Adults vs. children





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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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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.

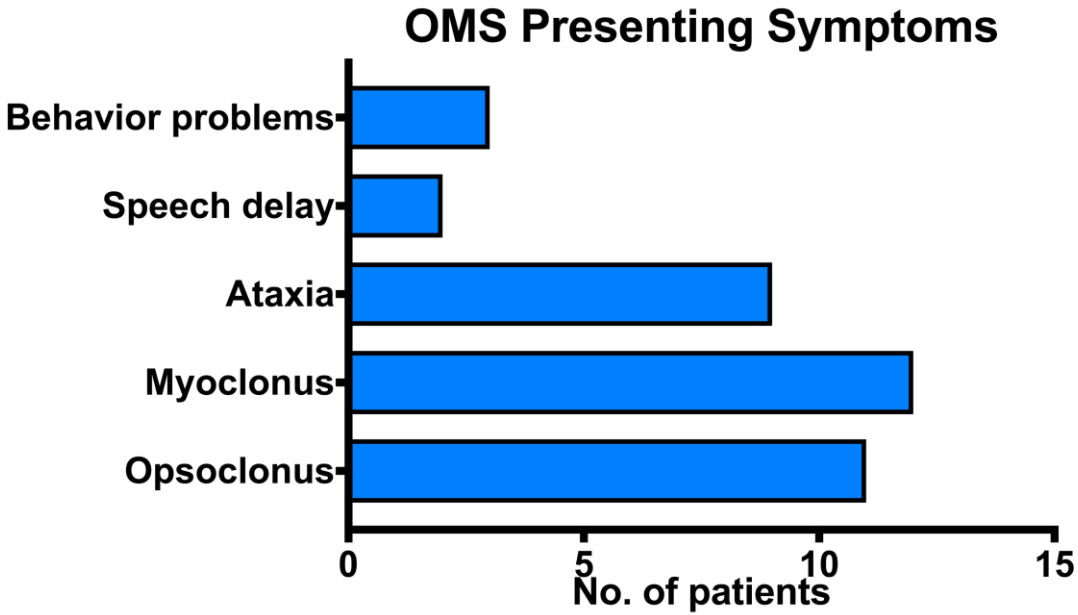
Methods

- 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



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Results cont.

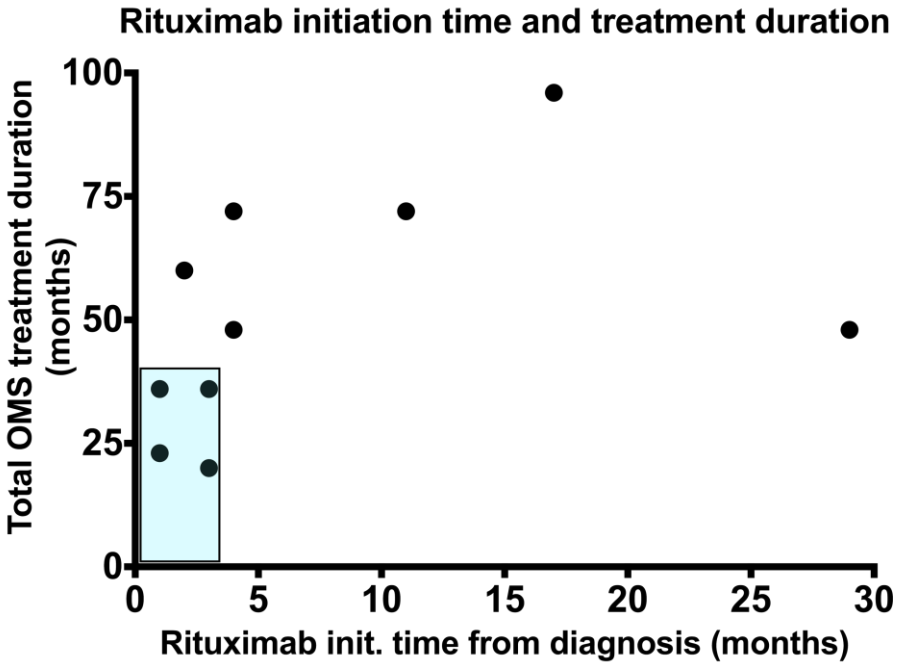
Treatment

Number	OMS Treatment	Treatment duration	OMS Relapse
1	I, A, D, R, C	48 months	Y
2	I, A, R, C	Transfer	N
3	I, A	Ongoing	N
4	I, A, R, C	72 months	Y
5	I, A, R	72months	Y
6		1 month	N
7	I, A, R	36 months	N
8	I, A, D, R	Transfer	N
9	I, A, D, R	Ongoing	N
10	I, A, R, C	48 months	Y
11	I, A, D, R	20 months	N
12	I, A, R, C	60 months	Y
13	I, A, R	23 months	N
14	I, A, D, R	36 months	N
15	I, A, R	96 months	Y

- Mean treatment duration: 47 months (range: 1 – 96 months)

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

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.

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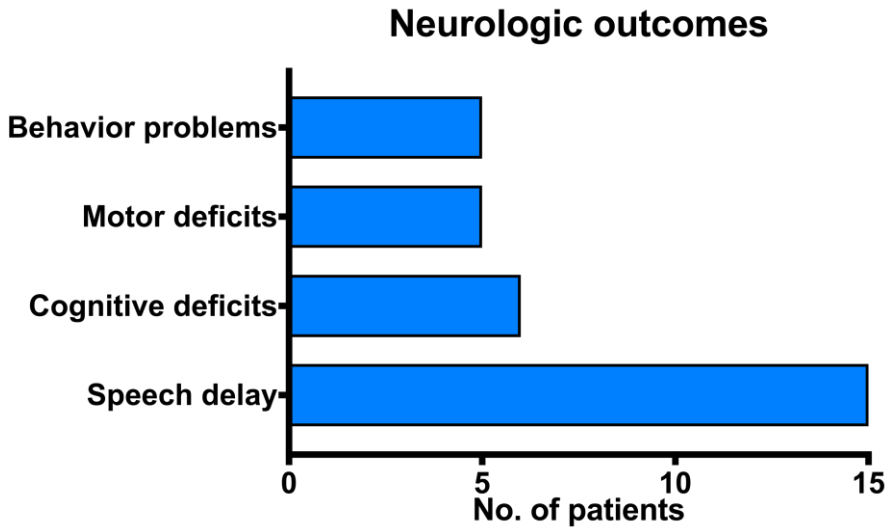
Results cont.

Outcomes

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



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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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