

OMS:

What we know, what we don't know

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Disclosures:

- OMSlife paid my airfare to come here, paid for my hotel and expenses
- I have no pharmaceutical industry funding for any of the medications I will discuss
- All treatments for OMS are “off label”

This talk is meant to provoke discussion

**Definite answers may not be available:
Be patient!**

**Some areas will be covered in more detail by other
speakers**

Outline of this discussion

- Step 1: making the diagnosis
- Step 2: finding the cause
- Step 3: initial treatments
- Step 4: weaning medications
- Step 5: what about relapses?
- Step 6: getting on with life

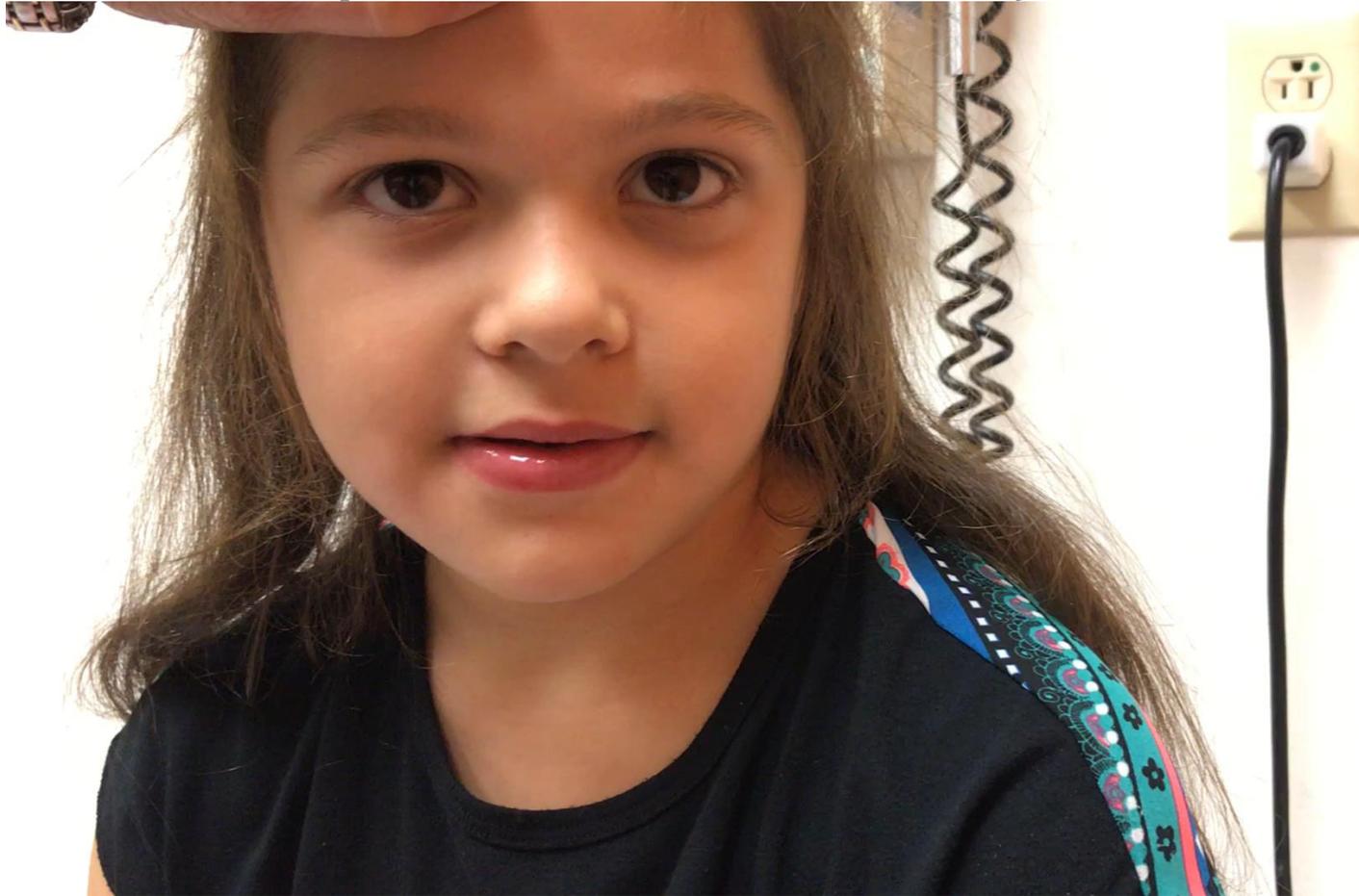
Step 1: recognizing OMS and it's variants

- Almost all children with OMS present with ataxia first
 - Acute cerebellar ataxia (ACA) in childhood is common
 - OMS is rare
- Almost all OMS is initially diagnosed as ACA initially
 - Ataxia is present in OMS nearly 100% initially
 - Tremor or myoclonus is less common
 - Opsoclonus may appear days to weeks later, or not at all
 - Extreme irritability, sleep disturbance is common early, but not universal
 - Almost everyone in OMS age group has had some viral illness or immunization within past month

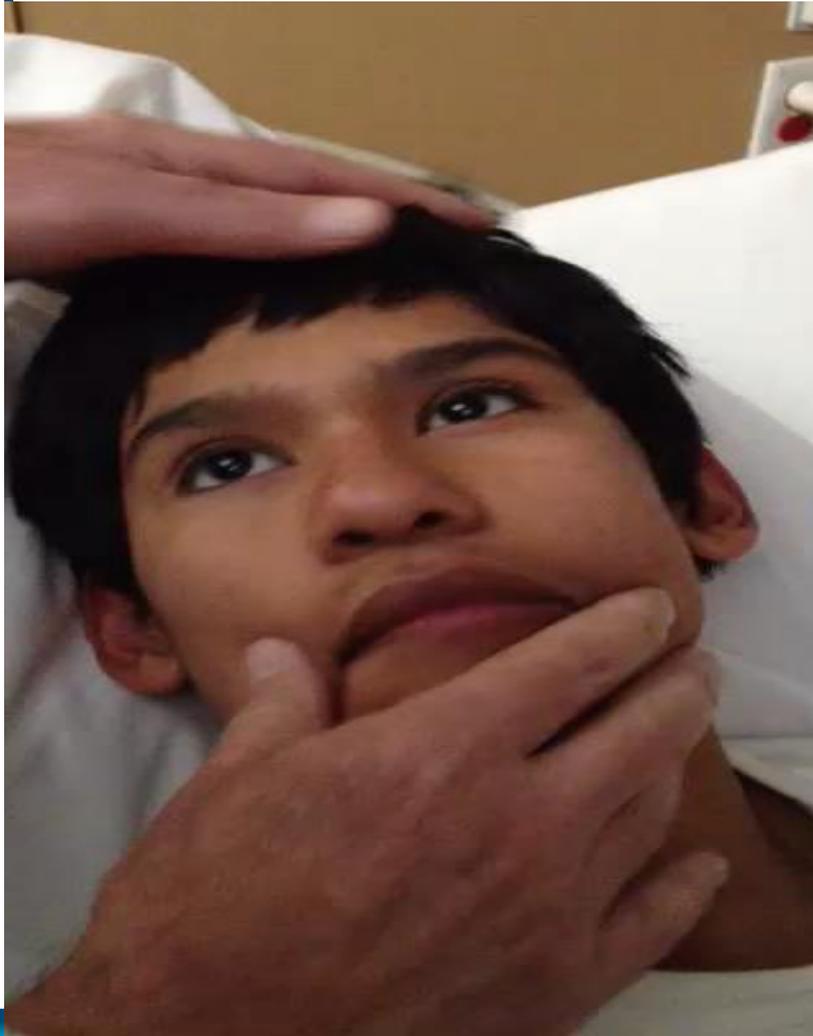
Step 1a: recognizing opsoclonus

- Opsoclonus is different from nystagmus or other abnormal eye movements in childhood
 - Opsoclonus can be seen through lightly closed eyelids or with squeeze test
- **Acquired** opsoclonus in infants/toddlers is almost always OMS
- Congenital opsoclonus or opsoclonus noted in first few months is usually NOT OMS
- Most pediatricians, ER doctors, and even many child neurologists have never seen opsoclonus
- Cel phone videos are very helpful: if in doubt, video eye movement!
 - Send video to your child's doctor, neurologist, etc
 - For follow-up, learn to do squeeze test and video it!

Squeeze test, courtesy of Eden



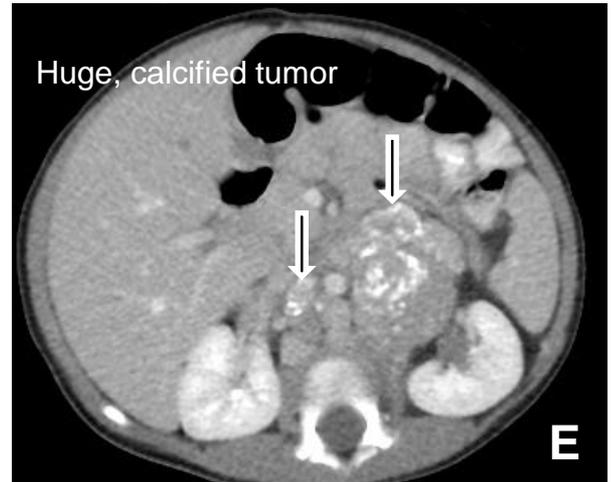
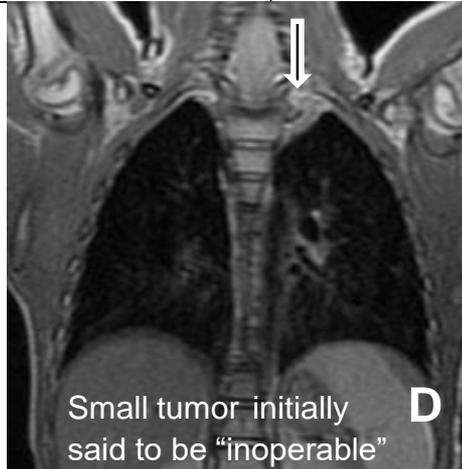
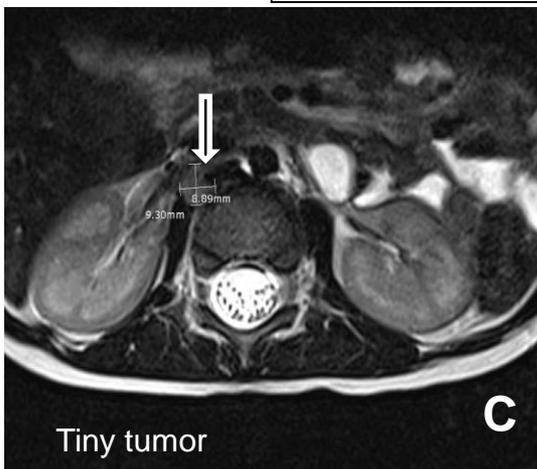
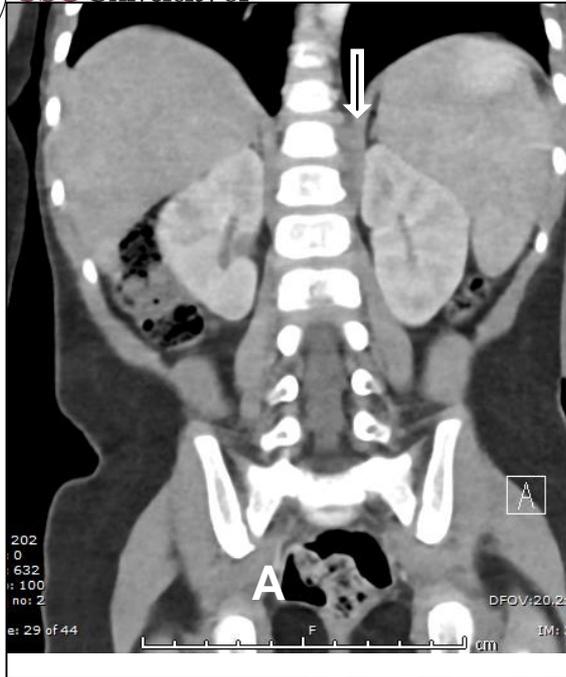
Squeeze test of an older child



Step 2: determine the cause/trigger

Do ALL infants/toddlers with OMS have NB?

- **MAYBE:**
 - In our hands, over 80% of children with OMS (between 9 months and 5 years) are found to have small neuroblastomas
- **MAYBE NOT:**
 - Other series with less aggressive imaging have between 10% and 50% neuroblastomas
- Inexperienced radiologists may miss or discount small masses which are neuroblastomas or ganglioneuroblastomas
- However, despite thorough and repeated searches, in some, no NB is ever found
 - NBs may have regressed beyond the point of detection



Do infections and immunizations cause OMS?

- Occasionally, OMS symptoms seem to start right after a viral illness or immunization
 - It is rare to find child between 9 months and 4 years who has not had some illness or immunization in the prior 6 weeks
- There may be an interaction of illness or immunization with the immune system which triggers OMS, even in children with NB

Step 3: Initial treatment to control symptoms

There is no protocol that is “best”, but some are better

- General principle: At least 2, preferably 3 agents combined
- HIGH doses to start, VERY SLOW wean of ACTH or steroids
- **MEDS SHOULD NOT BE WEANED UNTIL MAJOR OMS SYMPTOMS ARE CONTROLLED**
 - Do not accept “good enough” when symptoms are only partly controlled.
 - If initial treatment is ineffective, “move on” to something else

Step 3: Initial treatment to control symptoms

- Remove neuroblastoma if found
- Start corticotropin (ACTH) or high dose oral or IV corticosteroids
 - High doses of ACTH or steroids rapidly improve symptoms, but cause significant side effects and cannot be kept at maximum doses for very long
 - Various schedules for ACTH: 40 U daily (0.5 ml) or even more
 - Various schedules for IV methylprednisolone: 30mg/m²/day for 5 days then high dose oral prednisolone or prednisone
 - Dexamethasone 20mg/m² per day, divided in 3 doses, 3 days per month
- Start IVIG, usually 2 grams per kilogram body weight every 4 weeks
- Add a third immunosuppressant early
 - Current preferred treatment is rituximab (2 or 4 doses)
 - Ofatumumab may replace this eventually
 - COG study used cyclophosphamide (monthly for 6 months)

More on early treatment

- **Control symptoms if severe**
 - Nausea/vomiting
 - Sleep and behavior
- **Control side effects of ACTH/steroids**
 - Blood pressure control
 - High dose vitamin D and calcium to prevent bone loss
 - Antacid or PPIs (acid blockers)
 - Low salt, low sugar diet
- **Prevent infections**
 - Trimethoprim-sulfa 3 days per week to prevent pneumocystis pneumonia
 - NO immunizations for OMS child; immunize family, particularly flu vaccine (shot, not spray)

As improvement begins:

- PT, OT and speech therapy or “infant stimulation” via Regional Center, insurance or other agencies.
 - During the initial very acute phases, therapies are poorly tolerated and not very helpful
 - As child improves, they are more easily engaged in therapies
- Carefully watch nutritional status: corticosteroids or ACTH can promote very rapid weight gain.
- School enrollment at or before age 3 years to obtain services.
 - Need signed medical exemption from immunizations
- Begin treating of behavior outbursts as “2 year old tantrums” not as acute OMS symptom

If no neuroblastoma was found initially:

- Very few neuroblastomas are found late, but not zero
- Reimage with full body scans (usually MRI, not CT) at least once
- Despite CT being slightly more sensitive, limit full body CT with fine cuts to one time (too much radiation exposure)
- MIBG scans are not generally useful

Step 4: Beginning to wean medications

- **Very slowly reduce ACTH or corticosteroids**
 - Daily to alternate day dosing first, then very slowly lower dose
 - Or staying with daily doses, gradually reducing
 - Months or even years of treatment maybe needed
 - “Suggested” schedules don’t work for everyone, individualize!
 - Support medicines (sedatives, blood pressure meds, antacids) can be reduced as steroids are lowered and symptoms improve
- **Once off steroids/ACTH, begin reducing IVIG**
 - After several months of stability on monthly IVIG alone, space out from every 4 weeks to every 6 weeks, then every 8 weeks, etc
- **If rituximab was used, follow peripheral CD19+ counts. Once normal, ok to stop trimethoprim-sulfa**

Step 5: Recognize the difference between residual symptoms and true relapse

- “Minor” ups and downs are common
 - When overtired, sick, stressed
- True relapses as medication is weaned, often after viral illness, are (sadly) also common
 - At least one “step” higher OMS score in gait, tremor or opsoclonus
 - Behavioral deterioration is rarely the only symptom
- Watchful waiting for minor “bumps” in symptoms during illness
- Increase or restart treatment for true relapses

Issues to consider with recurrent symptoms: Determine if it is a true immunological relapse

- If recently treated with rituximab, assess peripheral CD19 count
 - If still very suppressed, additional rituximab is not likely to help
- If CD 19 cells have recovered peripherally, repeat CSF lymphocyte flow cytometry and “MS panel” to assess whether there is active neuroinflammation
 - If CSF has elevated CD 19+ cells and oligoclonal bands, consider repeat course or partial course of rituximab
 - If CSF does not have CD 19+ cells and does have oligoclonal bands consider cyclophosphamide or other agents
 - If no signs of neuroinflammation, the symptoms may not represent true immunological relapse, and further immune suppression may not be helpful

Step 6: Getting on with life

- **Some OMS warriors have long-term learning and behavioral issues**
 - Appropriate IEP for school-age (3 years and over)
 - Behavior therapy to “unlearn” OMS related explosive behavior and tantrums
 - Ongoing speech therapy, OT are generally helpful, PT less useful
 - Occupational planning/vocational training in adolescence
 - Some may benefit from ADHD medications
 - Neuropsychological evaluation may be helpful at school age
- **Some OMS warriors return to their pre-illness developmental progression**
 - May still qualify for special needs programs in public schools from age 3 years as “other health impaired”

Getting on with life: Parents' Needs

- OMS parents/caregivers have long-term issues with “fragile child syndrome”
 - While your OMS child is very ill, you do everything possible to comfort them and keep them happy
 - Some OMS children learn to manipulate parents' anxieties and continue to have oppositional behavior and tantrums even when OMS is otherwise controlled
 - Child needs to begin to learn “normal” coping mechanisms for age
 - Even if your OMS child is completely back to normal and off all treatment, parental anxiety may be problem
 - Consider working with therapist

Step 6b: Being healthy

- Health monitoring:
 - If your OMS child had a neuroblastoma, oncology monitoring
 - If your OMS child had chemotherapy, other specific protocols
 - If neuroblastoma was removed near spine, watch for scoliosis
- Immunizations:
 - Wait to restart *at least* 1 year after last rituximab and at least 6 months off IVIG (preferably 1 year)
 - Resist requests to “catch up everything immediately”
 - Seasonal flu vaccine comes FIRST
 - Live virus vaccines come last
 - Special circumstances: if traveling out of country, or other high exposure risk. Measles exposure is a major risk in Europe

Thank you!

