# OMS:
# What we know, what we don't know


- Wendy Mitchell MD
- Professor, Neurology and Pediatrics
- Keck School of Medicine, University of Southern California
- Children's Hospital Los Angeles

# 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”

Children's Hospital LOS ANGELES
We Treat Kids Better

USC University of Southern California

# 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

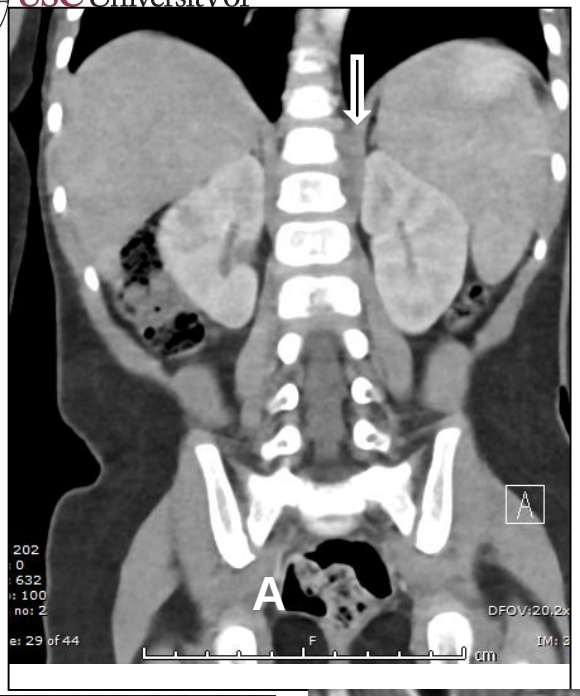
- Almost all children with OMS present with ataxia first
  - Acute cerebellar ataxia (ACA) in childhood is common
  - OMS is rare
- Almost all OMS is initially diagnosed as ACA initially
  - Ataxia is present in OMS nearly 100% initially
  - Tremor or myoclonus is less common
  - Opsoclonus may appear 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

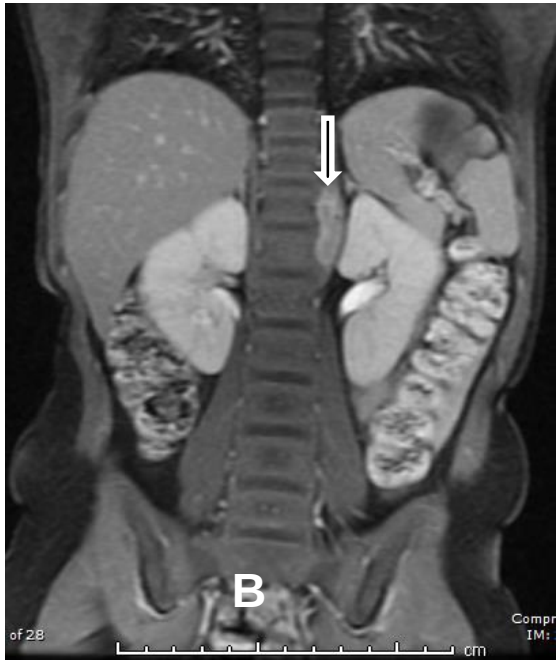
# Step 1a: recognizing opsoclonus

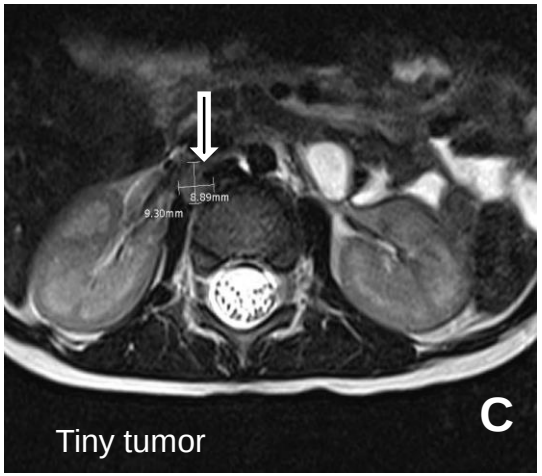
- Opsoclonus is different from nystagmus or other abnormal eye movements in childhood
  - Opsoclonus can be seen through lightly closed eyelids or with squeeze test
- **Acquired** opsoclonus in infants/toddlers is almost always OMS
- Congenital opsoclonus or opsoclonus noted in first few months is usually 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!

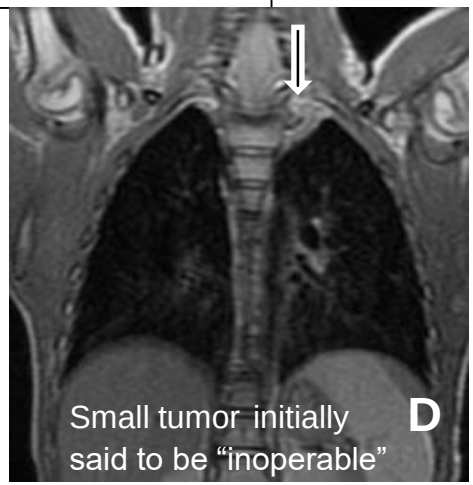
# Step 2: determine the cause/trigger
# Do ALL infants/toddlers with OMS have NB?

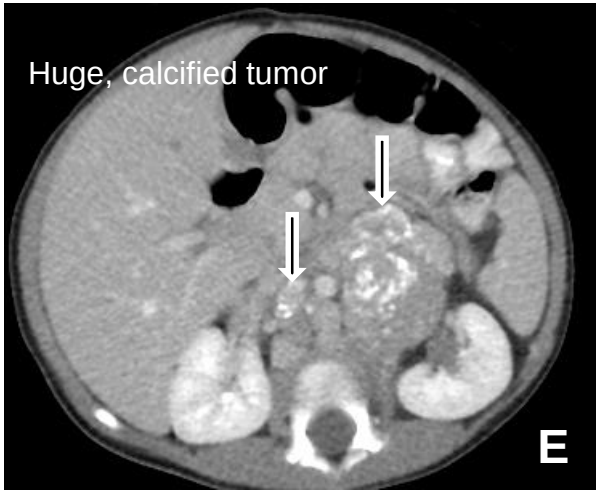
- MAYBE:
  - In our hands, over 80% of children with OMS (between 9 months and 5 years) are found to have small neuroblastomas
- MAYBE NOT:
  - Other series with less aggressive imaging have between 10% and 50% neuroblastomas
- Inexperienced radiologists may miss or discount small masses which are neuroblastomas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


A
DFOV:20.2x
cm


B
cm


8.89mm
9.30mm
Tiny tumor
C


Small tumor initially said to be “inoperable”
D


Huge, calcified tumor
E

# 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

Children's Hospital LOS ANGELES
We Treat Kids Better

USC University of Southern California

# Thank you!