Opsoclonus-Myoclonus and Neuroblastoma
An introduction:

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Todays Talk:

1. High correlation of Neuroblastoma and OMA
    - Need for surveillance

2. What is Neuroblastoma?
    - How does Neuroblastoma present?
        - Not one disease – range of presentations
        - What ‘causes’ neuroblastoma?
        - Treatment: vary according to stage

3. Does Neuroblastoma cause OMA?
        - Or OMA cause Neuroblastoma?
            - Or neither ?

4. Managing Neuroblastoma and OMA at the same time

Questions / Concerns?

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Correlation of OMA and Neuroblastoma:

Neuroblastoma is rare:

>90% of cases are in children under 5yrs of age
Approximately 8-10 cases per million children (varies with age)
about 700 cases/ year in usa
Distribution between boys and girls about equal

OMA is *very* rare:

About 0.2 cases per million - 50X less common than neuroblastoma
--only about 2% of neuroblastoma cases involve OMA

Compare to childhood diabetes 3-400 cases per million.

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Two Rare Diseases:

Neuroblastoma is detected in about 50-60% of all OMA patients
even though both diseases are rare,
This is a very high concordance.

OMA is a ‘paraneoplastic syndrome’ for neuroblastoma

Association is not Causation:
We don’t know how OMA develops or if neuroblastoma induces OMA

Surveillance:
But we do know that we need to look for Neuroblastoma in OMA patients

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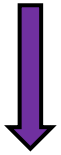
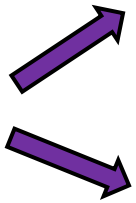
Neuroblastoma



Activated Inflammation Signals

Immune response

B-cells
T-cells
Dendritic cells
macrophages



Possible connections:
cross reactive antibodies

GOOD:
Anti-tumor
immune response
Clears cancer

BAD
Uncontrolled inflammation
Auto-immune antibodies
Cross-reactive to nerves?

Opsoclonus-Myoclonus with no neuroblastoma - ? Other inflammatory signals?
Infections, autoimmunity, other?

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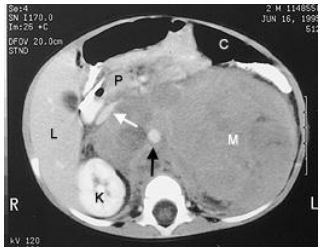
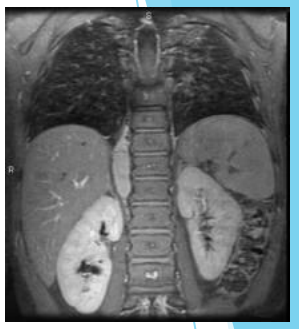
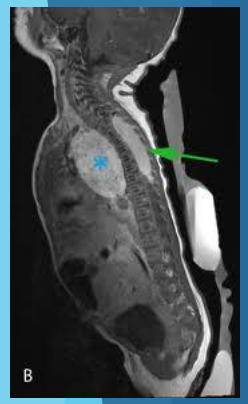
Surveillance- Detection of Neuroblastoma:

Radiology:
MRI scans, CT scans –
detects masses
in chest/abdomen/pelvis

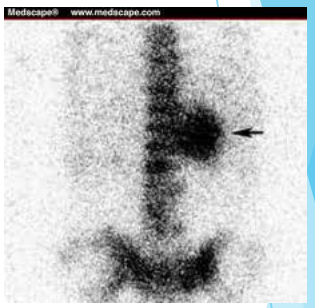


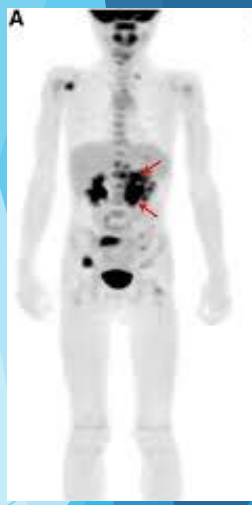




Nuclear scans:

MIBG – specific for most neuroblastoma (*not all*)
(Uptake of metaiodobenzylguanidine)





Urine Tests:
HVA/VMA –
specific for metabolic products of most neuroblastomas
(*not all*)

Should used combined modalities for first year (or until all negative) then decrease frequency of monitoring.
MIBG alone is not sufficient
MRI is typical these days for anatomic imaging.

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Biomarkers for OMS and Neuroblastoma:

Need: sensitive marker that corresponds to disease severity
or recurrence.

New markers for neuroblastoma: circulating (blood) microRNAs
DNA,
May reflect inflammatory response

Will these also be useful in OMA?

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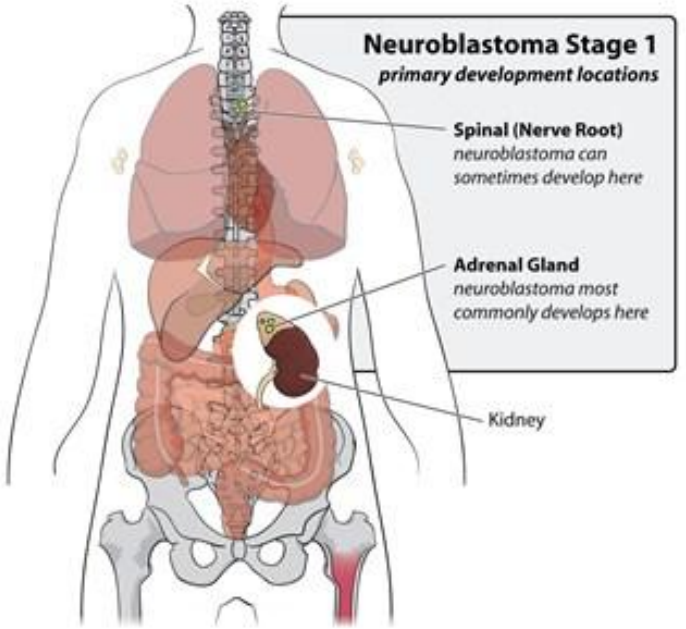
Neuroblastoma 101:

NOT a Brain Tumor:

Arises from peripheral sympathetic nervous system:



Tumors in the abdomen and chest and pelvis

- Paraspinal – 50% (chest and abdomen)
- Adrenal gland – 30%
- 20% other sites (pelvis, head, and neck)

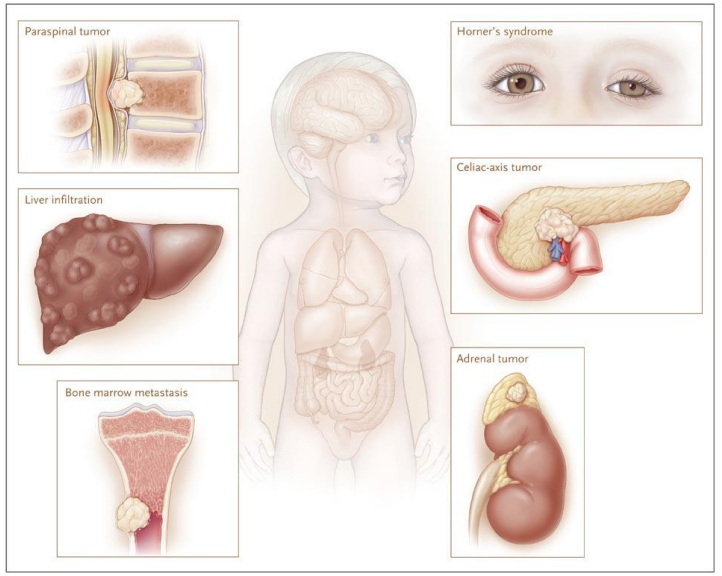
95% of cases in children less than 5 years of age
Most in children less than 2 years of age

Presentation varies dramatically:

Stage 1 – solitary tumor,
Stage 2 spread to local lymphnodes
Stage 3 larger tumor, + lymphodes
Stage 4 metastatic –

- Bone, Bone marrow, liver
- Skin, lymphnodes, kidney
- Almost never to the lungs or brain

(unlike other types of cancers



Special Stage 4S – metastatic but regresses

- (more later)

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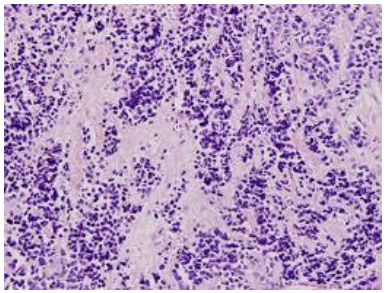
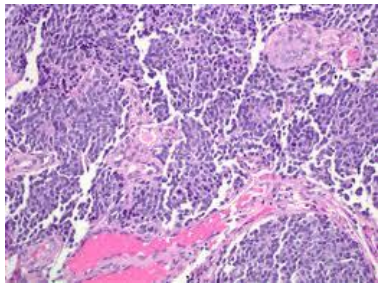
Neuroblastoma is *not* a single disease: Treatments depend on spread and biology

Very low risk (stage 4s, infants):	observation-regression
Low Risk (stage 1-2) no MYCN:	observation, small chemo, ?radiation
Intermediate risk (larger tumors), histology:	more chemo, surgery, radiation
High risk (metastatic), aggressive:	Intensive chemo, immunotherapy, surgery Radiation, MIBG radiation, others

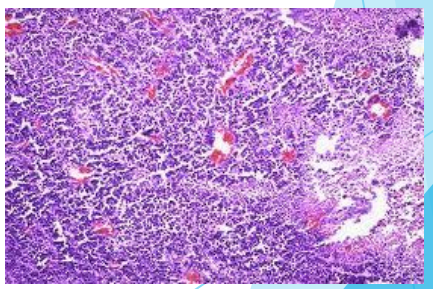
Differentiated



Poorly differentiated



Undifferentiated



Less aggressive → More aggressive

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Neuroblastoma 101: treatments

1. **Low risk**: (most common for OMA patients)
   Biopsy and observation
   intermittent MRI/MIBG and urine tests (interval 3-6 months, then yearly)
   These tumors most often regress by themselves
   Or 'mature' and don't grow
   {Stage 4s (for special)- about 10 % of cases
   often spontaneously resolves and does not return.
   This is the only case of a metastatic tumor that resolves by itself.}

2. **Intermediate risk**: larger tumors, spread to nodes
   Biopsy, then chemotherapy
   4-8 cycles of moderate intensity chemotherapy (about 6 months)
   Then observation

3. **High risk**: metastatic disease or multiple risk factors
   Biopsy, then chemotherapy
   More intensive, about 9-12 months, requires long term follow up
   Risk for relapse

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Take home points:

Neuroblastoma in OMA is typically:
Low Risk: - a single lesion, no MYCN amplification, etc.
Observation, and frequent surveillance

Neuroblastoma can be MIBG negative- need additional imaging
Urine catacholamines also can be negative

Treatment of intermediate or high risk neuroblastoma requires chemotherapy and close follow up.

Surveillance includes MRI/CT scans, MIBG scans, Urine markers
Tumor doesn't grow very fast (unlike leukemia)

Our understanding of immunology and 'auto-immune' responses to cancer is rapidly evolving.
New research into how cancer alters the immune system may be applicable to OMS in the future.

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Some recent references:

Update on diagnosis, treatment, and prognosis in opsoclonus–myoclonus–ataxia syndrome
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Thank you !

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