Infantile Spasms

Manisha Kak, MS4
Newborn Nursery
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What are infantile spasms?

- Infantile spasms (IS) is a convulsive disorder with onset in infancy or early childhood, associated with EEG changes and developmental regression.
- 90% present at less than 1 yr of age, with peak incidence b/w 3 and 7 months.
- Spasms are typically symmetric and synchronous, including flexor, extensor, and flexor-extensor.
- West Syndrome: triad of spasms, arrest of psychomotor development, hypsarrhythmia.
Incidence: 1.6 – 4.5 per 10,000 live births
Up to 93% have developmental retardation
Up to 33% mortality rate
Tends to be refractory to conventional antiepileptic drugs, but may respond to hormonal therapy

http://www.youtube.com/watch?v=86b9WufaQ1k&feature=related
Etiology

- Most cases are sporadic
  - Genetic susceptibility likely plays a role
  - X-linked inheritance in rare cases

- Symptomatic
  - Identified etiology and/or developmental delay at time of onset
  - Prenatal: CNS malformations, neurocutaneous disorders (TSC), chromosome abnormalities (DS), inborn errors of metabolism (PKU), congenital infections
  - Perinatal: hypoxic-ischemic encephalopathy, neonatal hypoglycemia
  - Postnatal: near-drowning, traumatic injury, CNS infection

- Cryptogenic
  - No known etiology; normal development at time of onset; normal EEG, imaging, and exam
Diagnosis

- Done with EEG and video monitoring of spasms, and should be followed by neuroimaging to work up possible lesions.
- Can also work up metabolic etiologies; the rest are called idiopathic or cryptogenic.
- Most parents underestimate seizure frequency by 5 to 10-fold.
The most common EEG finding in IS: high-voltage, random slow waves and spikes in all cortical areas.
Seizure types other than spasms occur in 1/3 to ½ of pts with IS

DDX includes:
- Hyperirritability
- Exaggerated startle response
- Colic
- Benign myoclonus of early infancy
- Sleep myoclonus
- Tonic reflex seizures of early infancy
Treatment

- First-line Tx: Corticotropin (ACTH)!
  - Better response in cryptogenic
  - Relapse rate up to 33%
  - High side-effect profile – most commonly HTN
- Can try Prednisone if no response to ACTH
- Antiepileptic drugs: Vigabatrin
  - Other AEDs not recommended
  - High side-effect profile – most notably vision loss
Other Therapies

- Pyridoxine
  - Some evidence of efficacy in West Syndrome
- Surgery
  - If focal cortical structural defect
- Ketogenic diet
  - Ketones may have inhibitory effect on neuron potassium channels
  - High-fat, low-carbohydrate
  - Concern for reducing linear growth of child
The relationship of ketosis and growth to the efficacy of the ketogenic diet in infantile spasms (Numis et al., 2011)

- Retrospective chart review on 26 patients with medically refractory IS at Mass Gen Hospital
- After 1-3 mo of ketogenic diet, 46% of pts had a >90% reduction in IS
- No changes in growth parameters noted due to KD
- Initiation of KD resulted in lower blood glucose levels and higher β-hydroxybutyrate levels, but these did not correlate with level of seizure reduction
**Efficacy of the ketogenic diet.**

Reduction in baseline seizure frequency and median age

<table>
<thead>
<tr>
<th>Age (mo)</th>
<th>&gt;50% %, Age (mo)</th>
<th>50—90% %, Age (mo)</th>
<th>&gt;90% %, Age (mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infantile spasms after KD initiation</td>
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<tr>
<td>1—3mo after (n = 26)</td>
<td>15%, 19</td>
<td>39%, 20</td>
<td>46%, 19</td>
</tr>
<tr>
<td>5—7mo after (n = 21)</td>
<td>0%, N/A</td>
<td>48%, 24</td>
<td>52%, 25</td>
</tr>
<tr>
<td>10—13mo after (n = 19)</td>
<td>16%, 29</td>
<td>21%, 36</td>
<td>63%, 28</td>
</tr>
<tr>
<td>Other seizure types after KD initiation</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>1—3mo after (n = 16)</td>
<td>31%, 19</td>
<td>44%, 25</td>
<td>25%, 19</td>
</tr>
<tr>
<td>5—7mo after (n = 15)</td>
<td>40%, 24</td>
<td>33%, 25</td>
<td>27%, 24</td>
</tr>
<tr>
<td>10—13mo after (n = 13)</td>
<td>54%, 29</td>
<td>8%, N/A</td>
<td>38%, 27</td>
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</tbody>
</table>

Abbreviations: KD: ketogenic diet; mo: months.

Note: Denominators in each time point include those patients continuing on KD only.
West Syndrome: early remission is not assurance of normal final outcome

(de Queiroz Campos Araujo et al., 2010)

- Retrospective case series on 37 infants with WS in Brazil from 1990-2005
- Most pts were symptomatic and had neonatal history of hypoxia as most frequent etiology
- 20 of the 37 pts had favorable short-term outcome with AED and steroid use, but only 3 had normal development and were seizure free after 2 yrs of age
- Conclusion: long term prognosis for seizure remission is poor even in those with initial favorable responses to treatment
# Features according to outcome

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<thead>
<tr>
<th></th>
<th>Good</th>
<th>Bad</th>
<th>( P )</th>
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</thead>
<tbody>
<tr>
<td><strong>Short Term</strong></td>
<td>n = 20</td>
<td>n = 17</td>
<td></td>
</tr>
<tr>
<td>- Age of onset (months, mean, SD)</td>
<td>4.9 (1.86)</td>
<td>4.1 (2.92)</td>
<td>0.18</td>
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<tr>
<td>- First consultation (months, mean, SD)</td>
<td>7.1 (3.04)</td>
<td>12 (9.01)</td>
<td>0.01</td>
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<tr>
<td>- Sex (male)</td>
<td>17 (85%)</td>
<td>7 (41%)</td>
<td>0.05</td>
</tr>
<tr>
<td>- Hypsarrhythmia (typical)</td>
<td>16 (80%)</td>
<td>14 (82%)</td>
<td>0.59</td>
</tr>
<tr>
<td>- Symptomatic</td>
<td>15 (75%)</td>
<td>14 (82%)</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Long term</strong></td>
<td>n = 3</td>
<td>n = 32</td>
<td></td>
</tr>
<tr>
<td>- Age of onset (months, mean, SD)</td>
<td>6 (1)</td>
<td>4.5 (2.38)</td>
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</tr>
<tr>
<td>- First consultation (months, mean, SD)</td>
<td>8.3 (0.57)</td>
<td>9.8 (7.26)</td>
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</tr>
<tr>
<td>- Sex (male)</td>
<td>100%</td>
<td>21 (66%)</td>
<td></td>
</tr>
<tr>
<td>- Hypsarrhythmia (typical)</td>
<td>2 (67%)</td>
<td>26 (81%)</td>
<td></td>
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<tr>
<td>- Symptomatic</td>
<td>2 (67%)</td>
<td>25 (78%)</td>
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Glaze, DG. Infantile Spasms. *UpToDate*. 2012