A 6 month old ex-full term previously healthy male presents to his primary care doctor for his well child check. He has been generally healthy, aside from a recent viral URI. He was noted to be developing appropriately at the 4 month visit. Parents have no major concerns, except they do happen to mention that their son started making some “funny jerking movements” a couple weeks ago. The parents show you a video they took on their cell phone.
DIFFERENTIAL DIAGNOSIS

• Infantile spasms
• Exaggerated startle response
• Altered life threatening event (ALTE)
• Colic/Hyperirritability
• Benign myoclonus of early infancy
• Sleep myoclonus
YOUR PATIENT’S EEG
NORMAL EEG
INFANTILE SPASMS AND DEVELOPMENT
CLINICAL FEATURES

• **Onset**
  - 90% before 1 year of age
  - Peak onset 3 to 7 months
  - Onset after 18 months is rare

• **Age range**
  - 1 day to 4.5 years

• **Incidence**
  - 2-5 per 10,000 live births worldwide

• **West syndrome**: The triad of
  - Spasms, arrest of psychomotor development, and hypsarrhythmia

CLINICAL FEATURES

- Spasms usually symmetric & involve the neck, trunk muscles, and/or extremities
- Often difficult even for practitioners to detect & diagnose
- 2 phases: Sudden, brief contraction (<2 seconds) followed by longer tonic phase (2-10 seconds)
- 80% occur in clusters (crescendo-decrescendo)

TYPICAL CLINICAL COURSE

• Initial stage: mild and infrequent
  • Even occasional infantile spasms associated with abrupt arrest and/or regression in development

• Second stage (most severe): peak activity reached
  • Often hundreds of spasms each day
  • Most profound developmental regression

• Third stage: Gradual decrease in spasms, resolution, or transition to overt seizures (Usually occurs before age 5)

ETIOLOGY OF INFANTILE SEIZURES

• Symptomatic IS: known underlying cause
  • 70-80% have cause found after clinical evaluation and neuroimaging
  • The percentage of IS cases classified as symptomatic has increased over time due to improved diagnostic techniques, such as metabolic and genetic testing and neuroimaging

• Cryptogenic IS: no known underlying cause, usually previously healthy child
  • Likely genetic cause
  • Outcomes are usually more favorable among this subset of infants

CAUSES OF SYMPTOMATIC IS

• **Prenatal/Genetic Causes:** Approximately 50%
  - Central nervous system malformation
  - Intrauterine insults
  - Neurocutaneous syndromes such as tuberous sclerosis complex (TSC)
  - Metabolic disorders
  - Genetic syndromes such as Down syndrome

• **Perinatal Causes:**
  - Hypoxic-ischemic Encephalopathy

• **Post-natal Causes:**
  - Infection
  - Trauma
  - Tumors (rare)

HYPSARRYTHMIA

- Characterized by very high voltage and slow waves/spikes in all cortical areas
- Most often present in Stages 2 and 3 of non-REM sleep
- May precede onset of spasms
CURRENT TREATMENTS

- Treatment is thought to be an “all-or-none” principle. Complete resolution of spasms and hypsarrythmia

- Practice guidelines from the American Academy of Neurology and the Child Neurology Society for the medical treatment of IS:
  - ACTH – Probably Effective
  - Vigabatrin – Possibly effective

- Pathophysiology:
  - stress/corticotropin-releasing hormone (CRH) hypothesis - increased release of stress-activated mediators in the brain, especially CRH in the limbic and brain stem lead to spasms
  - ACTH suppresses CRH

## SPECIFIC TREATMENTS

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<th>Specific therapy</th>
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<td>Sturge-Weber syndrome</td>
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<td>Tuberous sclerosis complex</td>
<td>Vigabatrin, ACTH (if vigabatrin fails), and possibly surgery if medications fail</td>
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<tr>
<td>Cortical dysplasias: focal cortical dysplasias, hemimegalencephaly</td>
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<td>Malformations of cortical development</td>
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OUTCOMES OF INFANTILE SPASMS

• Retrospective review of 44 children with untreated IS
• Cumulative spontaneous remission rate of spasms
  • 2 percent at one month
  • 5 percent at three months
  • 25 percent at twelve months
• Most resolve by 3-4 years of age
  • Often progress to other seizure disorders
  • Often with permanent developmental delay

Abstract

Objectives: The aim of this study was to provide additional evidences on prognostic factors for infantile spasms and the possible role of a ketogenic diet. Methods: A retrospective analysis was performed for patients with infantile spasms who had been followed up for more than 6 months between January 2000 and July 2012 at Samsung Medical Center (Seoul, Republic of Korea). We analyzed the association between possible prognostic factors and seizure/developmental outcomes. Results: Sixty-nine patients were included in this study and their mean follow-up duration was 52.5 (9–147) months. In the patients who had been followed up for more than 2 years, 53.6% \( (n = 30/57) \) remained seizure-free at the last visit. Sixty patients (86.9%) showed developmental delay at last follow-up. Forty-two patients (60.9%) became spasm-free with one or two antiepileptic drugs, one patient with epilepsy surgery for a tumor, and seven patients with a ketogenic diet after the failure of two or more antiepileptic drugs. The etiology and age of seizure onset were the significant prognostic factors. Conclusions: In this study, about 60% of the patients became spasm-free with vigabatrin and topiramate. Ketogenic diet increased the rate by 10% in the remaining antiepileptic drug resistant patients. However, 86.9% of the patients showed developmental delay, mostly a severe degree. Early diagnosis and prompt application of treatment options such as antiepileptic drugs, a ketogenic diet or epilepsy surgery can improve outcomes in patients with infantile spasms.
PROGNOSTIC FACTORS OF IS

- Review performed in 2010 of European literature show:

  - Cryptogenic spasms - cease and result in normal or almost normal development in about 80% of patients.

  - Symptomatic spasms - the spasms will cease in 50% but development is normal in only roughly 20%.

  - A rather benign course is associated with spasms due to: Down’s syndrome, neurofibromatosis-1, periventricular leucomalacia due to prematurity, and neonatal hypoglycemia

PROGNOSTIC FACTORS OF IS

“Factors associated with a favorable outcome include:

• No other seizures before onset of infantile spasms.
• Absence of atypical spasms, partial seizures and asymmetric EEG abnormalities.
• Age of onset after the age of 4 months.
• Early and sustained response to treatment.
• Short duration of hypsarrhythmia”

LONG TERM OUTCOMES

- In Finland 214 children were followed up for 20–35 years or until death.
- Prospective study in which children either received high dose ACTH (for 6 weeks) or low dose ACTH treatment.
- The long-term intellectual outcome was better treated with lower doses than with larger doses.
- 1/3 of Children died (Of which 1/3 were under the age of 3).
- 25% of children were found to have normal IQ scores, however 40% of these children had a specific learning deficit:
  - Psychiatric disorders, hyperkinetic behavior and infantile autism.

• In 70% of the children found to have autism in the Finnish study, an abnormality was identified in the temporal lobe.

• Chugani et al. and De Long and Heinz also found that 70% of patients with infantile spasms and autism had bitemporal hypometabolism.


ASSOCIATION OF IS WITH AUTISM SPECTRUM DISORDERS

Saemundsen et al., 2008

- Retrospective case-control study of 95 children (34 boys, 61 girls)
- Cases: children with autism
- Exposure: history of infantile spasm
- OR for ASD with exposure of IS: 5.53 (1.25-23)
- Conclusion: Infantile spasms predicted high risk for ASD, but association was mostly secondary to underlying cause for seizures