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CSI

ASHEVILLE

Case Studies In Epilepsy
Slides Posted

- http://neuron.med.unc.edu/neurology
Invisible Evidence

CSI 76. 4- 7 404 13 Nov 03
Case 1
Infant with Seizures

- Full term infant born meconium stained, low Apgar scores and found to have low platelets. He stayed in neonatal intensive care for three days.
- Development was slow. He did not sit until 9 months of age.
Case 1
Seizures

- Onset 4 months of age. The seizures were described by mother as episodes of quick jerks so that the head would fall and his upper extremities would stiffen. The seizures came in clusters at times of sleep transition.
- Generalized clonic seizures began at 8 months of age
Case 1

EEG

- EEG- 8 months old- bitemporal and generalized epileptiform discharges
- Video EEG at 10 months- video EEG monitoring which showed high amplitude generalized spike and polyspike waves and right and left temporal focal slowing greatest on the right.
- Video EEG at 16 months- Electro-clinical infantile spasms and Left temporal/parietal spikes awake, multifocal epileptiform discharges asleep.
Video-EEG
Case 1
Questions

- What is the cause and how to find it?
- What treatment should be used for the seizures?
Case 1
Imaging

- 3T MRI- Normal
Case 1
Laboratory Testing

- Amino acids- slight elevation of citrulline, proline and phenylalanine. Nondiagnostic.
- Organic acids- increased methylmalonic acid. Rule out B12 deficiency.
- Acylcarnitine profile-normal
- CSF for neurotransmitters could not be obtained
- Karyotype- normal male karyotype
Case 1

Treatment

- Phenobarbital - ineffective
- Topiramate, leviteracetam and clonazepam - Initial reduction of seizure frequency followed by gradually increasing seizures.
- Zonisamide caused vomiting and extreme restlessness.
- Lamotrigine - no improvement when added to medications above.
- Prednisolone - Seizures stopped and did not return after taper off.
Case 1
Further Genetic Testing

- Heterozygous variant 345 T>C in SCN 1A gene
<table>
<thead>
<tr>
<th>Gene</th>
<th>Protein</th>
<th>Neuronal Function</th>
<th>Epilepsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCN 1A</td>
<td>α1 Na Subunit</td>
<td>Membrane charge &amp; action potential</td>
<td>Generalize epilepsy and febrile seizures (GEFs)</td>
</tr>
<tr>
<td>SCN 2A</td>
<td>α2 Na Subunit β1 Na Subunit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SCN 1B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GABR gamma 2</td>
<td>GABA receptor</td>
<td>Inhibition</td>
<td>GEFs</td>
</tr>
<tr>
<td>GABAR(A) α 1 subunit</td>
<td>GABA receptor</td>
<td>Inhibition</td>
<td>Juvenile myoclonic epilepsy</td>
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<tr>
<td>KCNQ2</td>
<td>V-Sensitive K+ channel</td>
<td>Membrane charge &amp; after hyperpolarization</td>
<td>Benign Neonatal Seizures</td>
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<tr>
<td>KCNQ3</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>KCNA1</td>
<td>low V-Sensitive K+ channel</td>
<td>Membrane charge &amp; after hyperpolarization</td>
<td>Familial Temporal Lobe</td>
</tr>
<tr>
<td>CNRN alpha 4</td>
<td>Nicotinic α4 subunit</td>
<td>Excitation</td>
<td>Familial Frontal Lobe</td>
</tr>
<tr>
<td>CHRNB2</td>
<td>Nicotinic β2 subunit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cav2.1 subunit</td>
<td>voltage-gated Ca2+ channels</td>
<td>Excitation or inhibition</td>
<td>Absence epilepsy</td>
</tr>
</tbody>
</table>
The Unusual Suspect

CSI 135. 6-18 618 30 Mar 06
Case 2
Case History

- Normal child with onset of seizures at age 10 months. No etiology was identified.
- His seizures were tonic clonic. He had some isolated myoclonic jerks of his arms or legs when on antiepileptic medication.
- No family history of seizures.
Case 2
Seizure Characterization- EEG Studies

- Routiein EEG bitemporal delta slowing
- Video EEG – showed bihemispheric delta slowing and voltage suppression perhaps more prominent in the left temporal lobe. Neocortical onset was supported by frequent secondary generalization.
Case 2
Seizures Characterization- Imaging

- MRI - normal except for venous angioma in left parietal region

- SPECT -
  1. Multiple foci of seizure activity demonstrated in bilateral temporal and parietal lobes.
  2. Focal hypoperfusion in the mesial inferior aspect of the left temporal lobe as well as some hyperperfusion in the right temporal lobe. EEG at the time showed occasional spike wave complexes most prominent in the left frontal temporal areas with occasional independent sharp waves on the right side.
  3. Increased uptake in the right temporal lobe relative to the left, which may represent the patient’s seizure focus.

- PET - no clear focus of decrease uptake.

- MEG - showed discharges in the left mesial posterior temporal lobe.
Case 2
Treatment

- Meds- Felbamate, lamotrigine phenytoin, topiramate
- Surgery evaluation failed twice
- VNS- 3/96
Case 2
Question

- What does he have?
- What is the cause?
Case 2
Reflex Epilepsy

- One year after VNS- Video
  - Facial twitching only when he was reading and usually while reading aloud.
- Five years after VNS
  - Facial twitching while speaking
<table>
<thead>
<tr>
<th>VNS Complication</th>
<th>Onset After VNS</th>
<th>Settings</th>
<th>Resolution</th>
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<tbody>
<tr>
<td>Hiccups &amp; increased seizures</td>
<td>12 months</td>
<td>1.5 mA, 30 sec on, 5 min off</td>
<td>Reduction to 0.5 mA, 10 min off</td>
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<tr>
<td></td>
<td></td>
<td>Increased with 1.75 mA setting</td>
<td></td>
</tr>
<tr>
<td>Increased seizures</td>
<td>1 month</td>
<td>1.75 mA, 30 sec on, 5 min off</td>
<td>Current reduced to 0.5 mA &amp; VNS finally removed</td>
</tr>
<tr>
<td></td>
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<td>More seizures with increased current</td>
<td></td>
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<tr>
<td>Intractable hiccups after VNS</td>
<td>4 months</td>
<td>New VNS, 2.75 mA</td>
<td>Reduction to 1 mA</td>
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<tr>
<td>replacement</td>
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And Then There Were None

CSI 32. 2-9 209 22 Nov 01
Case 3
History

- A 6-year-old presented for evaluation of precocious puberty and spells.
- Product of a full-term normal pregnancy and uncomplicated delivery.
- Good health and normal milestones until 5 years of age.
Case 3
Spells

- Episodes of inappropriate laughter, hyperactivity, and giddiness, followed by profuse sweating, severe chills, and retching, and ending in abdominal pain and vomiting
- Occurred daily and lasted 1-4 hours
- No loss of awareness
Case 3
EEGs

- Two EEGs were normal
- A typical spell lasting 2 hours was captured on video EEG monitoring. The EEG did not show any seizure activity.
Case 3
Questions

- What are the spells and what is causing them?
- How can we treat them?
Case 3
Imaging Studies

- MRI - 6-mm mass in the tuber cinereum consistent with a hamartoma
- PET- No abnormality noted
## Case 3
Hormone and Stimulating Hormone Changes

<table>
<thead>
<tr>
<th>Time</th>
<th>Interval from Sz Onset</th>
<th>Prolac. ng/ml</th>
<th>ACTH pg/ml</th>
<th>TSH uU/ml</th>
<th>LH mIU/ml</th>
<th>FSH mIU/ml</th>
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<tbody>
<tr>
<td>900</td>
<td>Baseline</td>
<td>7</td>
<td>47</td>
<td>2.8</td>
<td>2.9</td>
<td>7</td>
</tr>
<tr>
<td>1700</td>
<td>Sz onset</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1715</td>
<td>15min</td>
<td>32</td>
<td>84</td>
<td>2.9</td>
<td>2.1</td>
<td>4.3</td>
</tr>
<tr>
<td>1730</td>
<td>30min</td>
<td>34</td>
<td>58</td>
<td>2.9</td>
<td>3.0</td>
<td>4.5</td>
</tr>
<tr>
<td>1750</td>
<td>50min</td>
<td>0.3</td>
<td>13</td>
<td>2.1</td>
<td>3.2</td>
<td>3.9</td>
</tr>
<tr>
<td>1900</td>
<td>120min</td>
<td>18</td>
<td>NA</td>
<td>1.8</td>
<td>1.9</td>
<td>3.3</td>
</tr>
</tbody>
</table>
Case 3
Treatment

- GnRH analogue (Lupron) 15-mg IM injection every 28 days
- Her seizures improved in the first few weeks and by 8 weeks she was seizure free
Viva Las Vegas

93. 5- 1 501 23 Sep 04
Jackpot

CSI 75. 4- 6 407 6 Nov 03
Gestation, labor and delivery were unremarkable except for transient neonatal jaundice.

Development proceeded normally until onset of infantile spasms at 4 months of age. After this development slowed.
Case 4
History Continued

- Admitted to Brenner Children’s Hospital where the diagnosis of infantile spasms was made and an evaluation for the etiology was performed.
- He was initially treated with phenobarbital and then placed on ACTH for 28 days.
- He was treated with zonisamide after the ACTH but when the seizures increased again he was given another course of ACTH.
Case 4
History Continued

He was seen by Roy Elterman for a second opinion and he confirmed the diagnosis of infantile spasms and recommended further work up and a trial of vigabatrin.

When first seen at UNC at 9 months old he was on ACTH 80 units subcutaneously q.a.m., Zonegran 100 mg b.i.d., Vitamin B6 100 mg p.o. t.i.d. and Phenobarbital 90 mg p.o. q.h.s.
Case 4
Seizures and EEG at 9 Months

- Seizures
  - Clusters of head drops several times each day
- EEG showed an abnormal background pattern consistent with a modified hysarrhythmia pattern.
Case 4
Imaging

- MRI- diffuse atrophy
- MRS-
  - Long echo spectra - normal.
  - Short echo spectra - elevation of glutamine and glutamate containing compounds seen in the frontal lobes bilaterally of uncertain significance.
Case 4
Laboratory Tests

- Normal venous lactate, urine organic and amino acids, acylcarnitine profile, carbohydrate deficient transferrin, CSF protein, CSF glucose, CSF amino acids, CSF lactate, and karyotype.
- Negative TORCH titers.
- VLCFA- slight increase in the C24/22 ratio which could have been secondary to liver dysfunction or another metabolic disorder affecting liver function.
- CSF neurotransmitters were sent.
Case 4
Treatment

- He was discharged on tapering doses of ACTH and phenobarbital.
- He was started on another treatment and when seen three months later he had no seizures and was developing normally.
Case 4
Question

What was the treatment that stopped the seizures?
Case 4

- Folinic acid (Leucovorin)
Vitamin Responsive Epilepsy

- Biotinidase deficiency
- Pyridoxine-dependent epilepsy
- Pyridoxal phosphate dependent epilepsy
- Folinic acid-responsive seizures
Case Studies In Epilepsy
Waiting For Relief
Overload

CSI 26. 2-3 203 11 Oct 01
Crash and Burn

CSI 63. 3-17 317 13 Mar 03
Fallen Idols

CSI 158. 7-17 717 22 Feb 07