Pediatric Epilepsy Surgery

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PEDIATRIC EPILEPSY SURGERY
A THING OF BEAUTY…IF DONE RIGHT
PEDIATRIC EPILEPSY SURGERY

But........

MAKE SURE YOU KNOW WHAT YOU ARE DOING
Overview: Epilepsy Surgery in Pediatric Patients

- Surgical candidates ➔ Who
- Developmental issues ➔ When/Why
- Evaluation of patients ➔ Where
- Outcomes ➔ What
- Other Surgical Approaches ➔ Gamma knife, VNS, CC, MSTs
Age of Onset of Epilepsy Disorders That May Lend Themselves to Surgical Approach

- Gelastic seizures (HH)
- Infantile spasms
- Epil. encephalopathy
- Sturge-Weber
- Inf. hemi epilepsy
- Lennox-Gastaut
- Rasmussen
- CPE (tumor/CD)
- CPE (MTS)
- Trauma

Bars indicate unique pediatric onset and “Adult” concepts.

Age 0 5 10 15
Who Should be Considered for Resective Surgery?

- Medically intractable seizures (What defines intractable?)
- Localizable brain abnormality
  - Accessible for Cortical resection
  - Assessment of anticipated neurologic deficit
  - Reasonable assumption that the remainder of the brain is normal and/or patient will be significantly improved if seizures are controlled
  - Good-bad vs. bad-worse

- Resection of Hypothalamic Hematoma
Who Should be Considered for Surgery?

- Medically intractable seizures (What defines intractable?)
  - Do you need to try everything?
    - 21 AED’s currently approved
      - 1 new med every 2 months = 3 ½ years
    - 2 drug combinations @ 1 drug change/2 months
      - 440 combinations = 72 years
    - 3 drug combinations @ 1 change/2 months
      - 8421 combinations = 1400 years
Who Should be Considered for Surgery?

- Medically intractable seizures  (What defines intractable?)

  - Sequential study of 780 adolescents and adults prescribed their first AED

  - Overall response rates with the first, second and third treatment schedules were 50.4, 10.7 and 2.7%, respectively, with only 0.8% patients responding optimally to further drug trials.

? Applicability to younger patients

Overview

- Surgical candidates → Who
- Developmental issues → When/Why
- Evaluation of patients → Where
- Outcomes → What
- Alternatives to cortical resection → Gamma knife, VNS, CC, MSTs
Overview

- Developmental issues → When / Why

*Older children*, i.e., those with CPS or similar issues, seizure control or tumor removal is generally the primary goal.

*Younger Children*: Seizure control is important but the real goal of surgery in very young children with catastrophic epilepsies is to provide an opportunity for the child to have the best possible long-term development by removing the noxious effects of seizures and abnormal brain tissue.
When Should Surgery Become a Consideration?

If seizure control is primary then:

- There is time to be circumspect and cautious
- Be deliberate in seeking all *appropriate* medical therapies

*Time from intractability to surgery ~ 10 years in typical TLE patients*

If improved development is primary then:

- There is urgency to make therapeutic decisions before the opportunity for improved development is lost

*Clearly can’t spend 10 years getting to surgery!!*
Overview

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Concept of 

*Epileptic Focus*
Concept of Epileptic Focus: Applicable in Many Pediatric Patients

- CPE (MTS)
- Some neonatal seizures
- Sturge-Weber
- Some Infantile hemiplegic epilepsy with partial only seizures. (i.e., stroke)
- Rasmussen
- CPE (MTS or tumor)
- Trauma
Case 1

- 8-year-old girl
- FC at 14 and 16 months; typical
- At 2½ yrs, onset of episodes characterized by
  - Appears frightened
  - Runs to parents to be picked up
  - Babbles, picks at her clothes
  - Stiffens for 20-30 seconds then goes limp
  - Post ictal state for minutes to hours
  - Occur Q 2 weeks
MTS
CD and MTS
Case 1

- 8-year-old girl
- What else do we need to know before deciding on surgery?
  - ? PET/SPECT
  - ? Neurocogs
  - ? Wada/fMRI for language, memory
Wada Test: Language and Memory Testing

(a) Left common carotid artery
Sodium amytal
Dye for angiography

(b) What is it I gave you?
Nothing.

(c)
fMRI for Language
Case 2

- 15-year-old right-handed boy, nl cognitively, excellent student; long-distance runner

- Onset of spells at age 12
  - Sometimes has vague feeling of lightheadedness
  - 20 sec later visual disturbance described as “objects blend together and faces look like a Picasso”
    - Improved on AEDs but still has 2/wk
  - Does not lose awareness, never had T-C seizures
  - VEEG: vague slowing R hemisphere with some spells, no change with others
  - MRI
Tumor: Suspect DNET
15-year-old boy

What else do we need to know before deciding on surgery?

- ? PET/SPECT
- ? Neurocogs
- ? Wada/fMRI for language
- ? Other studies
Case 2

- Resection of tumor in 2008
  - DNET

- Seizures free after surgery
  - He stopped his LTG on his own; he was told to continue to take it for now

- One seizure a year later when he “forgot” to take his LTG. Seizure free after restarting

✓ DRIVER’S LICENSE ISSUE
Case 3

- 8-year-old girl
- Onset seizures at 2; dx: FC
- Next seizure at 6 CPS c 2° generalization
  - Eye deviation to right, right focal seizure
  - CPS 5/day, T-C 1/month
  - Failed numerous medications
- Mild right hemiparesis
- VEEG: frequent left frontal discharges
- Major learning set back after each T-C seizure; language, learning seem to wax and wane
Perinatal Stroke
What is it?

5 year old with partial seizures. Infrequent at first but now occur many times per day. Always with the same semiology involving left face and arm.
RASMUSSEN
**CONCLUSIONS**

- CERTAIN PATIENTS WITH INTRACTABLE HAVE LESIONS SIMILAR ENOUGH TO ADULT PATIENTS THAT THEY CAN BE APPROACHED FOR SURGICAL EVALUATION IN THE SAME WAY.

- EXAMPLES:
  - STURGE WEBER SYNDROME
  - INFANTILE HEMIPLEGIC EPILEPSY
    - (SOME PATIENTS HAVE GENERALIZED SEIZURES)
  - RASMUSSEN ENCEPHALITIS
  - MTS
  - TUMOR
Concept of Epileptic Focus: But Not Applicable in Others, Especially “Generalized” Seizures

- Infantile spasms
- Other early-onset epileptic encephalopathies
- Gelastic seizures
- Lennox-Gastaut syndrome

Therefore a different concept – the Zone of Cortical Abnormality (ZCA)
Zone of Cortical Abnormality

- EEG ictal onset
- Increased delta
- Decreased beta
- MRI abnormal
- PET
- +/- MEG focus
VEEG Monitoring

- There may not be an *ictal* focus
  - However, focal changes *may* precede or follow generalized seizure such as IS
  - MISD not a contraindication
  - Generalized Hypsarrhythmia not a contraindication
  - Early EEG may show focus
- *Interictal* EEG abnormalities *may* be most important in identifying a ZCA
  - Focal slowing
  - Lateralized sleep spindles
  - Localized decrease in beta activity
- There may be *multiple* potential foci, i.e., TS
Figure 2 MRI of the patient Brain MRI demonstrates the presence of hemimegalencephaly with an enlarged left hemisphere, colpocephaly (A, B), midline shift of a dysplastic occipital lobe (occipital sign, A, B), white matter signal intensity changes (B, C) horn (arrow, C).

Bindu P S et al. Neurology 2010;74:e27
Focal CD, Right Frontal Lobe

At 6 months of age

At 3 years of age

References to Cortical Dysplasia in the Literature

Number of references

YEARS

References

3
0
1
8
3
0
1
8

YEARS

71-75
76-80
81-85
86-90
91-95
96-00
01 to 05
16-10
11-
Figure 1 Examples of difficult-to-identify type I cortical dysplasia from two patients with epilepsy (A and B) This **15-year-old patient began with seizures at age 4 years.** Interictal scalp EEG disclosed synchronous spikes from F4, C4, and T4 and rarer independent spikes from F3 and C3. Ictal events were associated with broad EEG changes over the right frontal–temporal electrodes. Two previous outside MRI scans had been read as normal, as had his initial fluorodeoxyglucose (FDG)-PET scan (grayscale). FDG-PET/MRI coregistration indicated a well-defined area of focal hypometabolism in the right superior temporal gyrus (B, arrow). Closer inspection of the structural MRI indicated less white matter signal on T2 imaging in the same area (A, arrow). (C and D) **This 8-year-old patient presented with seizure onset at age 3 years.** The seizures were characterized by right leg and arm tonic events with eye fluttering lasting from 15 to 45 seconds. Scalp EEG showed fairly regular synchronous interictal discharges coming from the Cz, C3, and Pz electrodes, with rarer spikes from C4. Scalp EEG ictal onsets were difficult to localize secondary to movement artifacts. A previous outside MRI scan had been read as normal. University of California, Los Angeles MRI was read as showing a subtle lesion consistent with CD (C, arrow). FDG-PET/MRI coregistration indicated a focal area of hypometabolism in the left superior parietal region just behind the sensory cortex (D, arrow).

Cortical Dysplasia Leading to Surgery at UCLA

A: Most Frequent Surgical Etiologies
Children <18 years at Surgery

B: Most Frequent Surgical Etiologies
Adults >18 years at Surgery
SURGERY FOR CORTICAL DYSPLASIA PATIENTS

UCLA EXPERIENCE
SURGICAL TREATMENT OF EPILEPSY ASSOCIATED WITH CORTICAL DYSPLASIA

- **DIAGNOSTIC ACCURACY**
  - EEG: Localizes accurately in 50-66%
  - MRI: Localizes accurately in 70%
    - Often not helpful in type 1 CD’s
  - FDG-PET 80-90%
    - MRI-PET fusion >90%

- **Post op OUTCOMES IN CD PATIENTS**
  - Overall 60% seizure free in short term
    - 80% if complete resection
    - 20% if incomplete resection
Final Surgical Decision

- **ZCA present**
  - Multiple lines of evidence point to one area or hemisphere as likely etiology of seizures

- **Risk : benefit assessment**
  - Often most difficult decision; some patients have such disastrous seizures that higher level risk of failure is acceptable
  - Good : bad vs. bad : worse

- **Never** talk family into surgery; surgery offered as option, not necessity

- **Resect vs. no resect**: decision is usually made in OR with ECoG guidance
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5 YEAR OUTCOME DATA

- UCLA patients operated at <18 years between 1986 and 2005
- N = 257
  - Continuously seizure free = 53%
  - Late seizure recurrence = 18%
  - Seizure free after initial failure = 3%
  - Never seizure free = 25%

Hauptman et al. Neurosurg Aug 14, 2012 (epub)
OUTCOME IN PEDIATRIC EPILEPSY SURGERY PATIENTS

- RATE OF SEIZURE CONTROL AND TIME OF SURGERY

<table>
<thead>
<tr>
<th>SURGICAL EPOCH</th>
<th>% CONTINUOUSLY SEIZURE FREE AT 5 YEARS</th>
</tr>
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<tbody>
<tr>
<td>1986-1990</td>
<td>46%</td>
</tr>
<tr>
<td>1991-1995</td>
<td>36%</td>
</tr>
<tr>
<td>1996-2000</td>
<td>61%</td>
</tr>
<tr>
<td>2001-2005</td>
<td>68%</td>
</tr>
</tbody>
</table>

Hauptman et al. Neurosurg Aug 14, 2012 (epub)
FIGURE. Box plots comparing for private and government (CCS/MediCal) insurance seizure onset to referral, referral (evaluation) to surgery, and seizure onset to surgery (SZ duration) (A) and pre- and post-surgery Vineland adaptive scores for private and government insurance (B). Mean (±SD) provided above each bar. A, the interval from seizure onset to referral (log-rank; \(P = .034\)) and seizure duration (\(P = .017\)) was longer for patients with government compared with private insurance. B, pre- (t test; \(P = .042\)) and postsurgery (\(P = .001\)) Vineland developmental quotients (DQs) were higher (better) for those with private compared with government insurance. Number of cases per blot noted for Vineland scores. CCS, California Children's Services; SD, standard deviation.
Hypothalamic Hamartoma (HH)

- Gelastic seizures begin in infancy
- CPS seizures often occur later
- May evolve to tonic/drops etc. with slow spike and wave
- Associated with:
  - Cognitive decline
  - Rage attacks
  - Precocious puberty
Treatment of HH

- AEDs generally don’t work very well
- Surgery
  - Sub-frontal or temporal approach
  - Transcallosal approach
  - Endoscopic/ventricular approach
  - Gamma knife
Transcallosal Resection of HH

- Success rates, 70-90% reported
- Problems with:
  - Increased appetite/obesity
  - Some memory disturbances
  - Somnolence
  - Temperature instability
Treatment of HH

- AEDs generally don’t work very well
- Surgery
  - Sub-frontal or temporal approach
  - Transcallosal approach
  - Endoscopic/ventricular approach
  - Gamma knife
Corpus Callosotomy: Indications

- Specific seizure considerations
  - Drop attacks
    - Atonic
    - Tonic
  - Secondarily generalized tonic-clonic seizures
  - Complex partial seizures

Not utilized much anymore
Alternative Therapies

Multiple Subpial Transection: Conceptual Framework

- Physiologic function based on vertically arranged columns
- Minimal volume of transversely arranged contiguous tissue necessary to generate an epileptiform spike

Morrell, 1997 in Epilepsy: A Comprehensive Textbook. Ch 177
FIG. 1. Artist's drawing to illustrate the technique of insertion and movement of the subpial transector. (From Morrell et al., ref. 40, with permission.)
Purpose of surgery must be clearly defined before surgery is performed.

Seizure control is important but it is not always the primary goal in young children with catastrophic epilepsy; improved development is often the goal.
Concept of Epileptic Focus: Applicable in Many Pediatric Patients

- CPE (MTS)
- Some neonatal seizures
- Sturge-Weber
- Infantile hemiplegic epilepsy (stroke)
- Rasmussen
- CPE (tumor)
- Trauma
TAKEAWAY MESSAGES

Concept of Epileptic Focus: But Not Applicable in Others, Especially “Generalized” Seizures

- Infantile spasms
- Other early-onset epileptic encephalopathies
- Gelastic seizures
- Lennox-Gastaut syndrome

DON’T DEPEND TOO HEAVILY ON THE EEG IN THESE CASES, REMEMBER

THE “ZCA” CONCEPT