Autoimmune Epilepsy: Recognition & Treatment

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Faculty/Presenter Disclosure

• Faculty: Jeffrey W. Britton, MD

• Relationships with financial sponsors:
  – Grants/Research Support: None
  – Speakers Bureau/Honoraria: None
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  – Patents: None
  – Other: Co-investigator (unpaid) in:
    • A Randomized Double Blind Placebo Controlled Study of IVIG in Patients with Voltage Gated Potassium Channel Complex Antibody Associated Autoimmune Epilepsy
    • GW Pharma “Cannabidiol in refractory epilepsy related to tuberous sclerosis” An open label extension study to investigate the safety of cannabidiol (GWP42003-P; CBD) in children and adults with inadequately controlled Dravet or Lennox-Gastaut Syndromes.
Disclosure of Financial Support

• **Potential for conflict(s) of interest:**
  – Mayo Clinic receives payments covering costs of subjects enrolled in
    • Grifols Pharmaceuticals sponsored trial of IVIG in VGKC encephalitis, a maker of IVIG which is a product that will be discussed in this program
    • GW Pharma “Cannabidiol in refractory epilepsy related to tuberous sclerosis” An open label extension study to investigate the safety of cannabidiol (GWP42003-P; CBD) in children and adults with inadequately controlled Dravet or Lennox-Gastaut Syndromes.
Mitigating Potential Bias

- All unapproved treatments marked as unapproved in slides
- Efficacy of several immunosuppressants other than IVIG discussed with respect to management
Objectives

At the end of the session, the learner will:

1. Recognize the clinical features suggesting the diagnosis of autoimmune epilepsies
2. Be aware of the characteristic radiologic, EEG features and spinal fluid findings in autoimmune epilepsies
3. Determine features suggesting likelihood of positive antibody test results and positive therapeutic response
Case 1

- 39 yo F, 3 years déjà-vu, olfactory auras, few/month
- 7 months prior – “waves”, chills – 20+/d
- 2 months prior – left hemiconvulsive seizures
- Also memory loss, 20 # weight loss
- Valproate, pregabalin, lacosamide – minimal effect
- EEG negative during “waves”; witnessed convulsive events deemed “atypical” – dx PNES at NAEC level IV center
- 2nd opinion – subtle temporal discharge in 4 of 20 “waves”
- CSF neg, ANA 1:120, SSB+
Case 1 (cont’d)

• Neuroimmunology panel + VGKCc 0.62 nmol/L (<0.01 nmol/L)
• IV methylprednisolone* (IVMP) 1 gram daily x 5, then weekly x 12
• “wave” seizures stopped by week 2 for 6 weeks, then recurred at rate of 6 per week
• Mycophenolate* 500 mg BID, ↓ IVMP
• After 8 weeks, “waves” increased 20/d, ↑ IVMP then Rituximab* no benefit
• CBZ helped, seizures ↓ 6 per wk
• 2 years after dx – IVMP* d/c’d, 3 years after dx – mycophenolate* d/c’d; auras 5-6 per week

*not approved for use for this indication
AUTOIMMUNE EPILEPSY: WHAT IS IT?
Immunologically mediated CNS disorder in which recurrent seizures are a primary feature
Autoimmune etiology suggested by:
• detection of neural autoantibodies
• inflammatory changes on CSF or MRI
• other etiologies excluded
Antibodies or clear signs inflammation may be absent

Quek, Britton, Pittock et al. Arch Neurol 2012; 69: 582-93
Autoimmune encephalitis and Autoimmune epilepsy – Why two terms?

• While epilepsy clearly complicates encephalitis, and presence of evidence of encephalitis clarifies etiology...
• Some pts with inflammatory etiologies lack all signs of encephalitis, leading to diagnostic delay
• Not all autoimmune epilepsies have identifiable antibody
• Failure to identify inflammatory etiology may lead to omission of effective treatment
HOW COMMON IS IT?  WHEN IS ANTIBODY POSITIVITY SIGNIFICANT?  WHAT ABOUT FALSE POSITIVES?
Autoimmune encephalitis epidemiology

• Annual incidence encephalitis ~ 5 to 8 cases per 100,000 persons, 40 to 50% idiopathic¹
• Autoimmune 3rd most common
  – NMDA surpasses that of any single infectious agent²
• NMDA 1% of all young adult ICU admissions³
• LGI1 incidence 0.83 per million/year⁴
• overall autoimmune epilepsy incidence unclear
  – Seronegative cases

Neural Ab prevalence persons with epilepsy

• N=124 children with focal epilepsy
  – 5 (4%) had neural Abs\textsuperscript{1}
• N=66 adults >55 yrs new onset epilepsy
  – 4 (6%) had evidence autoimmune cause\textsuperscript{2}
• N=112 consecutive pts cryptogenic epil
  – Abs (all) 39 (34.8\%)\textsuperscript{3}
• N=82 with DRE unknown cause, 17 (22\%) Ab+\textsuperscript{4}

Neural Abs in disorders other than epilepsy

• N=70 achalasia, n=161 controls\(^1\)
  – Neural antibodies: 25.7% vs 4.4% (\(p<10^{-4}\))
  – GAD65 21.4% v 2.5% (\(p<10^{-4}\))

• GAD65 9-13yrs in n=4496 non-diabetics (Norway)\(^2\)
  – 1.7% GAD65+ initially; 54% became neg over time
  – 0.4% initially neg became +
  – GA65 associated w TPO Ab+, HLA-DQA1/DQB1

CLINICAL FEATURES
Clinical features suggesting autoimmune epilepsy

- Focal epilepsy
- Subacute onset
- High seizure frequency
- Certain MRI, fdg-PET, EEG features
- Risk factors for Ca, autoimmunity present
- Additional neurologic symptoms
- Nonimmunologic causes excluded

Autoimmune epilepsy work-up warranted

CLINICAL FEATURES –
MAYO AUTOIMMUNE EPILEPSY SERIES

N=32; median age = 56 years (5-79)
Seizure duration = 5 months (3 weeks – 12 years)
All had focal (partial) seizures
Median anticonvulsants tried = 3
Seizure frequency – daily 26 (81%)

Quek, Britton, Pittock et al. Arch Neurol 2012; 69: 582-93
LGI-1 clinical manifestations - frequency

- Video-EEG analysis seizures in 16 LGI-1 pts
- 14 with 86 faciobrachial dystonic sz
  - $\mu=0.4$/hr (0.1-9.8)
- 11 non-FBD (53) seizures alone or in addition
  - $\mu=0.1$/hr (0.1-2)

Aurangzeb et al. Seizure 2017; 50:14-7
Phenotypes, outcomes LGI-1 & CASPR-2

• N=196 LGI1, n=51 CASPR2, n=9 dual in lab database
• CNS: LGI1 81%, CASPR2 47% (p<0.00001)
• Limbic encephalitis, cognitive, depression more common with LGI1 than CASPR2
• Paroxysmal dizzy spells 17% LGI1

Faciobrachial dystonic seizures
Faciobrachial dystonic seizures
Ictal fear, panic—multiple per day
**Table 1**
Comparison between antibody-positive cases, antibody-negative cases, and MTLE-HS (control)

<table>
<thead>
<tr>
<th>Seizure characteristic</th>
<th>Positive (n = 30)</th>
<th>Negative (n = 22)</th>
<th>( P^1 ) value</th>
<th>Control (n = 22)</th>
<th>( P^2 ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset (y), median(^b)</td>
<td>58</td>
<td>45</td>
<td>0.320</td>
<td>13.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of seizures (mo), median(^a)</td>
<td>2</td>
<td>7.5</td>
<td>0.007</td>
<td>138</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Seizure type</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>SPS</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPS duration (sec), median(^a)</td>
<td>8</td>
<td>7</td>
<td>0.456</td>
<td>30</td>
<td>NA</td>
</tr>
<tr>
<td>SPS frequency</td>
<td></td>
<td></td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Daily, ( n ) (%)</td>
<td>7 (100)</td>
<td>7 (100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly, ( n ) (%)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Monthly, ( n ) (%)</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>CPS</td>
<td>15</td>
<td>16</td>
<td>0.922</td>
<td>95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CPS duration (sec), median(^a)</td>
<td>11</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPS frequency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily, ( n ) (%)</td>
<td>14 (93.33)</td>
<td>16 (100)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weekly, ( n ) (%)</td>
<td>1 (6.67)</td>
<td>0</td>
<td>12 (60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monthly, ( n ) (%)</td>
<td>0</td>
<td>0</td>
<td>8 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postictal confusion, ( n ) (%)</td>
<td>0</td>
<td>0</td>
<td>18 (81.82)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGTC circadian rhythm(^b)</td>
<td>23</td>
<td>14</td>
<td>0.705</td>
<td>8</td>
<td>0.002</td>
</tr>
<tr>
<td>Sleep, ( n ) (%)</td>
<td>18 (78.26)</td>
<td>10 (71.43)</td>
<td></td>
<td>1 (12.50)</td>
<td></td>
</tr>
</tbody>
</table>

NMDA encephalitis – Initial clinical features

NMDA - catatonia
NMDA – oral dyskinesias
NMDA – speech disorder, behavior, seizures, dyskinesia
EEG
EEG in autoimmune epilepsy

- Abnormal in 80%
  - May be normal if not encephalopathic
- Bitemporal sharp waves and seizures
- Generalized rhythmic delta – “extreme delta brush” - NMDA
- Multifocal epileptiform abnormalities

EEG in ANNA-1 encephalitis – limbic & non-limbic

Left temporal seizure – VGKC (LGI-1)
Right temporal seizure – VGKC (LGI-1)
EEG depends on seizure type

- N=18 pts
- 4-faciobrachial dystonic (FBD) seizures only
  - Ictal EEG normal in all
- 6-non-FBD seizures only
  - EEG abnormal in all
- 8-FBD + other seizure types
  - Typically FBD then temporal seizure
  - EEG abnormal in all

Chen et al. Epilepsy Behavior 2017; 77:90-5
EEG in LGI-1 FBD seizures

- N = 4 patients with FBD seizures, LGI-1
- Low frequency analog 0.07 Hz filter
- Pre-spasm infraslow activity (ISA) preceded clinical spasm by 1.2 sec
- Contralateral to spasm

Wennberg et al. Clin Neurophys 2018; 129:59-68
Generalized rhythmic delta 48 F \((NMDA)\)
NMDA – 48F - 4 months later
NMDA – 24 F – evolution of EEG patterns
EEG in autoimmune epilepsy

• Ab+ PWE (20) vs seronegative PWE (21) (blind)
• 71% Ab+ continuous θ or Δ, compared to only 25% of those who were seronegative
• 40% Ab+ showed FIRDA, compared to 24% seronegative group
• Delta brush only seen in NMDA

Hashimoto’s – EEG manifestations

- All showed mild to severe generalized slowing
- Triphasic waves, IEDs, photoparoxysmal
- Recorded myoclonus in 8, no EEG correlate

VGKCC (not subtyped) – neuroimaging

- 33/42 patients (78.6%) showed mesial temporal enlargement, T2-hyperintensity
- Hippocampal atrophy - 16/33 (48.5%)
- Restricted diffusion on DWI in 8/13 (61.5%)
- Basal ganglia can be involved (T1 or T2 hyperintensities caudate, putamen)

NMDA – structural & functional MRI

• Structural imaging normal in 50-75%
• Functional imaging
  – reduced functional connectivity between hippocampi & default mode network
  – DTI - extensive white matter changes, most prominent in the cingulum

- Claustrum FLAIR hyperintensity

- All 4 - explosive onset seizures, cognitive and behavioral disturbance

- EEG - frontal, parasagittal epileptiform activity

- 1 GAD-65, 1 Ma2, 2 seronegative

CASE SELECTION FOR TESTING AND TREATMENT
CASE SELECTION IMPORTANCE

• Antibodies of uncertain significance may be encountered
• Some Abs/syndromes less responsive to immunotherapy than others
• Work up and treatment are costly and have risks
CLINICAL APPROACH

1. Clarify syndrome, and Ab type if present
   – determines immunotherapy potential, tumor risk
2. Determine duration since symptom onset
   – Shorter the better re: chances of success of immunotherapy
3. Determine cognitive status, risk, and review imaging to gauge irreversibility
4. Identify metrics you can follow to assess progress
   – seizure frequency, cognitive testing, imaging, EEG
Diagnostic criteria: Definite autoimmune encephalitis

Diagnosis can be made when all four* have been met:

1. Subacute onset (rapid progression < 3 mos) working memory deficits, altered mental status, psychiatric symptoms
2. Bilateral brain abnormalities on T2/FLAIR MRI or fdg-PET highly restricted to the medial temporal lobes
3. At least one of the following:
   – CSF pleocytosis (WBC > 5 cells per mm³)
   – EEG with temporal epileptic or slow-wave activity
4. Reasonable exclusion of alternative causes

* = if neural Ab positive, only 2 of first 3 required

May be too restrictive, impacting sensitivity

Who to test, who to treat? *APE and RITE*

- **APE** – *Antibody Prevalence in Epilepsy*
  - Predicts likelihood of antibody positivity
  - Score $\geq 4$: sens 97.7%, spec 77.9%
- **RITE** – *Response to Immunotherapy in Epilepsy*
  - Determines potential for response to immunotherapy
  - Score $\geq 7$: sens 87.5%, spec 83.8%
- **APE$^2$, RITE$^2$** – improved specificity

## Antibody Prevalence in Epilepsy (APE²)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Yes/No (Y/N)</th>
</tr>
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<tbody>
<tr>
<td>New onset, rapidly progressive (1-6 weeks) mental status changes or seizures, within 1 year of eval</td>
<td>1 pt</td>
</tr>
<tr>
<td>Neuropsychiatric (agitation, aggression, emotion lability)</td>
<td>1 pt</td>
</tr>
<tr>
<td>Autonomic dysfunction (sustained supra/bradycardia, OH, hyperhidrosis, labile BP, VTach, asystole) if no prior hx</td>
<td>1 pt</td>
</tr>
<tr>
<td>Viral prodrome (in absence Ca history last 5 yrs)</td>
<td>2 pt</td>
</tr>
<tr>
<td>Facial dyskinesia in absence FBD seizures</td>
<td>2 pt</td>
</tr>
<tr>
<td><strong>Faciobrachial dystonic (FBD) seizures</strong></td>
<td><strong>3 pt</strong></td>
</tr>
<tr>
<td>Seizures refractory 2 or more AEDs</td>
<td>2 pt</td>
</tr>
<tr>
<td>CSF inflammatory (protein &gt; 50 mg/dL, WBC &gt; 5 cells/μL)</td>
<td>2 pt</td>
</tr>
<tr>
<td>MRI findings of limbic encephalitis (T2/FLAIR hyperintensity one or both medial temporal lobes, or multifocal grey/white matter or both c/w demyelination/inflammation) (no MRI=&quot;n&quot;)</td>
<td>2 pt</td>
</tr>
<tr>
<td>Underlying malignancy &lt; 5 yrs neurologic onset</td>
<td>2 pt</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0 Abnl &gt;= 4</td>
</tr>
</tbody>
</table>

## Response to Immunotherapy in Epilepsy (RITE2)

<table>
<thead>
<tr>
<th>RITE2</th>
<th>Yes/No (Y/N)</th>
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<tbody>
<tr>
<td>New onset, rapidly progressive (1-6 weeks) mental status changes or seizures, within 1 year of eval</td>
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<td>Autonomic dysfunction (sustained supra/bradycardia, OH, hyperhidrosis, labile BP, VTach, asystole) if no prior hx</td>
<td>1 pt</td>
</tr>
<tr>
<td>Viral prodrome (in absence Ca history last 5 yrs)</td>
<td>2 pt</td>
</tr>
<tr>
<td>Facial dyskinesia/FBD movements</td>
<td>2 pt</td>
</tr>
<tr>
<td><strong>Faciobrachial dystonic (FBD) seizures</strong></td>
<td>3 pt</td>
</tr>
<tr>
<td>Seizures refractory 2 or more AEDs</td>
<td>2 pt</td>
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<td>2 pt</td>
</tr>
<tr>
<td>Underlying malignancy &lt; 5 yrs neurologic onset</td>
<td>2 pt</td>
</tr>
<tr>
<td>ImmunoRx within 6 months onset</td>
<td>2 pt</td>
</tr>
<tr>
<td>Neural plasma membrane autoantibody detected (NMDAR, GABAAR, GABABR, AMPAR, DPPX, mGluR1, mGluR2, mGluR5, LGI1, IgLON5, CASPR2 or MOG)</td>
<td>2 pt</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0 Abnl &gt;=7</td>
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</table>
# Autoimmune epilepsies - management

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Tumor screen</th>
<th>ImmunoRx?</th>
<th>Other Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>LGI1/CASPR2</td>
<td>10% thymoma</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>VGKC (-/-)</td>
<td>10% thymoma</td>
<td>Poor response</td>
<td>No</td>
</tr>
<tr>
<td>NMDA</td>
<td>Ovarian teratoma</td>
<td>Yes</td>
<td>Teratoma surgery</td>
</tr>
<tr>
<td>GAD65</td>
<td>Low yield</td>
<td>Poor response</td>
<td>None</td>
</tr>
<tr>
<td>GABA-B</td>
<td>Small cell lung</td>
<td>Yes</td>
<td>Cancer</td>
</tr>
<tr>
<td>GABA-A</td>
<td>Thymoma</td>
<td>Yes</td>
<td>Thymoma</td>
</tr>
<tr>
<td>AMPA</td>
<td>SCLung, Thym, Breast</td>
<td>Yes</td>
<td>Cancer</td>
</tr>
<tr>
<td>Ma2</td>
<td>Testicular seminoma</td>
<td>Poor response</td>
<td>Cancer</td>
</tr>
<tr>
<td>Hashimoto’s TPO</td>
<td>Low yield</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Onconeural Ab</td>
<td>Yes</td>
<td>Poor to moderate</td>
<td>Cancer</td>
</tr>
<tr>
<td>SLE</td>
<td>No</td>
<td>Moderate</td>
<td>No</td>
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<tr>
<td>Celiac</td>
<td>No</td>
<td>Unknown</td>
<td>Diet</td>
</tr>
<tr>
<td>SNALE</td>
<td>Unknown</td>
<td>Moderate</td>
<td>Unknown</td>
</tr>
<tr>
<td>NORSE/FIRES</td>
<td>Low yield</td>
<td>Poor response</td>
<td>Anakinra? Others?</td>
</tr>
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</table>
TREATMENT APPROACH AND PUBLISHED OUTCOMES
AEDs do have a role in autoimmune epilepsy

- Metanalysis 6 autoimmune epilepsy studies
- N=139 patients
- **AEDs efficacious in 10% overall:**
  - Seronegative = 18%, VGKC = 11%, GAD65=8%
- 73% of AED responders did so to Na+ channel blockers
AEI

• N=50 autoimmune patients
• Levetiracetam used by 42/50, unhelpful in all
• 27/50 seizure-free
  – 18 (36%) with immunotherapy alone
  – 5 (10%) AEDs alone
  – 4 (8%) AEDs after immunotherapy
• Sodium channel blockers most effective

Feyissa et al. Neurol Neuroimmun Neurolinflamm. 2017; 4:e353
Surgery in autoimmune epilepsy

- **N=13**, sz onset age $\mu=23$ yrs, epil duration not stated, seizure rate: $\mu=20$/month, 5 encephalitic phase

- All had temporal lobe surgical procedures (1 RF)
- MRI: unilateral temporal abnl 9, bilateral 3, normal 1
- Abs: GAD65 (8), Ma2 (2), Hu(1), LGI-1(1), CASPR2(1) (five discovered after surgery)

- 2/13 were Engel I, 3/13 Engel II (38% Engel I or II)
  - 2 GAD65, 1 Ma2, 1 LGI-1, 1 Hu

- Path: perivascular lymphocytic infiltrates 7/12

Autoimmune epilepsy diagnosed

If No: Stop, consider trial of acute option not previously used or consider other immunotherapies (rituximab*, others?)

IV methylprednisolone* 1 g IV or IVIG* 0.4 -1 g/kg IV daily for 3-5 days, then weekly x 6 wks then every other week x 6 weeks or PLEX* (severe attacks)

? Improved

If yes: Gradual taper IVMP/IVIG over 6 mos Consider chronic immunosuppressant (e.g. mycophenolate*, azathioprine*, cyclophosphamide*, methotrexate*)

*None are approved for use by FDA for this indication

Immunotherapy results

• N=29 patients treated (23 IVMP, 6 IVIG)
• 18 (62%) responded, 15 to first selection
  – 10 seizure free (34% of whole cohort)
  – 12/15 responders did so in first 4 weeks, 6 within first week
• Earlier treatment correlated with response
  – Responders: treatment median 9.5 mos after seizure onset, nonresponders 22 mos ($p = 0.048$)

Toledano, Britton, Pittock Neurology 2014; 82(18):1578-86
Immunotherapy – Antibody type matters

Toledano, Britton, Pittock Neurology 2014; 82(18):1578-86
LGI-1 encephalitis and FBD seizures – early Rx

• N=103 pts - FBD seizures & LGI-1 Abs
• 9/89 (10%) controlled w AEDs alone
• 51% experienced control w immunoRx in 30d
  ‒ earlier in cognitively normal pts

Thompson et al. Brain 2018; 141:348-56
Predictors of outcome in autoimmune epilepsy

- meta-analysis, 46 studies – 186 responders, 96 non-responders

- Responders:
  - Older - \( \mu=43 \text{yrs} \) vs 31 yrs (\( p<0.01 \))
  - Cell-surface Abs – 68% vs 39% (\( p<0.05 \))
  - Shorter duration symptom onset to treatment – 80 vs 554 days (\( p<0.01 \))

Dubey et al. Ther Adv Neurol Disord. 2016; 9:369-77
Autoimmune epilepsy outcome

• N=34 pts, retrospective; μ=44.9 yrs
• Abs+ in 26/34 (76.5%):
  – VGKC (8), NMDA (7), TPO (5), GAD (4), GABA-B (2)
• 19/32 (63.3%) >50% seizure reduction
  – 5/8 seronegative responded to immunoRx
• time from symptom onset, dx shorter in responders than non-responders (p<0.005)

Dubey et al. Seizure 2015; 29:143-7
Seronegative autoimmune limbic encephalophathy (SNALE)

- N=28 recent onset TLE, MRI and clinical indicators limbic encephalitis
- 100% had seizures, 86% impaired cognition
- Following pulse steroids*:
  - 13 (46%) seizure-free (>2 months)
  - 48% MRI improved
  - 57% cognition improved, 32% worsened

*=treatment not approved for this indication

Autoimmune epilepsy seropositive and seronegative treatment response

• N=61 with autoimmune epilepsy
• Abs+ in 39
  – VGKC 23, NMDA 9, GABA-B 6, anti- amphiphysin 1
• Seronegative = 22
• Ab status affected ImmunoRx efficacy:
  – 84.6% Ab+ responders versus 40% of seronegative

MRI amygdala enlargement - possible sign of autoimmune epilepsy?

Responder – A1 before, A2 after Rx – decreased amygdala size

Non-responder – D1 before, D2 after Rx – no change in amygdala size

NMDA treatment results

All 472 treated

N=251 Pts who responded to 1st line Rx

N=96 failed 1st line, no 2nd line Rx

N=125 failed 1st line, received 2nd line

Rituximab in autoimmune LE

- N=80 (controls)
- Treatment group: 30 surface Ab+ (NMDA 27, LGI1 3), 15 (onconeural), 35 (seronegative)
- Efficacy not affected by Ab status (onconeural group improved as well)

*not approved for this indication

Lee et al. Neurology 2016; 86:1683-91
TCZ -
N = 91
30 –
TCZ naïve
Majo imprc

*Tocilizumab – not approved for this indication

Lee et al. Neurotherapeutics. 2016; 13:824-32
Interleukin-2* in autoimmune encephalitis

- IL-2 restores balance regulatory and effector T-cells
- N=10 low-dose IL-2
- 6 improved MRS by 1 point (p=0.014) compared to baseline

Lim et al. 2016; 299:107-11;
*IL-2 not approved for this indication
CONCLUSIONS

• Autoimmune epilepsies and encephalitis are potentially treatable with immunotherapy – recognition essential
• Case selection helps identify persons with autoimmune epilepsies and identify those most likely to respond to treatment
• Weighing clinical factors can inform decisions about selection of patients for testing and treatment in those diagnosed
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Questions?
References

References

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