Contemporary Neurology 2025
Case 2

Dane Chetkovich, MD, PhD

DISCLOSURES

- **Name:** Dane M. Chetkovich, MD, PhD
- **Relevant Financial Relationships:** None
- **Consultant for:** None
- **Speaker's Bureau for:** None
- **Grant/Research Support from:** NIH (NINDS, NIMH)
- **Stockholder in:** None
- **Employee of:** Vanderbilt University Medical Center
- **Off-Label Use:** I will/will not discuss off-label use of medications/devices.

Learning Objectives

At the conclusion of this activity/session, participants will be able to:

1. Determine localization of neurological disease in a patient presenting with unique symptoms
2. Create a differential diagnosis for patients presenting with unique symptoms
3. Describe the diagnostic criteria for specific neurological diseases
4. Demonstrate the proper use of diagnostic testing to determine the neurological cause of specific unique symptoms

History of present illness

- 58-year-old male bank executive with past medical history significant for type 2 diabetes and asthma
- Wife noted he had been “distracted” and irritable for the past month.
- Left Nashville 1 week ago for “Guys Trip” fishing in rural Montana
- In rental cabin friends noted he was not sleeping, perseverating on topics and saying “odd things”
- Patient was initially evaluated in a hospital in Helena, MT who believed that symptoms were secondary to psychiatric illness. Wife signed patient out AMA and presented to VUMC for further evaluation.

Exam

- GENERAL: No acute distress, left tongue laceration, bruise on forehead
- MENTAL STATUS:
  - Attention and concentration: impaired, unable to answer questions appropriately
  - Orientation: oriented to person and place, not time
  - Memory: impaired short-term recall
  - Language: fluent speech
  - Fund of knowledge: does not know current president
- CRANIAL NERVES: II-XII intact; Intermittent twitching of the left platysma
- MOTOR: Paratonic tone throughout; 5/5 strength
- SENSORY: intact to light touch throughout
- REFLEXES: 2/4 upper and lower extremities; Toes equivocal
- COORDINATION: no ataxia with FNF bilaterally
- GAIT: normal casual gait

Initial work-up in the ED

Labs:

- WBC 10.9
- Na 133
- Vitamin B12 422
- Thiamine 130
- Folate 11.1
- TSH 0.7
- Anti-thyroglobulin negative
- Ammonia 27
- HIV non-reactive
- UA noninfectious
- UDS negative

CT head non-contrast: no acute abnormalities

Then admitted to the general neurology service

Differential Diagnosis?
Next Steps?

Differential diagnoses

Infection

- HSV
- Neurosyphillis
- PML
- CJD

Metabolic, including Wernicke Syndrome

Autoimmune

- Systemic- SLE, Antiphospholipid syndrome
- Neuro-immune
  - Autoimmune encephalitis
  - Paraneoplastic

Neurodegenerative

- AD
- Lewy Body Dementia
- FTD

Malignancy

- Lymphoma, Glioma

Other

- Non-convulsive status
- Vasculitis

EEG

- **EEG findings**:
  - Intermittent generalized irregular delta and theta activity
  - Abundant right hemispheric (predominantly temporal) irregular delta activity
  - Three right temporal subclinical ictal discharges
  - Occasional right temporal LPDs+R

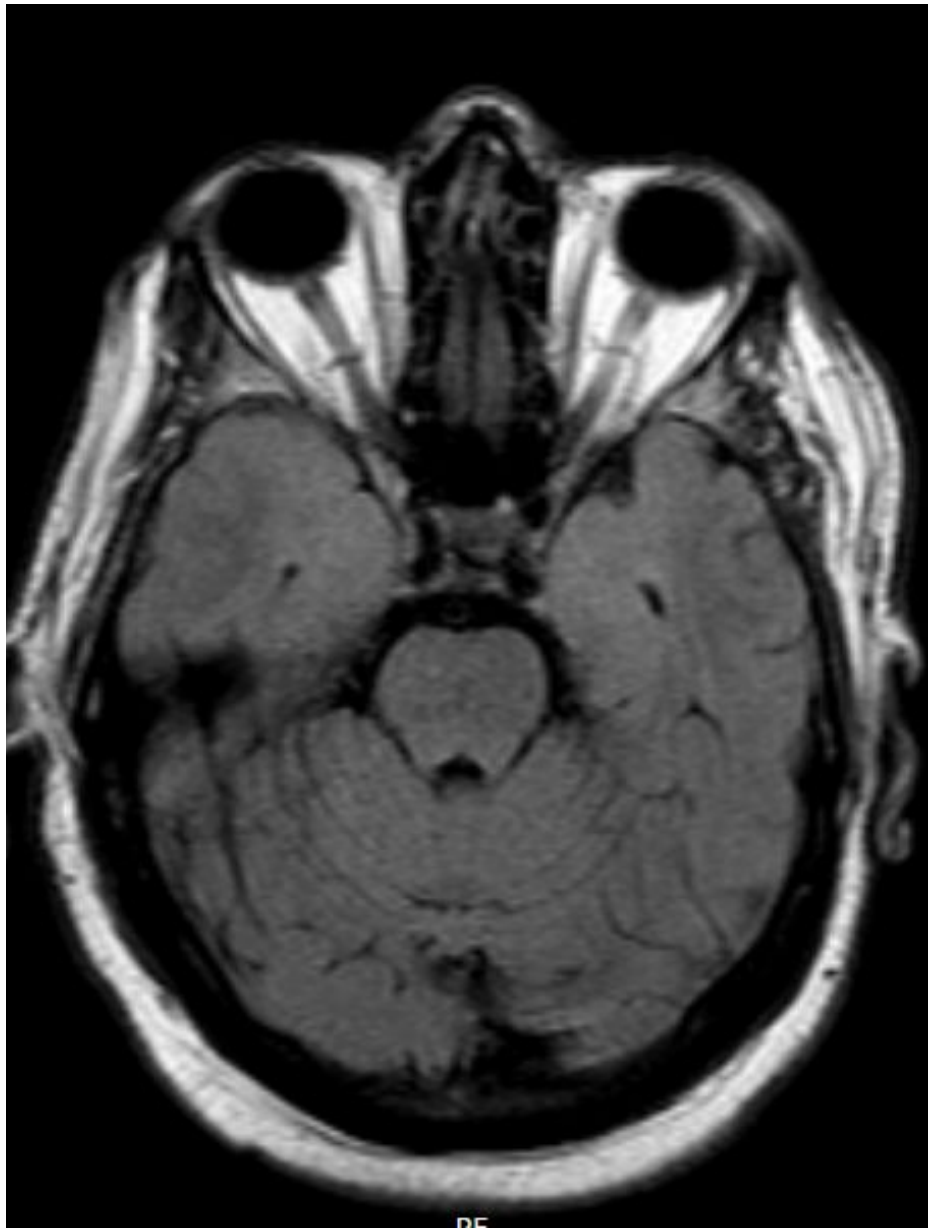
- **Clinical interpretation**: This EEG demonstrates an active epileptogenic focus in right temporal region with three ictal discharges recorded. There is evidence of right hemispheric dysfunction superimposed on mild generalized cerebral dysfunction. No ictal correlate seen with pushbutton events.

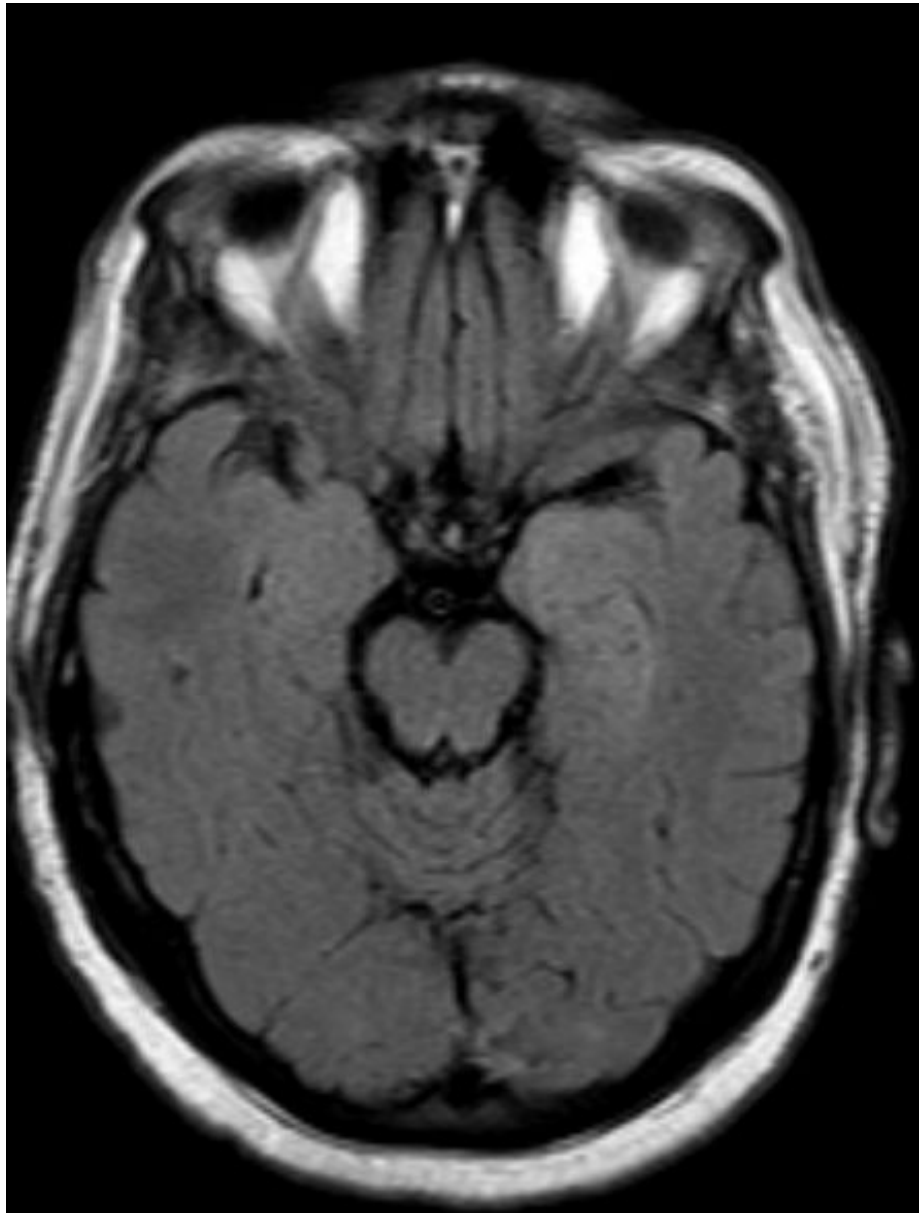
Treatment Initiated

Received 4500mg levetircetam load and 2mg lorazepam

Started on 750mg levetiracetam twice daily maintenance therapy

Next Step?





CSF studies

- Opening pressure 12
- Nucleated cells 2 (85% lymphocytes)
- RBCs 0
- Protein 55
- Glucose 89
- MEP negative (including HSV/VZV)
- Cytopathology negative for malignancy

Thoughts?

Differential diagnoses

- ~~Infection~~
  - ~~HSV~~
  - ~~Neurosyphillis~~
  - ~~PML~~
  - ~~CJD~~
- ~~Metabolic, including Wernicke Syndrome~~
- Autoimmune
  - ~~Systemic- SLE, Antiphospholipid syndrome~~
  - Neuro-immune
    - Autoimmune encephalitis
    - Paraneoplastic
- Neurodegenerative
  - AD
  - Lewy Body Dementia
  - FTD
- ~~Malignancy~~
  - ~~Lymphoma, Glioma~~
- ~~Other~~
  - ~~Non-convulsive status~~
  - ~~Vasculitis~~

Overall, clinical presentation was concerning for an autoimmune or paraneoplastic limbic encephalitis

Evaluation for underlying malignancy

- CT chest/abdomen/pelvis with contrast: No evidence for primary or metastatic malignancy
- Testicular US: Bilateral small hydroceles. Right scrotal pearl. No other scrotal abnormalities demonstrated

Inpatient cognitive testing

Impression:

"Moderate cognitive communication deficits with difficulty appreciated in areas of orientation, recent and delayed recall, attention, trail making, and verbal fluency."

Agitation

- Agitation was initially an issue during hospitalization for which psychiatry was consulted.
- The patient pulled out IV, removed EEG leads, and would jump off the bed over the side rail.
- Due to prolonged QT interval, antipsychotics were initially avoided. Patient was initiated on Depakote 250mg twice daily and subsequently increased to 250mg in the morning and 500mg in the evening. Repeat EKG showed improved QTc so quetiapine 25mg QHS was added.

Memory impairment

- Psych progress note (11/30): "He was somewhat distressed and states he just "found out I am divorced." He reports wife will be at hospital later in the day though. Interview was limited today as pt asked the provider to terminate interview due to distress. Pt declined further support."
- Primary team progress note (11/30): "[patient] reporting that his wife is coming to the hospital later although he is not married anymore."
- SLP progress note (12/2): "states he is unsure if he is married or divorced."
- Outpatient follow-up note (12/9): "he has also been texting his ex-wife of 6 years repeatedly."

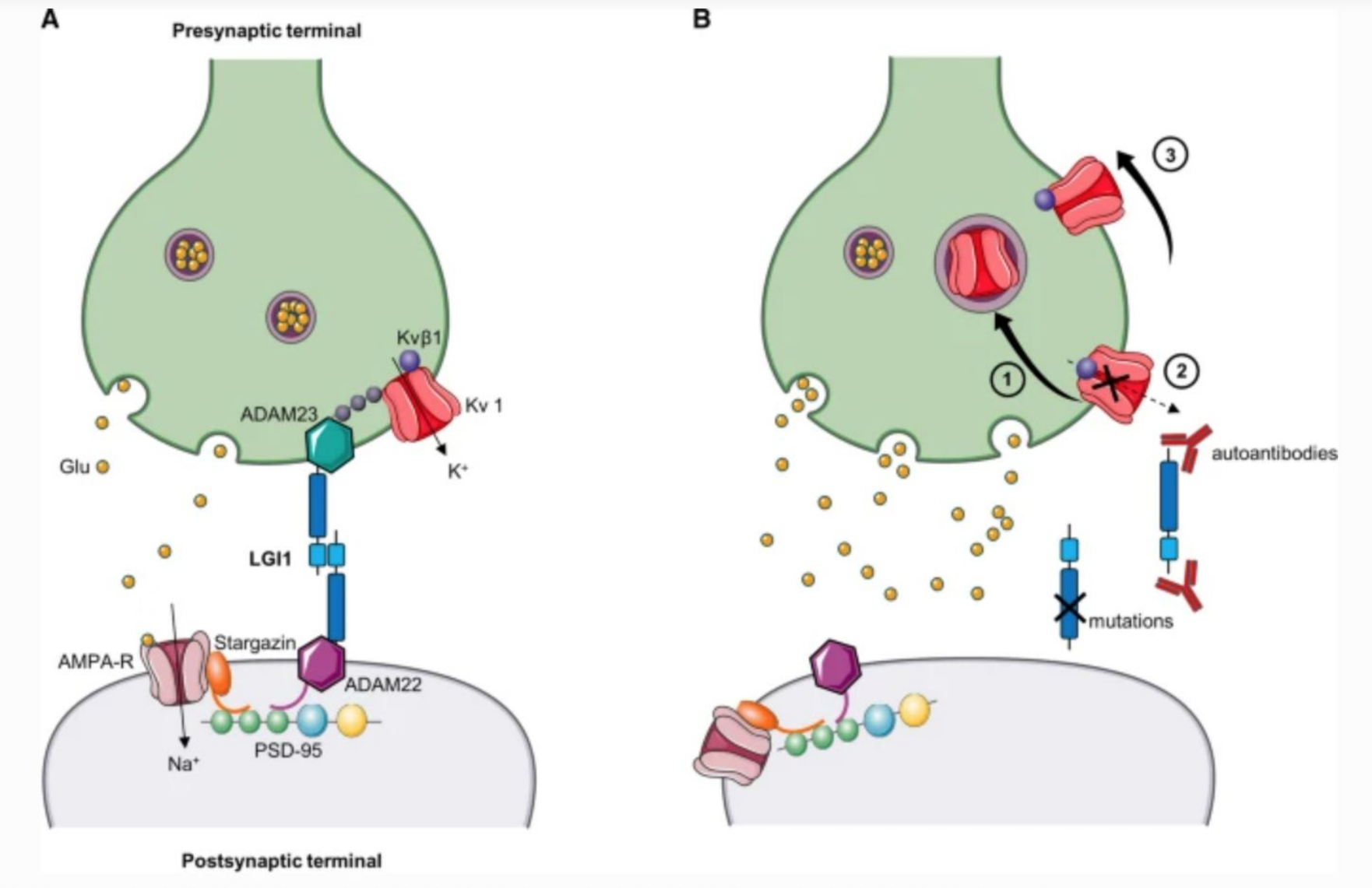
Diagnosis

- Serum encephalopathy panel pending at time of discharge.
- Later, it returned positive for LGI-1.

Treatment

- Inpatient: 5-day course of IVMP with improvement in mental status
- At time of discharge: IVMP 1g weekly for the next 6 to 12 weeks on an outpatient basis
- At time of outpatient follow-up: replace IVMP with IVIG and prednisone 80mg daily, planning to begin taper of steroids in 1-2 months by 10mg monthly if clinically stable

LGI-1 Antibody Encephalitis

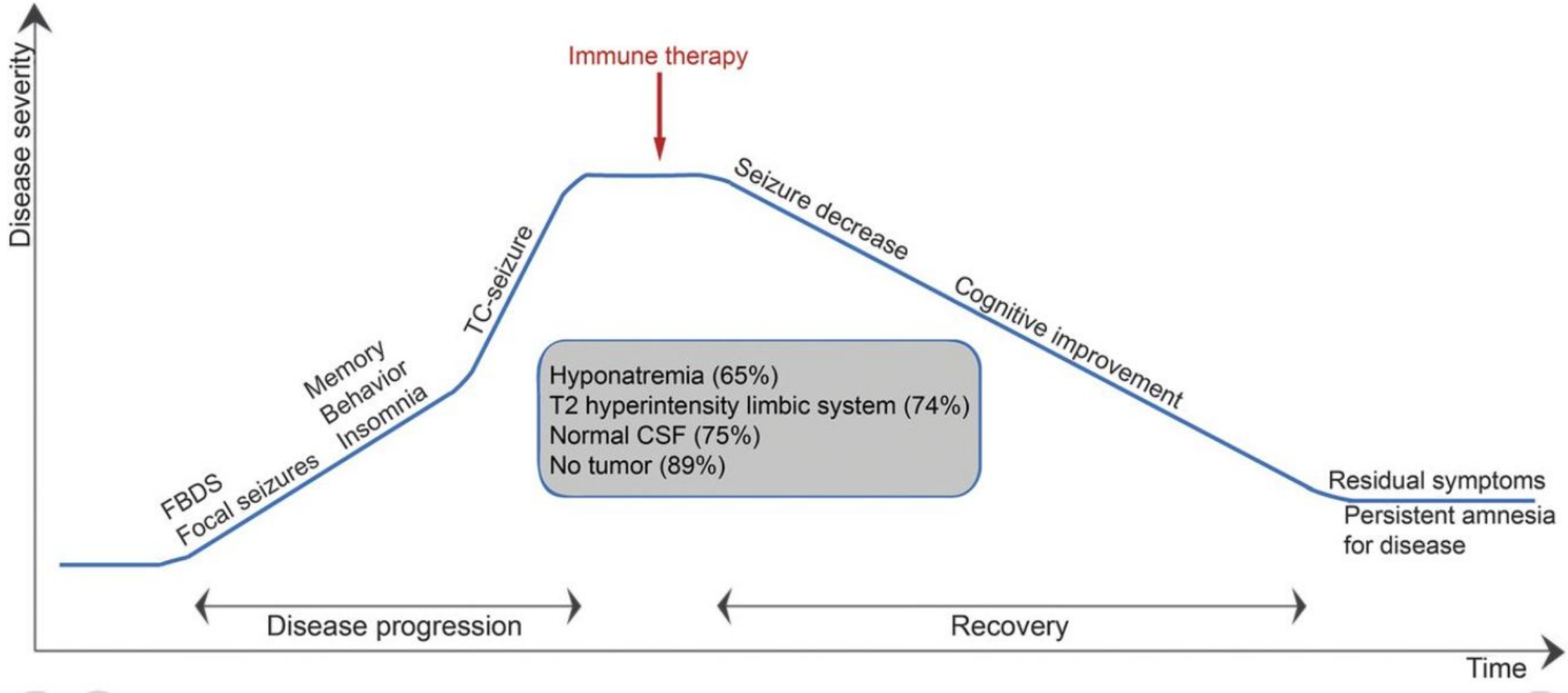


Baudin, P., Cousyn, L. & Navarro, V. The LGI1 protein: molecular structure, physiological functions and disruption-related seizures. Cell. Mol. Life Sci. 79, 16 (2022)

Overview

- Demographics:
  - 2:1 male predominance
  - Median age 55-65
- Clinical presentation:
  - Cognitive impairment
  - Psychiatric features
  - Seizures
- Time course:
  - 3-6 months to reach peak severity

Clinical manifestations



Van Sonderen, A., et al. (2016). Anti-LGI1 encephalitis: Clinical Syndrome and Long Term Follow-up. Neurology, 87 (14), 1449-1456

Seizure types

Table 2. Three different subtypes of seizures in anti-leucine-rich glioma-inactivated 1 encephalitis

	Faciobrachial dystonic seizures	Focal seizures	Tonic–clonic seizures
Description	Short (few seconds) involuntary unilateral contractions of the face and arm (or leg).	Subtle dyscognitive or autonomic features ('indefinable feelings' or 'goosebumps')	Generalized tonic–clonic seizures
Frequency	Up to 100 per day	~10 per day	Few (~3) in total
Incidence	50%	65%	60%
Onset	Regularly before cognitive decline	Regularly before cognitive decline	Later in disease course
Remarks	Almost invariably EEG shows no epileptic discharges		

EEG, electro-encephalogram; FBDS, faciobrachial dystonic seizures.

Bastiaansen A.E.M. et al "Autoimmune encephalitis with anti-leucine-rich glioma-inactivated 1 or anti-contactin-associated protein-like 2 antibodies (formerly called voltage- gated potassium channel-complex antibodies)" Curr Opin Neurol 2017, 30:302 – 309

Faciobrachial dystonic seizures

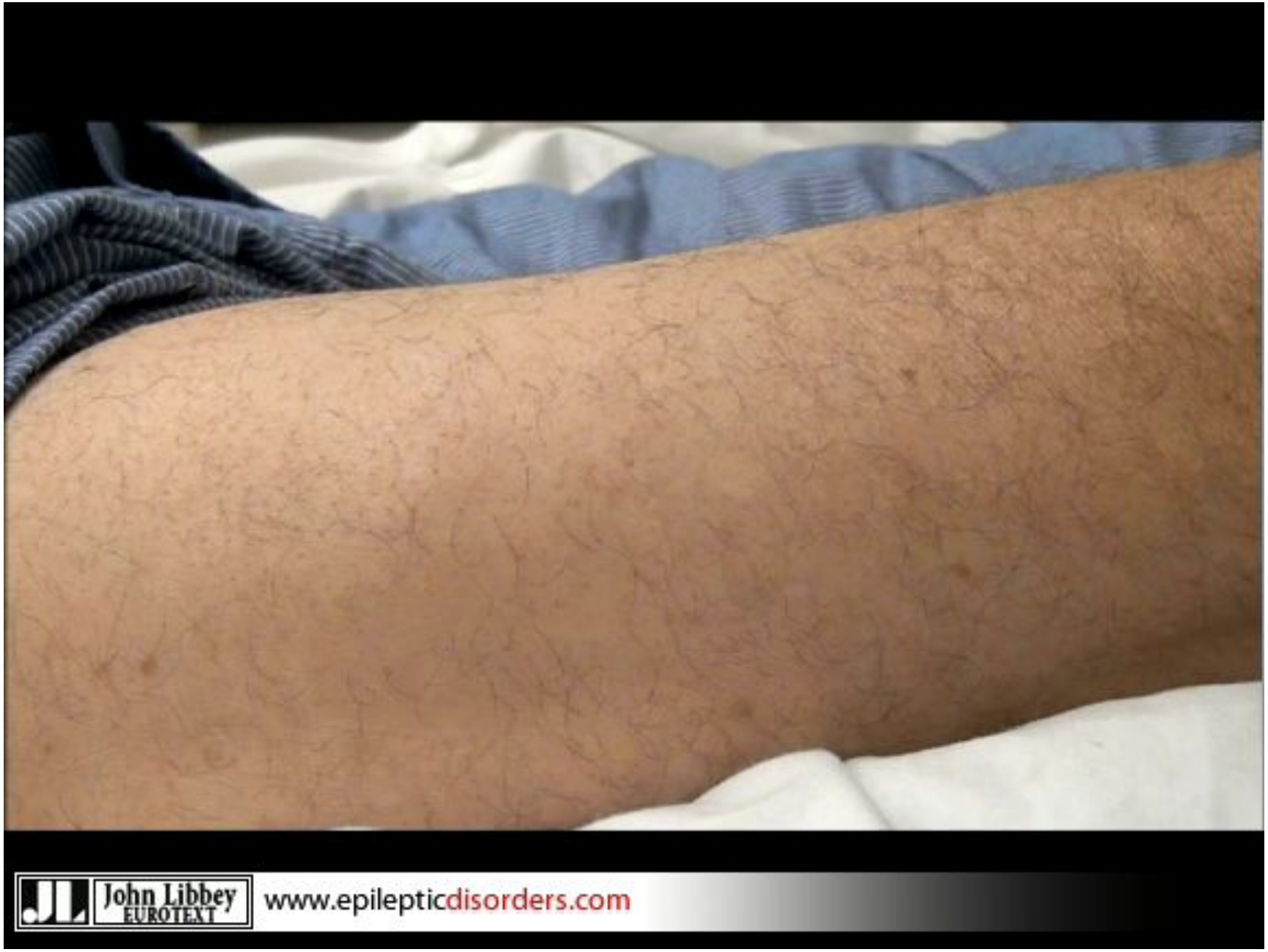
- Pathognomonic for LGI-1 antibody encephalitis
- Dystonic posturing of hemiface, arm, and possibly leg
- Brief lasting 1-3 seconds
- Very frequent (up to 200 times per day)

Kim DD, et al. Recurrent Involuntary Contractions of the Face, Arm, and Leg in an Elderly Man. *JAMA Neurol.* 2019;76(6):728–729.

Sen, A. et al. Pathognomonic seizures in limbic encephalitis associated with anti-LGI1 antibodies (2018) Lancet (383): 933

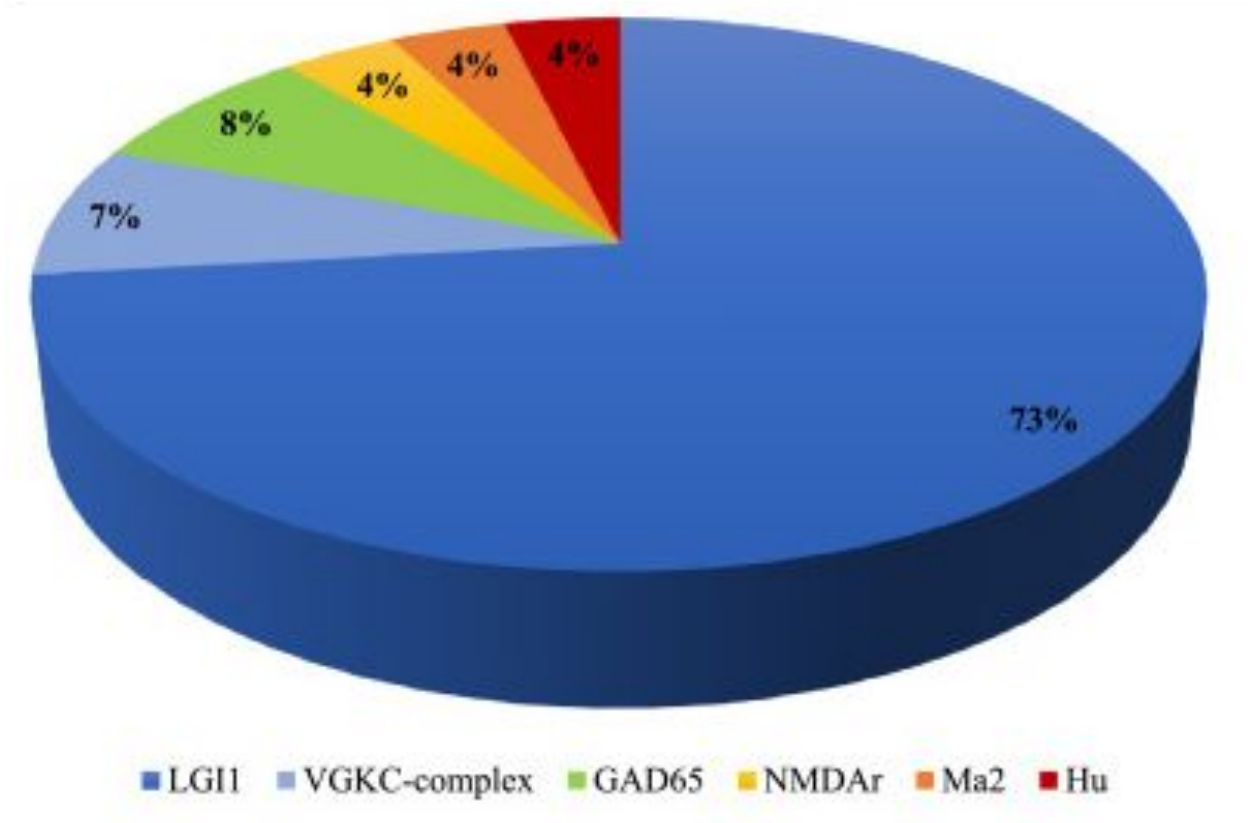
Focal seizures

- Likely to arise from the mesial temporal lobe
- Clinical manifestations may vary- Can present as piloerection
- Brief duration, lasting less than a minute
- Very frequent, up to 30-40 per day



Haykal MA, Abou-Khalil B. Pilomotor seizures: a video case report. Epileptic Disord. 2012 Mar;14(1):76-9.

Limbic encephalitis manifesting as ictal piloerection



Pondrelli, F. et al. (2022) Pilomotor seizures in autoimmune limbic encephalitis: description of two GAD65 antibodies- related cases and literature review. Seizure. (98): 71-78.

Treatment

First line:

- IVMP 1g per day for 3–7 days
- IVIG 2g/kg over 2-5 days
- PLEX 5-10 sessions every other day

Second line:

- Rituximab
- Cyclophosphamide

Long term outcomes

Typically follows a monophasic course

Relapses occur at a rate of 30% at 2 years from disease onset

May have persistent cognitive impairment and psychiatric features

Questions