

# ACP Conference WI 2017

Marvi Verma Rijhwani MD

Karina Arkush MD

Aurora Health Care, Milwaukee WI

# Case Presentation

- Patient is 63 year old female who presented to the emergency department with increasing confusion for several months
- Patient was unable to provide any details of her symptoms
- Per family members,
  - Patient was recently fired from job since she could not remember things or complete assignments
  - She also stopped speaking English and would primarily converse in Spanish
  - She had episodes of staring blankly, involuntary arm movements, and surprised look with twitches on her face several times a day
  - Denied any obvious seizure activity
- Review of systems otherwise negative

# Case Presentation

- Past Medical History

- None

- Medications

- None

- Family History

- HTN in mother

- Social History

- Lives alone in an apartment
- Independent
- Worked as a secretary at a day care center
- Never smoker
- Denies alcohol use
- Denies illicit drug use

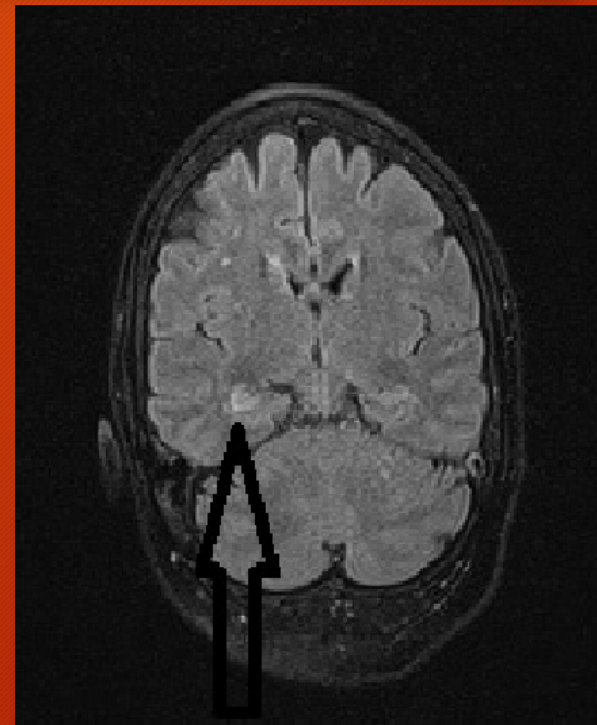
# Clinical Course

- Physical exam
  - General: Appears to be confused and is not oriented to time or place
  - Tongue: 1 cm area of erythema/purple plaque consistent with hematoma
  - Neuro: CN II-XII intact. No facial droop. Motor/sensory exam intact.
  - Psych: Pleasant and not agitated
- Basic lab evaluation
  - CBC, CMP without pertinent positive findings

# Clinical Course

- Imaging

- CT Head → Age indeterminate sub-centimeter lacunar infarct in right basal ganglia
- MRI Brain → T2/FLAIR hyper intensity involving the mesial left temporal lobe and left hippocampus



# Clinical Course

- Patient admitted to the Neuro floor for further evaluation
- The next morning, patient was noticed to have a tonic-clonic seizure
- Video EEG
  - Partial non-convulsive status epilepticus originating from the left anterior quadrant

# Clinical Course

- Paraneoplastic panel was ordered to evaluate for possible underlying malignancy
  - Positive for → Neuronal VGKC-complex (voltage gated potassium channel) antibody 0.25 (High)
- Oncologic evaluation did not reveal any malignancy
- Further testing revealed LGI1 (leucine-rich glioma inactivated 1) antibody positivity

# Anti-LGI1 Limbic Encephalitis



<https://aealliance.org/jama-a-case-of-anti-lgi1-encephalitis/>



# Anti-LGI1 Limbic Encephalitis (LE)

- Rare cause of autoimmune encephalitis
  - Estimated annual incidence was <1 per million
- Affects medial temporal lobe
- Limbic Encephalitis is usually a paraneoplastic syndrome
- Recently, antibodies that target neuronal cell surface antigens, ion channels, and ligand-gated ion channels (VGKC, NMDA, GABA receptor channels) → Not usually related to tumors/malignancy
- Antibodies to LGI1 protein were discovered in 2010 → Cause Anti-LGI1 Limbic Encephalitis

# LGI1 Antibodies/Protein

- Leucine-rich glioma inactivated-1 (LGI1) protein
  - Encoded by LGI1 gene on chromosome 10
  - May be a metastasis suppressor
  - Expressed in neural tissues
  - Expression is reduced in low grade brain tumors and significantly reduced or absent in malignant gliomas
  - Is a target for autoantibodies associated with VKGC complex



# Autoimmune Encephalitis

- First group includes the classic paraneoplastic disorders associated with antibodies to intracellular antigens
  - Strongly cancer associated and involve T-cell responses targeting neurons
- Second group involves autoantibodies to extracellular epitopes of ion channels, receptors and other associated proteins, such as the NMDA receptor or LGI1 protein
  - Cancer associations are variable

# Clinical Features

- Patients present with facio-brachial seizures (FBDS), memory loss, and confusion
- Memory and cognitive deficits are preceded by FBDS
  - FBDS → frequent, brief dystonic seizures that predominantly affect the arm and ipsilateral face
- Occasional development of hyponatremia
  - Syndrome of inappropriate secretion of Antidiuretic Hormone by the LGI1 expression in the hypothalamus and the kidney
- Tonic-clonic seizures may be seen later in the disease process

# Diagnosis

- History/Clinical features
- MRI → may or may not show changes in temporal lobe
- EEG
- Specific antibody testing

# Treatment

- Steroids
- IVIG
- Mycophenolate mofetil
- Cyclophosphamide
- Plasma exchange
- Rituximab

# Prognosis

- May recover, completely or partially, and then experience worsening symptoms
- Long term outcome of surviving patients is mostly favorable
- Relapses are common

## Back to our patient

- Unfortunately, patient continued to have seizures despite multiple anti-epileptic drugs
- She underwent plasma exchange and IVIG without improvement
- She was started on Rituximab and has stabilized clinically
- Seizures have not recurred
- However, her confusion and memory loss continue to deteriorate
- Currently a nursing home resident



## References

- Bhardwaj K, Sharma SK, Pandey AK, et al. A Case of Limbic Encephalitis: Antibody LGI1 Associated Encephalitis. *J Neurol Neurosci*. 2016, 7:4
- Irani, SR. Faciobrachial dystonic seizure precede Lgi1 antibody limbic encephalitis. *Ann Neurol*. 2011 May; 69 (5):892-900.
- Jung-Ju, L. Anti-LGI1 Limbic Encephalitis Presented with Atypical Manifestations. *Exp Neurobiol*. 2013 Dec; 22 (4):337-340.
- Lancaster, E. The Diagnosis and Treatment of Autoimmune Encephalitis. *J Clin Neurol*. 2016 Jan; 12 (1):1-13.
- Van Sonderen, A. From VGKC to LGI1 and Caspr2 encephalitis: The evolution of a disease entity over time. *Autoimmunity Reviews*. Elsevier. 2016.

Questions?