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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

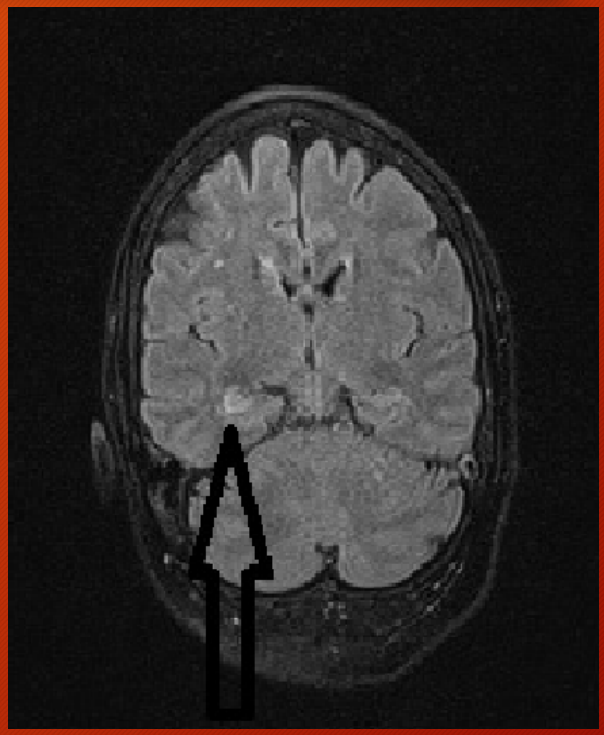
- Past Medical History
  - None
- Medications
  - None
- Family History
  - HTN in mother
- Social History
  - Lives alone in an apartment
  - Independent
  - Worked as a secretary at a day care center
  - Never smoker
  - Denies alcohol use
  - Denies illicit drug use

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

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Questions?