Clinical commentary

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Response to immunotherapy in a patient with Landau-Kleffner syndrome and *GRIN2A* mutation

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Epileptic Disorders

Laundau-Kleffner Syndrome (LKS)

- Rare epileptic encephalopathy characterized by acute or gradual loss of speech abilities (aphasia)
- Occurs in children between 2 to 12 years of age (peak incidence between 5-7 years) who are usually previously developmentally normal
- Children may or may not have accompanying seizures, typically clonic or generalized tonic-clonic
- EEG in LKS is characterized by:
  - Bilateral centrotemporal spikes and sharp waves
  - Electrical status epilepticus in sleep (ESES)
- Cause unknown in most cases but there is evidence to support an autoimmune aetiology and some cases have been shown to be associated with *GRIN2A* mutations

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LKS Treatment

- Typically consists of using antiepileptic drugs and/or immunotherapy
- Antiepileptic drugs used:
  - Valproic acid, diazepam, ethosuximide, clobazam, clonazepam
  - Avoid carbamazepine , phenytoin, phenobarbital
- Response to steroids and to intravenous immunoglobulin has also been well described in the literature

GRIN2A

- The *GRIN2A* gene encodes for the NMDA 2A receptor/channel. Gain of function mutations of this gene have been associated with various forms of epilepsy, including epilepsy-aphasia syndromes such as LKS.

- Optimal treatment modalities for *GRIN2A* mutation positive patients is still unclear but typically consists of AED use.

- Memantine therapy, to block the above NMDA channel, has also been considered.

- Our observation of an LKS patient with a *GRIN2A* mutation who responded to immune therapy with steroids and with IVIG suggests that such therapy may be an option in patients with *GRIN2A* mutations and LKS

Epileptic Disorders

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Epileptic Disorders