A Rare Cause of Neonatal Seizures: *KCNQ2*-Related Epilepsy

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INTRODUCTION

While the majority of neonatal seizures are due to acute symptomatic causes, approximately 15% of neonatal seizures are a consequence of epilepsy syndromes.
In well appearing neonates with an otherwise negative workup, recurrent neonatal seizures may be due to a genetic epilepsy syndrome such as Benign Familial Neonatal Epilepsy.

CASE

PRESENTATION:

- AA is full term 3-day-old female who presented to clinic for a newborn visit and was observed having apneic events.
- Mom described shaking episodes in the nursery that were attributed to benign myoclonus of infancy.
- Given concern for seizures, 911 was called.

EMERGENCY DEPARTMENT:

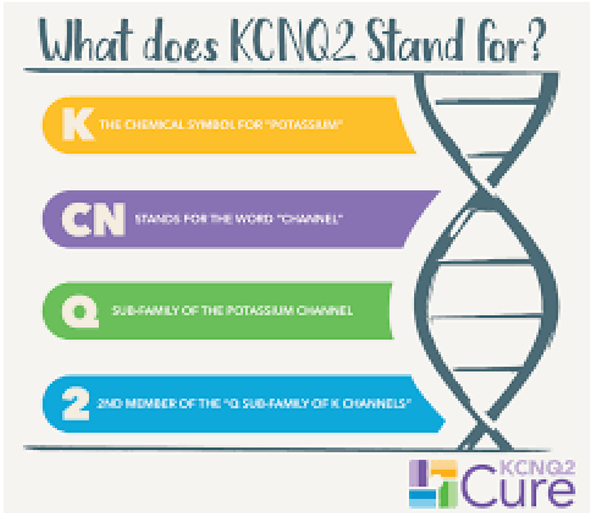
- On arrival, the patient was intubated for apnea and a full septic and metabolic workup was initiated.
- She was started on empiric antibiotics and given a loading dose of levetiracetam.
- A CT head was negative for an acute hemorrhage.

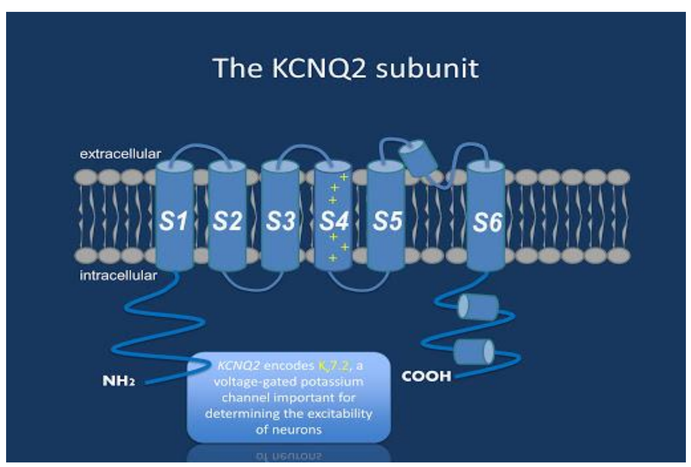
PICU:

- She was admitted to the PICU, where a brain MRI was normal and an EEG was remarkable for seizure activity and interictal sharp waves.
- She ultimately required maintenance levetiracetam, phenobarbital, topiramate, and pyridoxine for seizure control.
- Ultimately, she was discharged home seizure-free.

OUTCOME

- A comprehensive genetic epilepsy panel resulted with a variant of uncertain significance in KCNQ2, which is associated with benign neonatal seizures.
- A detailed family history revealed that both mother and maternal grandmother of the patient had similar episodes of seizure activity requiring antiepileptic therapy during infancy.
- Given the patient's presentation and family history, this variant is presumed to be pathologic and the cause of her seizures.





DISCUSSION

Benign Familial Neonatal Epilepsy (BFNE) is a rare genetic seizure disorder that results in afebrile seizures occurring within the first days of life in otherwise healthy newborns. Pathologic variants in the KCNQ2 gene are the most common cause of BFNE, and are inherited in an autosomal dominant pattern.

KCNQ2 belongs to a large family of genes that code for proteins that make up voltage gated potassium channels in neurons found in the brain. Mutations in the KCNQ2 gene alter the regulation of neuronal excitability by improperly suppressing neuronal firing, resulting in seizure activity.

Seizures generally occur on the second or third day of life, are brief, and can occur up to 20-30 times per day. Seizures are mixed type starting with apnea and tonic posturing, progressing to motor automatisms, and may evolve to status epilepticus. Patients will have a brief post-ictal state involving fatigue, and generally display normal behavior between seizures. This syndrome is considered benign because initial studies suggested no long-term neurologic sequelae, however newer studies have found a higher incidence of post-neonatal epilepsy.

CONCLUSION

- Epilepsy syndromes should always be considered in cases of neonatal seizures.
- Early genetic testing can be essential in identifying the etiology of neonatal seizures.
- Accurate family history and follow up familial testing is necessary in reclassifying genetic variants.

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