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ED Management of Status Epilepticus in Pediatric Patient with Dravet Syndrome

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Abstract

Dravet Syndrome is a rare, early-onset pediatric epilepsy characterized by prolonged, treatment-resistant seizures and a spectrum of neurodevelopmental delays (2). It is a sodium channelopathy, most commonly caused by a mutation in the alpha-1 subunit of voltage-gated sodium channel gene (SCN1A) (2). Dravet Syndrome is estimated to affect 1 in 15,700 - 40,000 live births (2), with onset of seizures typically between 1-18 months old. Diagnosis and management is challenging as there is lack of universal diagnostic guidelines and treatment protocols. Furthermore, seizures associated with Dravet Syndrome are typically refractory to medical management and routinely present in status epilepticus. The mainstay treatment algorithm for status epilepticus, being Sodium Channel blocking agents, are contraindicated in treating patients with Dravet Syndrome. It is essential for Emergency Medicine Physicians to not only recognize Dravet Syndrome, but to be familiar with appropriate treatment and management of these patients presenting in status epilepticus. This disease carries high morbidity and mortality, making quick intervention a necessity for these patients.

Case Presentation

- 21moF with known Dravet Syndrome presented to the ED for witnessed unilateral convulsive seizure. Symptoms started 20 minutes prior to ED arrival and were continuous since onset. She was given 2 doses of Diastat 5mg PR at home without response. Patient was at baseline prior to symptom onset, without fever, recent illness, vaccinations, or photic stimuli. She has been compliant with all prescribed anti-epileptics. Mother provided ED staff with a list of anti-epileptics she was unable to receive, that was provided by patients Neurologist.
- On arrival to the ED, Initial vital signs: T 36.7 ° C (rectal),HR 159 bmp, RR 18, SpO2 82-85% RA, POC glucose 130. Patient was unresponsive, with focal hemiclonic seizure activity. Initial ED interventions: ABC's, IV established, supplemental oxygen via blow-by nasal cannula, 20cc/kg IVF bolus infused. Patient was given 0.2mg/kg Versed IM without response. She was intubated with RSI for airway protection given low GCS and respiratory failure with hypoventilation. CBC, BMP, magnesium, urinalysis all within normal limits
- Therapeutic Interventions used in ED with successful termination of status epilepticus: IV Benzodiazepine, Levetiracetam, Phenobarbital, continuous infusion of midazolam
- Total seizure lasted approximately 60 minutes. She was transferred from the ED to a tertiary care PICU for escalation of care. Patient was extubated on hospital day 2. She regained full neurologic recovery to baseline mental status. Remainder of hospital workup was unremarkable.
- Patient was discharged on an increased dose of Keppra and recommendation for a secondary antiepileptic. Addition of Midazolam was added to Diazepam for home abortive medications.

Tables

Figure 1. Clinical Features of Dravet Syndrome

Clinical features of Dravet syndrome

Clinical features	Presentation in young children	Presentation in older, previously undiagnosed children or adults
Age of onset	• Between 1 and 18 months	• Early childhood or unknown
Seizures	• Recurrent generalized tonic-clonic or hemiconvulsive seizures (all patients), often prolonged • Myoclonic seizures, commonly seen by age 2 years • Obtundation status, focal dyscognitive seizures, and atypical absences, commonly seen after age 2 years • Typical absences and epileptic spasms are atypical	• Persisting seizures*, which include: • Focal and/or generalized convulsive seizures • Myoclonic, atypical, absence, and tonic seizures (less common) • Recurrent status epilepticus becomes less frequent with age, may not be seen in adolescence or young adulthood
Seizure triggers	• Hyperthermia, which may be associated with vaccination (most patients) • Flashing lights, visual patterns, bathing, eating, overexertion • Sodium channel blocking antiseizure drugs	• Hyperthermia (may become less problematic in adolescence and adulthood) • Sodium channel blocking antiseizure drugs
Development and neurologic examination	• Normal development and neurologic examination at baseline	• Intellectual disability (typically evident by 18 to 60 months of age) • Crouched gait, hypotonia, incoordination, impaired dexterity (typically evident by 3 to 4 years of age)
MRI	• Normal at onset	• Typically normal, may show mild generalized atrophy and/or hippocampal sclerosis
EEG	• Nonspecific findings at onset	• Diffuse background slowing, often with multifocal and/or generalized interictal discharges; photoparoxysmal response may be seen

EEG: electroencephalogram; MRI: magnetic resonance imaging.
* Some older adults may become seizure-free. It is not clear whether antiseizure drugs can be safely stopped in this group, however.

Original figure modified for this publication. Wirrell EC, Laux L, Donner E, et al. Optimizing the diagnosis and management of Dravet syndrome: Recommendations from a North American consensus panel. Pediatr Neurol 2017;68:18. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 112854 Version 1.0

Figure 2. Our ED Management of Status Epilepticus with seizure resolution

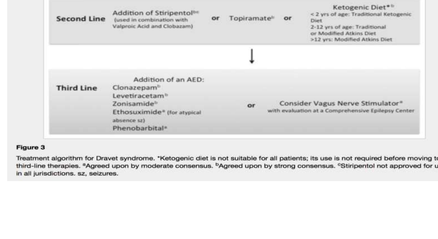

Figure 3. Current treatment algorithm for status epileptics in Dravet Syndrome patients

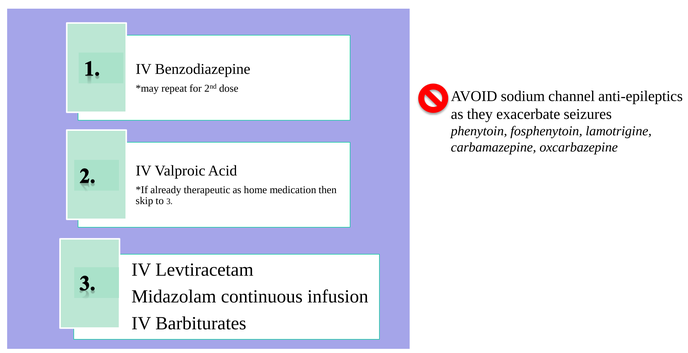

Figure 4. Maintenance Treatment Algorithm

Figure 3
Treatment algorithm for Dravet syndrome. *Ketogenic diet is not suitable for all patients; its use is not required before moving to third-line therapies. [a]Agreed upon by moderate consensus. [b]Agreed upon by strong consensus. [bm]Stiripentol not approved for use in all jurisdictions. sz, seizures.

Discussion

Dravet Syndrome, formerly known as "severe myoclonic epilepsy of infancy" is a rare form of infantile infantile-onset epilepsy syndrome characterized by prolonged, treatment-resistant seizures and a spectrum of neurodevelopmental delays after seizure onset (2). Reports from recent studies suggest Dravet Syndrome may account for 3-7% of epilepsy cases in patients whom initial seizure presentation occurs by 3 years old (2). Pathophysiology of disease is poorly understood, but believed to be due to a mutation in alpha-1 subunit of voltage-gated sodium channel gene (SCN1A) (2). This causes impaired action firing in GABAergic interneurons, leading to dysfunction of inhibitory interneurons (disinhibition), thus creating a hyperexcitable state.

Dravet Syndrome is primarily identified by key clinical features (Figure 1), and further supported by genetic testing, although it is not necessary for diagnosis. Criteria to help guide diagnostic, treatment, and management standards was recently created by The North American Consensus Panel. Seizures associated with DS are typically resistant to pharmacologic therapy. Complete seizure control is unlikely as most patients require 2-3 anti-epileptics to achieve optimal control.

The importance of ED recognition of Dravet syndrome is that treatment regiment is unique, in that typical treatment algorithms for status epilepticus is contraindicated in DS (ie Na channel blocking agents). For ED physicians, initial diagnosis is unlikely to take place in the Emergency Room, although, you may be treating young infants on initial seizure presentation. It is important to work with local neurologist and pediatric specialists to individual seizure protocol for when these patients presents to the local ED. It is equally important for parents of affected patients to have a home regiment of rescue medications (rectal diazepam, Buccal/nasal midazolam).

Conclusion

- Dravet syndrome is rare with high frequency of refractory status epileptics
- Disease carries high morbidity and mortality
- It is important for ED physicians to be familiar with disease in order to appropriately treat and avoid poor patient outcomes with use of exacerbating anti-epileptics
- Universal guidelines on in-hospital management is yet to be established. Although strong consensus that swift elimination of prolonged seizures or status epileptics is among the highest priorities in treatment.

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