Case report:

Dravet Syndrome -A case report from Aseer, Saudi Arabia

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Abstract:

Dravet syndrome (DS) is an epileptic encephalopathy that presents with protracted seizures in infancy, associated with fever, and frequently categorized as febrile seizure at first presentation. In the second year, myoclonia, atypical absence and complex partial seizures develop. The correct diagnosis of DS and appropriate follow-up are delayed until after appearance of signs of developmental regression in the second year of life. Timely detection and diagnosis of DS followed by management with suitable anticonvulsants and treatment plan may reduce the seizure burden and improve long-term developmental outcome. We present a case of 2 years old female with recurrent attacks of generalized tonic colonic convulsion after 1st febrile convulsion diagnosed as Dravet syndrome. The diagnosis was based on history and gene study (SCN1A).

Keywords: Dravet Syndrome, Refractory Seizure, SCN1A gene, Febrile Convulsion, Hypsarrythmia.

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Introduction:

Dravet syndrome is a rare and devastating form of epilepsy classified as an epileptic syndrome by the International League Against Epilepsy (ILAE).[1] First seizures present like febrile seizures and are often treated as such but later that may evolve into prolonged events (status epilepticus). In the second year of life, other seizure types emerge.[2]Early development of the child is normal while signs of regression appear in the second year of life. Thus, the diagnosis of DS and its appropriate management are usually delayed.[3] Diagnosis can be confirmed by genetic testing and shows mutations within the SCN1A gene. The prognosis for DS is severe for both epileptic seizures and cognitive impairment, and the mortality rate is significant.[4] Early diagnosis of DS can go a long way in reducing the seizure burden and improve long-term developmental outcome of the child. As this is a rare disease with important implications arising from early diagnosis, management and parent education we decided to present this case as we consider it will be useful for paediatricians and pediatric epileptologists in this region. Due care was taken for ethical issues by taking parental consent and ensuring that the institute has no objection for publishing this case report.

Case Report:

Our patient is a 2 years old girl who was the first of non- identical twins. She was born to a 33 years old multigravida at 31+ weeks of gestation whose previous three children are normal. The twins were delivered by emergency cesarean section due to early placental separation. Due to prematurity and respiratory distress the newborns were admitted

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to neonatal ICU(NICU) for 4 weeks. Standard protocol for treatment, meticulous nursing care and timely intervention, as proven in earlier studies[5], led to recovery and the twins were discharged in good condition. NICU admission was otherwise uneventful. The other twin is reportedly in good health and achieved normal milestones.

The child was healthy till the age of 6 months when she developed 1st episode of generalized convulsion consequent to an upper respiratory tract infection and fever. She was admitted to the regional pediatric hospital and underwent full septic screening including CSF analysis and culture which was negative. She was treated symptomatically with analgesics and antibiotics, believing the seizures to be febrile convulsions. She was discharged after one week in a good condition.

After one year she developed prolonged episode of generalized tonic clonic convulsions without fever. She was brought to the ER where the attack was subsequently aborted by lorazepam. She had to be intubated due to respiratory depression and was later shifted to PICU where she underwent investigations and treatment for 10 days. She did not have dysmorphic features and her growth parameters were within normal centiles. Her vital signs showed a heart rate of 120 beats/ minute, temperature of 36.5 Celsius, blood pressure of 96/65mmHg, respiratory rate of 22breaths/minute, and SPO2 of 94%.Neurological examination revealed delayed motor milestones. Her speech was reported to be delayed and she was noted to be speaking only disyllabic words. Other systemic examination was unremarkable. Her base line investigations were normal. CT&MRI were unremarkable. EEG showed continuous, high-amplitude, arrhythmic and asynchronous delta activities, interspersed with independent, multiple spikes (**Figure 1**). Considering the clinical presentation and EEG findings, DNA sequence analysis of the SCN1A gene was done which confirmed a diagnosis of Dravet Syndrome. Anticonvulsive therapy was initiated with phenobabitone and levetiracetam .The patient was discharged in a stable condition. The parents were advised on triggers and ketogenic diet. At the time of writing this report six months later, the patient was followed up and reported to have been doing well without any convulsive episodes.

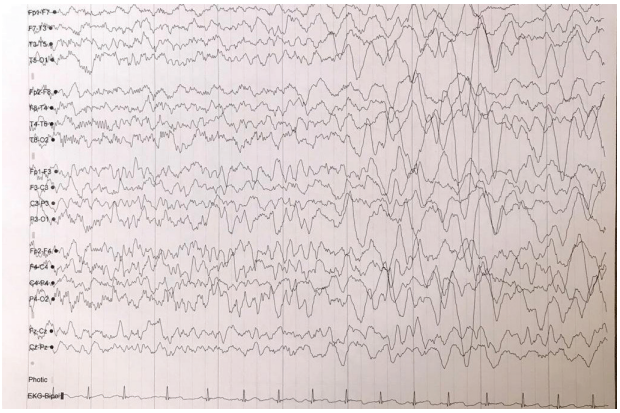

Figure 1: EEG showing hypsarrythmia in a case of Dravet Syndrome

Discussion:

History: In 1978, a new syndrome was described by Charlotte Dravet and named after her as Dravet syndrome (DS). International League Against Epilepsy since 1989has recognized it as an epileptic syndrome.[2] **Epidemiology**: It is a relatively uncommon condition, with a prevalence at1 in 40,000 members of the population[3] however with increased awareness and genetic testing, recent studies are reporting double of this prevalence.[6] **Clinical characteristics**: Our case had typical clinical features of DS. Infancy onset severe myoclonic epilepsy, refractory seizures, frequent episodes of status epilepticus and multiple seizure types that may be associated with fever.[7] Neurobehavioral impairment can be limited to minor learning difficulty or range up to a global developmental delay.[8,9] In our case neurological examination revealed delayed motor development specially speech difficulties. **Genetics:** As compared to other seizure disorders, family history of epilepsy or febrile seizures is less in DS.[10]In identical twins,it is very likely that the other twin will also have the condition. In our case the second of the twins is a fraternal twin and is normal. In more than three quarter of cases, DS is related to a genetic disorder, mostly carrying a de novo SCN1A mutation.[11] **Diagnosis:** The clinical diagnosis of DS is supported byEEG, neuroimaging, and genetic testing for SCN1A mutation.[2] EEG provides critical prognostic data and is used to determine the course of treatment.EEG istypically normal at onset, but later EEG might show focal or multifocal spike-waves, sharp waves, and slow waves and spikes activity.[12] Thiscase had hypsarrythmia on EEG at the second episode. Neuroimaging is generally normal as happened in this case. Our case was finally confirmed as Dravet syndrome after SCN1A

gene mutation testing. In the recommendations published in pediatric neurology, there was strong consensus that genetic testing should be pursued for all patients with a clinical picture suggestive of Dravet syndrome.[13] There is improved long term outcome for patients with improved cognition and seizure control associated with early diagnosis.[13] **Treatment:** DS is characterized by intractable seizures. Pharmacological treatment attempts have been carried out with oxcarbamazepine, phenytoin, bromides, topiramate, levetiracetam, vigabatrin, stiripentol (STP), valproicacid, clobazam.[14] Similar treatment protocol has been followed for this case. Counseling regarding avoidance of triggers, preventive measures like using cooling vests in hot weatheror wearing sunglasses if photosensitive, and home use of emergency benzodiazepine to prevent status epilepticus is recommended. **Prognosis:** In most cases, after 4 years of age,patients reach a steady state of intractable seizures, intellectual impairment, behavioral disorders,and neurologic abnormalities. The mortality rate is approximately 10-20% and is related to prolonged convulsive seizures, drowning, and sudden unexpected death.[15] **Conclusions:** Early detection and diagnosis of DS and management with suitable anticonvulsants and treatment plan may reduce the seizure burden and improve long-term developmental outcome.

Ethical Approval about publication from the concerned hospital:

Ethics approval not required. The patient's permission was obtained.

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References:

1. Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, Higurashi N et.al.Instruction manual for the ILAE 2017 operational classification of seizure types. *Epilepsia.* 2017;**58**:531–42. https://doi.org/10.1111/epi.13671. Epub 2017 Mar 8. PubMed 50 PMID:28276064.
2. Dravet C, Bureau M, Oguni H, et al. Dravet syndrome. *Adventures in Neurology*. 2005; 95: 72-102.
3. Hurst DL. Epidemiology of severe myoclonic epilepsy of infancy. *Epilepsia* 1990; **31**: 397-400.
4. Shmuely S, Sisodiya SM, Gunning WB. Mortality in Dravet syndrome: a review. *Epilepsy Behav*. 2016;**64**(Pt A):69–74.
5. Mannan, M. A., Dey, S., Karim, S., Iqbal, S., Yasmin, S., &Ferdous, N. Neonatal arterial blood gases & immediate outcome following perinatal asphyxia. *BJMS* 2019;**18**(2):238-243. https://doi.org/10.3329/bjms.v18i2.40692
6. Verbeek NE, van der Maas NA, Jansen FE, van Kempen MJ, Lindhout D, Brilstra EH. Prevalence of SCN1A-related dravet syndrome among children reported with seizures following vaccination: a population-based ten-year cohort study. PLoS One. 2013;8(6):e65758. Published 2013 Jun 6. doi:10.1371/journal.pone.0065758
7. Dravet C, Bureau M, Oguni H, Fukuyama Y, Cokar O. Severe myoclonic epilepsy in infancy: Dravet syndrome. *Adv Neurol*. 2005;**95**:71–102.
8. Korff C, Laux L, Kelley K, Goldstein J, Koh S, Nordli D Jr. Dravet syndrome (severe myoclonic epilepsy in infancy): a retrospective study of 16 patients. *J Child Neurol* 2007;**22**:185–194.
9. Villas N, Meskis MA, Goodliffe S. Dravet syndrome: characteristics, comorbidities, and caregiver concerns. *Epilepsy Behav*. 2017;**74**:81–6.
10. Patel, A. & Perry, S. Febrile Seizures: Evaluation and Treatment. *JCom* 2017;**24**(7); 325-334.
11. Marini C, Scheffer IE, Nabbout R, Suls A. The genetics of Dravet syndrome. Epilepsia. 2011;52(Suppl 2):24–9.
12. Baskar, K., &Karthikeyan, C. Review on diverse approaches used for epileptic seizure detection using EEG signals. *BJMS* 2018; **17**(4): 526-531. https://doi.org/10.3329/bjms.v17i4.38307
13. Connolly MB. Dravet syndrome: diagnosis and long-term course. *Can J Neurol Sci*. 2016;**43**(Suppl 3):S3–58.
14. McTague A, Appleton R, Avula S, Cross JH, King MD, Jacques TS, Bhate S, Cronin A, Curran A, Desurkar A, Farrell MA. Migrating partial seizures of infancy: expansion of the electroclinical, radiological and pathological disease spectrum. *Brain.* 2013;**136**(Pt 5):1578–91.
15. Cooper MS, Mcintosh A, Crompton DE, McMahon JM, Schneider A, Farrell K, Ganesan V, Gill D, Kivity S, Lerman-Sagie T, McLellan A, Pelekanos J, Ramesh V, Sadleir L, Wirrell E, Scheffer IE. Mortality in Dravet syndrome. *Epilepsy Res.* 2016 Dec;**128**:43-47. doi: 10.1016/j.eplepsyres.2016.10.006. Epub 2016 Oct 26. PubMed PMID: 27810515.