DRAVET SYNDROME
[Case of a 10 year old girl living with dravet]

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DEFINITION OF DRAVETS SYNDROME

- Dravet syndrome is a rare severe epileptic encephalopathy. It was formally known as severe myoclonic epilepsy of infancy. It is characterized by febrile or non-febrile seizures, that are resistant to antiepileptic therapy, starting within the first year of life. The seizures get worse as the patient ages and can ultimately become status epilepticus.
- It is characterized by frequent, prolonged seizures often triggered by high body temperature (hyperthermia). Developmental delay, speech impairment, ataxia, hypotonia, sleep disturbances, and other health problems are associated with it. DS is thought to be at the **severe end** of a spectrum of disorders associated with changes (mutations) in genes for the sodium ion channel.
- More than 80% of patients with Dravet syndrome have a mutation in the *SCN1A* gene .

OUTLINE

- The approach to this presentation would be using a clinical case ,from iashvilli hospital, as both an example and an explanation of this syndrome.
- We categorized the case study into 3 sections with different subtopics pointed out for better understanding of the syndrome.

- SECTION 1----- BEFORE DIAGNOSIS
  1. CLINICAL CASE
  2. PRESENTATION OF THE SYNDROME
  3. DIFFERNTIAL DIAGNOSIS
  4. PRECIPITATION OF SEIZURES

- SECTION 2------DIAGNOSIS OF DRAVET
  1. CLINICAL CASE CONTD
  2. DIAGNOSTIC CRITERIA
  3. COMORBIDITIES AND EFFECT OF LATE DIAGNOSIS

- SECTION 3-----AFTER MEDICATION
  1. CLINICAL CASE CONTD
  2. TREATMENT OF DRAVET
  3. COMPLICATIONS
  4. MAJOR CHALLENGE

SECTION 1; Before diagnosis

CLINICAL CASE

- **Our patient was born healthy by healthy parents with no problems during pregnancy or birth defects.**
- The seizures in this patient started few months after birth , febrile and nonfebrile seizures were diagnosed and antiepileptic drugs were given.
- She also presented with generalized convulsive seizures which caused her frequent admission to the hospital and use of multiple antiepileptic drugs like carbamazepine, gabapentin, felbamate and valproic acid.
- Due to recurrence of the seizures it was obvious that they were resistant to the drugs. Before age 3, she had recurrent status epilepticus and was often admitted to the ICU.

PRESENTATION OF DRAVETS SYNDOME

- Dravet syndrome is 1 of the most severe epilepsies in infancy.
- The onset is always in the first year of life in apparently normal infants,
- Most have had seizure onset less than 15 months of age; however, a small minority of cases have onset in the second year of life.
- The first seizure is associated with a fever in about 60% of cases. Not all patients start with febrile convulsions. Immunization may be a nonspecific trigger to the first seizure leading to an earlier age of seizure onset. Sensitivity of seizures to fever may persist throughout life.
- At around age 2, most infants with Dravet syndrome will begin to have myoclonic seizures, a type of muscle-twitching seizure for which the syndrome was initially known. But the disorder can cause numerous other types of seizures, including: ABSENSE SEIZURES, ATONIC SEIZURES, TONIC CLONIC SEIZURES, STATUS EPILEPTICUS.
- Over time ataxia and pyramidal signs may develop. Development is typically normal in the first year of life, with plateauing or regression in later years.

DIFFERNTIAL DIAGNOSIS

1

Febrile seizures

2

Myoclonic atonic epilepsy – characterizes with sudden drop attacks, which are unusual in Dravet syndrome.

3

Benign myoclonic epilepsy- excluded by the presence of other seizure types and an abnormal EEG.

4

Severe infantile multifocal epilepsy- SIMFE does not exhibit myoclonic seizures, absence seizures, or generalized epileptiform discharges present in dravet.

5

Lennox- Gastaut syndrome- LGS has a later onset, seizures that are more tonic and atonic, and slow spike and wave on EEG.

PRECIPITAION OF SEIZURES

seizure precipitants are as follows;

- Having a fever (97%)
- Having a cold (68%)
- Taking a bath (61%)
- Having acute moments of stress (58%)
- Engaging in physical exercise(56%).
- Seizure precipitants were often related to ambient warmth or cold-warmth shifts (41%) and to various visual stimuli (18%). others triggers are eating, bowel movements and rarely, touch.

MAJOR CHALLENGES IN THE FIRST SECTION;

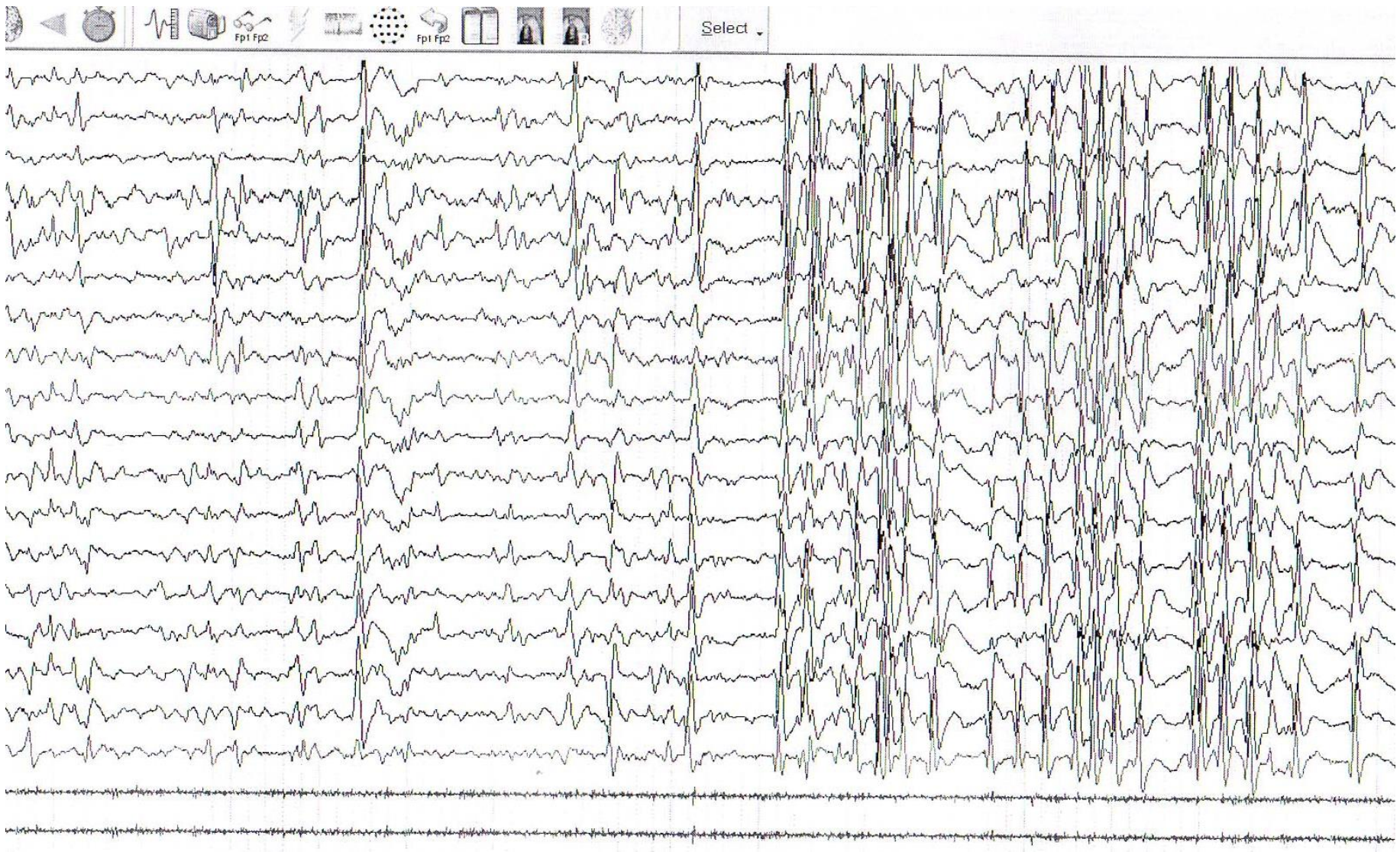
Rareness of the disease which made the doctors think they were faced with other forms of seizures allowing room for misdiagnosis.

Being unable to identify the precipitants of the seizures and isolating the patient from it, this increased the reoccurrence rates dramatically.

SECTION 2; DIAGNOSIS OF DRAVET

CLINICAL CASE contd

- In 2013, at age 5, she had an episode of hemi convulsive right-sided status epilepticus that lasted for six hours. This caused hemi edema and right hemiparesis.
- On physical examination the patient had a right sided hemiparesis with hemiparetic gait, contractures in the ankle joint foot deformities, dystonic movement in the fingers and reduced strength on the right side.
- This was the inciting event and reason for further examinations. A genetic test was performed and a SCN1A mutation was found, which is highly diagnostic of Dravet syndrome. On her EEG generalized spike-and-wave and multifocal discharges were seen.
- She was diagnosed with Dravets syndrome and was given valproic acid, clobazam and stiripentol to reduce the status epilepticus.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DIAGNOSTIC CRITERIA

- Normal development before the first seizure.
- Two or more seizures, with or without fever, before age 1.
- Two or more seizures that last more than 10 minutes.
- Seizures associated with fever due to illness or vaccinations.
- Seizures induced by prolonged exposure to warm temperature.
- Presence of other seizure types like myoclonic, hemi-clonic or tonic-clonic seizures.
- Seizures that do not respond to epilepsy medications, with seizures continuing past age 2.

COMORBIDITIES AND EFFECT OF LATE DIAGNOISIS

- Motor and coordination issues, such as a crouched gait, impaired dexterity, low muscle tone (hypotonia), loss of control of bodily movements (ataxia), and tremors
- Urinary tract and bowel issues, such as changes in eating and appetite, constipation and incontinence
- Communication issues, such as delayed language and ability to understand speech
- It can leads to cerebellar, cortical, and hippocampal damage which manifest as chronic encephalopathy and brain atrophy.
- Continuation of the seizure activity may lead to more pathologic states such as hypotension, myocardial dysfunction, hypoglycemia.

<u>MAJOR CHALLENGE IN SECTION TWO;</u>

Due to the effect of late diagnosis, our patient suffered extreme complications from the long standing status epilepticus. The complications were unfortunately irreversible even after diagnosis and treatment.

Section 3; AFTER MEDICATION

- CLINICAL CASE contd
- In 2017, at age 9, our patient was brought back to the hospital with complaints that she experiences multiple nightly seizures which presented with sudden opening of the eye, eye fixation, body rigidity and cyanosis. A deep breath usually signified the end of the seizures and she would fall back asleep. This lasted about 1-3 minutes, about 2-3 times a day or less.
- Subsequently she also suffered from partial seizures with body and eye deviation, eye fixation and falling. She presents with this 1-4 times in a month.
- On physical examination, she has marked developmental delay and apparent right sided hemiparesis with ankle recurvation.
- On MRI, there is presence of left hemispheric ischemia. EEG showed subclinical status epilepticus for one year.
- Clobazam was replaced with lorazepam and other drugs were continued unchanged I.e valproic acid and stiripentol.

Treatment

- First-line treatment of Dravet syndrome usually involves valproic acid or clobazam.
- **Physicians may prescribe** topiramate or stiripentol as second-line treatments for Dravet syndrome.
- For most people, Dravet syndrome is caused by a mutation in the SCN1A gene, which is involved in encoding sodium channels that allow neurons to transmit messages. Research shows that antiepileptic agents that act on sodium channels may worsen Dravet syndrome seizures. So DRUGS TO AVOID ARE---Carbamazepine, oxcarbazepine, lamotrigine, vigabatrin, phenytoin.
- KETOGENIC DIETS The ketogenic diet is a high-fat, adequate-protein, low- sugar diet. A Ketogenic diet has been proven to be of benefit.
- An elevated level of ketone bodies in the blood, a state known as "ketosis", can lead to a reduction in the frequency of epileptic seizures.

COMPLICATIONS

- Due to the decline in cognitive function and mild to profound intellectual disability the patients usually require 24-hour supervision.
- This disability can also cause them to suffer from severe anxiety and social isolation, which inevitably affects the quality of life of caregivers as well.
- The gait and balance problems associated with Dravet syndrome can result in falls. These falls, along with an increased risk of osteopenia and may cause bones to break.
- Seizures may cause drowning if they occur while a person is in or near water.
- The seizures can also increase the risk of pulmonary complications, such as aspiration pneumonia, which occurs when you inhale food, stomach acid, or saliva into your lungs, potentially resulting in sepsis.

Major challenges in section 3

- **There is no cure for Dravet syndrome, but medications can help manage seizures. This is the major challenge for doctors because patients still present with these seizures even though the drugs have reduced their frequency.**
- **Early undiagnosed stages of dravet syndrome are usually treated with antiepileptics that can even worsen the syndrome e.g. carbamazepine and phenytoin.**
- **Limited awareness.**

A few years ago dravet syndrome was extremely rare but it has started gaining recognition and is being reconsidered as a disease rather than a syndrome. This is because it is both epileptic and encephalopathic in nature and it appears to affect other systems, reduces life's expectancy and can drastically affect day to day activities.

Raise Awareness for
DRAVET'S SYNDROME

I love SOMEONE
WITH
DRAVET SYNDROME.

June 23
Dravet Syndrome Awareness Day

REFERENCES

- Our patient is an active outpatient of iashvilli children hospital, who stills comes for regular checkups.
- Supervisors and mentor; DR NANA TATISHVILI , EMAIL - n_tatishvilli@hotmail.com

DR ANNA BEDOSHVILLI

BOOKS AND JOURNAL REFERNCEs

- Medlink nuerology . P Panayiotopoulos MD PhD (Dr. Panayiotopoulos of St. Thomas' Hospital] and Dr Jerome Engel Jr MD PhD, editor. (Dr. Engel of the David Geffen School of Medicine at the University of California, Los Angeles]
- Everyday health, By Joseph Bennington-Castro Medically Reviewed by Samuel Mackenzie, MD, PhD
- Dove med articles


thank you!