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Síndrome de Dravet: caso clínico

Dravet syndrome: clinical case

[1] Ana Gabriela Romero Loja https://orcid.org/0009-0000-8170-0962
Catholic University of Cuenca, Cuenca, Ecuador.
ana.romero.63@est.ucacue.edu.ec

[2] Maria Fernanda Peralta Cardenas https://orcid.org/0000-0002-8183-9785
Catholic University of Cuenca, Cuenca, Ecuador.
mfperaltac@ucacue.edu.ec

[3] Rodrigo Jose Mendoza Rivas https://orcid.org/0000-0001-6020-9226
Catholic University of Cuenca, Cuenca-Ecuador.
rodrigo.mendoza@ucacue.edu.ec

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Palabras claves:
Epilepsia, síndrome de Dravet convulsiones, epilepsia infantil, encefalopatía epiléptica

Resumen

Introducción: el síndrome de Dravet es una condición genética poco común y grave, que se manifiesta con crisis epilépticas desde la infancia. Los pacientes pueden experimentar problemas de desarrollo, cognitivos, motores, conductuales, trastornos del sueño entre otros. Este síndrome generalmente se desarrolla por alteraciones genéticas en el gen SCN1A. No existe actualmente un tratamiento curativo por lo que el manejo se enfoca en controlar las convulsiones y promover el bienestar del paciente. Los medicamentos antiepilépticos, el régimen cetogénico y la cirugía son opciones que se pueden emplear para tratar el síndrome de Dravet. **Objetivo:** Determinar el manejo y terapéutica de Síndrome de Dravet genético en un historial clínico, con el propósito de identificar y destacar componentes innovadores y prácticos sobre la enfermedad. **Metodología:** El procedimiento consistió en la revisión detallada del historial clínico del paciente, así como de la patología, utilizando diversas bases de datos reconocidas. Estas bases de datos incluyeron publicaciones de los últimos cinco años en español e inglés. Se respetaron los procesos ético-legales, incluyendo la firma del consentimiento o asentimiento por parte del paciente. **Resultados:** Se detalla el caso de una niña de 44 meses de edad que experimentó convulsiones recurrentes durante episodios febriles. Su desarrollo motor y del lenguaje fue atípico, con inicio de la marcha a los 2 años y 2 meses y una capacidad verbal limitada. La sospecha de epilepsia, en particular del tipo Dravet, se basó en la recurrencia elevada de las convulsiones, la ausencia de mejoría con el tratamiento actual y los hallazgos del examen físico. Se realizó una tomografía de cráneo y un estudio genético para confirmar el diagnóstico. Se introdujo topiramato en el tratamiento para mejorar el control de las crisis. **Conclusión:** El caso ilustra las características del síndrome de Dravet y la importancia de un diagnóstico preciso para un manejo adecuado. **Área de estudio general:** medicina. **Área de estudio específica:** cardiología. **Tipo de estudio:** Casos clínicos.

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Keywords:
Epilepsy, Dravet syndrome, seizures, childhood epilepsy, epileptic encephalopathy.

Abstract

Introduction: Dravet syndrome is a rare and severe genetic condition, which manifests with epileptic seizures since childhood. Patients may experience developmental, cognitive, motor, behavioral, sleep disorders and other problems. This syndrome usually develops due to genetic alterations in the SCN1A gene. There is currently no curative treatment, so management focuses on controlling seizures and promoting the patient's well-being. Antiepileptic drugs, ketogenic regimen and surgery are options that can be used to treat Dravet syndrome. Objective: To determine the management and therapeutics of genetic Dravet syndrome in a case history, with the purpose of identifying and highlighting innovative and practical components of the disease. Methodology: The procedure consisted of a detailed review of the patient's clinical history, as well as the pathology, using various recognized databases. These databases included publications from the last five years in Spanish and English. The ethical-legal processes were respected, including the patient's signature of consent or assent. Results: We report the case of a 44-month-old girl who experienced recurrent seizures during febrile episodes. Her motor and language development were atypical, with onset of walking at 2 years and 2 months and limited verbal ability. Suspicion of epilepsy, particularly of the Dravet type, was based on high recurrence of seizures, lack of improvement with current treatment, and physical examination findings. A skull CT scan and genetic study were performed to confirm the diagnosis. Topiramate was introduced in the treatment to improve seizure control. Conclusion: The case illustrates the characteristics of Dravet syndrome and the importance of an accurate diagnosis for proper management.

Introduction

Dravet Syndrome (DS), also known as severe myoclonic epilepsy of infancy (SMEI) (1), was initially described in 1978 by Dr. Charlotte Dravet. Over the years, other research has confirmed and detailed the characteristics of this syndrome. Based on the clinical

manifestations, two main forms have been identified: the typical form (SMEI) and the borderline form (SMEIB), in which the myoclonic component may be absent or subtle.(1).

The disease described is an encephalopathic and developmental epileptic disorder(2), originating from mutations due to a disappearance of the function in the replication of the SCN1A gene (haploinsufficiency), located on chromosome 2q24, which causes a decrease in the function of the Nav1.1 sodium channels in the GABAergic inhibitory interneurons(3). Resistant to pharmacological treatments in the first 12 months of life and is characterized by seizures generally associated with hyperthermia. These crises can be prolonged and generalized or hemiclonic.(4–8).

The incidence is low; it has been estimated that it occurs in approximately one in every 20,000 to one in every 40,000 live births.(8.9). Strzelczyk et al. (11) indicate in their study that the incidence of DS varied from 1:15,400 to 1:40,900, and the prevalence varied from 1.5 per 100,000 to 6.5 per 100,000. Mortality was estimated at 3.7% to 20.8% of patients with DS, mostly attributed to sudden and unexpected death in patients with epilepsy and status epilepticus.(10).

In Ecuador there are no studies or reports of DS incidence at the national level, in a study that was carried out in a hospital center of Specialties of the IESS in the city of Quito with a universe of 745 patients belonging to the pediatric neurology outpatient clinic in the years 2017 to 2018 with a diagnosis of epilepsy, of which 89 met the criteria of the International Organization against Epilepsy called ILAE according to the etiological classification only 1 patient corresponds to Dravet syndrome corresponding to a prevalence of 0.0013(11).

The mortality rate for Dravet syndrome is high, higher than the mortality rate for people with epilepsy in general. Mortality in adults is estimated to be approximately 15%. Sudden death in epilepsy (SUDEP) represents the most frequent cause of death, occurring mainly during sleep. The second most common cause of death is status epilepticus (SE) and its complications.(12,13).

Approximately 80% of cases of this syndrome are associated with the mutation of the SCN1A gene.(14), which encodes the voltage-gated sodium channel subunit IV Nav1.1 that causes neuronal circuit hyperexcitability and seizures(15–17). However, it can also be caused by inheritance from one of the parents who has less severe clinical manifestations or as a consequence of a somatic mutation.(18). Multiple epilepsy phenotypes originate from the SCN1A gene, including Dravet syndrome, febrile seizures (FS), and genetic epilepsy with FS plus. A hallmark is the phenotypic heterogeneity of SCN1A-related epilepsy, the causes of which have not yet been resolved.(19).

In the same context, Cetica et al. (21) conducted an article to explore the prognostic value of the initial clinical and mutational findings in infants with SCN1A mutations in 182 mutation carriers, evaluating the accuracy of associations such as sex, age/fever at first seizure, family history of epilepsy, EEG, and type of mutation to predict Dravet syndrome. The results showed that 48.5% had Dravet syndrome, and age at first seizure and frameshift mutations were associated with this syndrome. The risk of Dravet syndrome was 85% in the 0-6 month group, 51% between 6 and 12 months, and 0% after the twelfth month. ROC analysis identified onset within the sixth month as the diagnostic cut-off point for progression to Dravet syndrome with a sensitivity of 83.3% and specificity of 76.6%.(20).

Dravet Syndrome can manifest with a wide range of symptoms ranging from typical epileptic seizures, autism spectrum disorders and cognitive problems. These three conditions are known as the "neurotriad" (epileptic seizures, cognitive problems and autism).(8)The syndrome usually begins in the first 12 months of life of an infant with typical psychomotor development and is triggered under the influence of several factors, the most investigated currently being the previous occurrence of febrile episodes.(21).

Seizures in the first 12 months of life tend to manifest, frequently with fever, in boys or girls who were previously healthy. These seizures later evolve into forms that do not respond to anticonvulsant treatment and are associated with motor and cognitive impairment. Between five and ten percent of patients have a familial component, while the majority are due to de novo mutations. In addition, mosaicism situations can be observed. Approximately seventy to eighty-five percent of patients are associated with mutations in the SCN1A gene; however, various genes are identified as possible contributors. The incidence of this syndrome is approximately one in every twenty thousand to forty thousand live births, and its prevalence represents seven percent of epilepsies in children under 36 months of age, affecting boys and girls equally.(22).

Initial manifestations are the typical seizure at 2 to 15 months of age, in rare cases at 1 month or as late as 20 months. They present with recurrent febrile or afebrile focal clonic seizures, focal to bilateral tonic-clonic and/or generalized clonic seizures, which are generally prolonged. In addition, they develop other types of seizures between 1 and 5 years of age, which are myoclonic seizures, focal seizures with altered consciousness, atypical absence seizures, atonic seizures, nonconvulsive status epilepticus and tonic and tonic-clonic seizures that usually manifest during sleep and in clusters.(9).

From their perspective, Wheless & Fulton (24) in their study report that DS initially manifests with seizures, being the first symptom in previously healthy children, generally between one and eighteen months of age, with a higher percentage of cases between four and eight months. The classic onset is a prolonged and generalized or hemiclonic seizure induced by fever. The alternation of unilateral seizures helps to

differentiate DS from focal epilepsy. In the initial stages, electroencephalographic studies and magnetic resonance imaging generally do not show pathologies.(23).

The diagnostic process begins with a thorough review of the patient's medical history to identify the hallmark signs and symptoms of the condition. Electroencephalogram (EEG) and magnetic resonance imaging (MRI) can confirm the diagnosis of Dravet syndrome (DS) and rule out other possible reasons for the seizures. Genetic testing can also be performed to detect mutations in the SCN1A gene to confirm the diagnosis. It is crucial to assess the type and frequency of seizures in the patient to identify any other neurological abnormalities that may be related to Dravet syndrome.(24).

Between 1 and 5 years, patients develop drug-resistant seizures of various types, which become more frequent but shorter over time. Interdictal EEG shows background slowing and epileptic discharges. In older children and adults, neuroimaging may reveal generalized atrophy or hippocampal sclerosis. These patients present with persistent seizures, intellectual disability, and neurological abnormalities from age 5 years. Hyperthermia as a seizure trigger decreases, but sodium channel agents may worsen seizures. MRI may show hippocampal atrophy and sclerosis with age.(9).

The presence of an orthopedic disease often has other important manifestations, such as: Scoliosis, valgus foot, growth retardation, etc. Some commonly used medications carry a significant risk of seizures if an accurate diagnosis is not obtained. Delays in cognitive and psychomotor development occur from the second year of life.(5).

Although there is no literature to support the benefits of early diagnosis, experts have reached a moderate consensus based on their clinical experience that an early diagnosis improves the overall long-term outcome of patients by improving cognition and seizure control. An accurate diagnosis can be helpful at any age, not only to guide treatment options but also to connect families to support networks.(21).

Diagnosis is made by clinical evaluation, as magnetic resonance imaging (MRI) results are usually normal and electroencephalography (EEG) findings are nonspecific. The early clinical presentation of DS is distinctive, with the onset of recurrent and prolonged seizures, which are often triggered by fever in apparently normal developing infants.(21).

The pathophysiology of Dravet syndrome (DS) involves abnormalities in brain function that contribute to the initial manifestation of the clinical symptoms of the disease. The SCN1A gene is responsible for the synthesis of the alpha subunit of the NaV1.1 sodium channel, which is voltage-dependent, and is the main cause of the de novo mutations observed in Dravet syndrome. This channel plays an essential role in the control of neuronal excitability and signal transmission in the nervous system.(25).

Mutations in the SCN1A gene result in a functional decrease of the NaV1.1 channel, leading to abnormal neuronal excitability. This neuronal hyperexcitability results in the generation of seizures.(26,27). In addition, it affects the function of GABAergic neurons, which are inhibitory and have a fundamental role in regulating the excitatory and inhibitory balance in the brain. The decrease in the function of GABAergic neurons contributes to neuronal hyperexcitability and the appearance of seizures.(25).

DS primarily affects children in the first twelve months of life, and the underlying pathophysiology results in febrile seizures that progress to a variety of more severe and treatment-resistant seizures.(28). Altered neuronal plasticity and persistent excitability contribute to the development of epileptic encephalopathy and the cognitive and behavioral disabilities observed in patients with DS.(29).

It is important to note that although mutations in SCN1A cause the majority of DS cases, there are cases in which mutations affect other genes related to ion channels and neurotransmitters, which adds complexity to the pathophysiology of Dravet syndrome. In order to advance in the development of more specific and effective therapeutic approaches for the treatment of this pathology described, it is essential to understand the underlying structures involved.(30–32).

According to the International Consensus Panel Study, the treatment recommendations indicate Valproate as a first-line drug; Fenfluramine, Stiripentol, and Clobazam as second-line drugs; Cannabidiol (pharmaceutical grade, Epidiolex) as third-line drugs; and Topiramate, a ketogenic diet, or a modified Atkins diet as fourth-line treatment. In addition, other treatments include vagus nerve stimulation, Levetiracetam, Zonisamide, Bromides, Clonazepam, and Ethosuximide.(9,33,34). Regarding treatment, in a review carried out, valproate and Clobazam are the most commonly used drugs in first-line management, while Clobazam is the most suggested in second-line.(35).

Results from randomized controlled trials support the efficacy of cannabidiol (CBD) in the treatment of epileptic seizures associated with Dravet syndrome. Despite the lack of global consensus among drug regulatory agencies, CBD shows promise as a treatment method for the control of epileptic seizures, according to well-designed studies. A good safety and tolerability profile is highlighted, although the need for long-term studies in pediatric patients is emphasized to confirm long-term utility and safety. The debate on the release of CBD as a therapeutic treatment continues, and the importance of further research to support its specific application in epilepsies that do not respond to conventional therapies in the pediatric population is underlined.(36).

On the other hand, eight placebo-controlled trials were included, with active treatments including stiripentol, pharmaceutical-grade cannabidiol, fenfluramine hydrochloride, and soticlestat. Pharmaceutical-grade cannabidiol showed a lower seizure response rate

compared with fenfluramine hydrochloride, whereas stiripentol showed a higher response rate than pharmaceutical-grade cannabidiol. Stiripentol had a lower likelihood of treatment discontinuation than pharmaceutical-grade cannabidiol, and cannabidiol showed a lower incidence of adverse events than fenfluramine hydrochloride. However, stiripentol had a higher risk of adverse events compared with pharmaceutical-grade cannabidiol.(37).

Likewise, fenfluramine, marketed as Fintepla, has emerged as a reliable and effective therapeutic option for patients with Dravet Syndrome (DS), recently approved by the FDA and EMA to address the lack of additional anticonvulsant options. Findings from placebo-controlled phase 3 and open-label studies were evaluated, consistently confirming a marked reduction in seizures. The serotonergic mechanism of action of fenfluramine is discussed, highlighting its future perspective in the treatment of DS. Fenfluramine has a potent anticonvulsant effect, generally well tolerated, although it needs dose adjustment with stiripentol. Preclinical studies suggest a specific and possibly disease-modifying impact in DS.(38).

The ketogenic diet represents a treatment option for Dravet syndrome, characterized by a high-fat, low-carbohydrate, moderate-protein diet. This dietary approach is individually tailored to reduce the brain's reliance on glucose as its primary energy source.(39)In a study conducted from March 2014 to March 2020, where the ketogenic diet was applied to 114 patients, it was concluded that this diet is effective as a treatment option and has a low incidence of adverse reactions.(40).

In the modern era, new genetic testing options will allow for diagnosis closer to the onset of the disease. Three new drugs—stiripentol, cannabidiol, and fenfluramine—have demonstrated documented efficacy and safety as adjuvant therapies to treat drug-resistant Dravet syndrome. Early diagnosis resulting in earlier treatment with these and other drugs may improve the prognosis for long-term outcomes, including less severity of cognitive, motor, and behavioral impairments.(23).

Furthermore, viral and non-viral gene therapies, as well as gene editing tools, are rapidly improving and offering new platforms for alternative and more effective medicinal treatments for Dravet syndrome. These strategies include gene supplementation, CRISPR-mediated transcriptional activation, and the use of antisense oligonucleotides.(41).

Selvarajah et al. (43) point out in their study that, in general, seizure frequency increases during the first decade of life. Subsequently, these seizures, such as myoclonic, focal with altered consciousness, and atypical absences, tend to decrease in frequency or even disappear in adulthood. Adults tend to have a marked reduction in status epilepticus, especially after age 30, with consequences such as parkinsonian features in patients as

young as 19 years and are more severe in older patients, suggesting a progression of parkinsonian symptoms. In adulthood, patients continue to present behavioral problems, which negatively affect the general well-being and health of the individual. The predominant cause of mortality reported in adults with DS is Sudden Unexpected Death in Epilepsy (SUDEP). Further studies in older adults are needed to understand the long-term outcomes of patients with DS.(42).

Methodology

This paper presents a case report together with a descriptive and retrospective bibliographic review on Dravet Syndrome. For the collection of data from the clinical case, a methodology was used that included an exhaustive review and thorough evaluation of the patient's clinical record. Vancouver style guidelines were followed for correct bibliographical reference, and the description of the disease was organized according to predetermined sections: definition, pathophysiological mechanism, risk factors, diagnosis, prognosis, clinical manifestations, implications and therapeutic options. Relevant information was obtained through a critical review of specialized literature from various recognized sources, among other relevant ones. These databases included publications from the last five years in Spanish and English. Respecting the ethical-legal processes, including the signing of consent or assent by the patient.

To systematize the information of this case, the data from the patient's medical history were extracted and thoroughly analyzed, considering it as a secondary source. The detailed aspects included the reason for consultation, the current disease upon admission, the diagnostic impression (IDX), relevant personal and family history, usual medications, complete physical examination, results of the first laboratory tests, the initial therapeutic management plan, complementary tests performed and the patient's clinical outcome, which was categorized according to improvement, lack of response or death.

In the discussion and synthesis of knowledge, the particularities that played an integral role in the patient's outcome were meticulously examined. To conclude, a comparison of the acquired information with previous research was made, with the aim of organizing the clinical case article in a systematic and contextualized manner.

Results

Case presentation

A 44-month-old patient was referred to the emergency department for recurrent febrile episodes accompanied by seizures. Born to non-consanguineous parents and after a planned pregnancy, the girl experienced a delay in neurodevelopment around 2 years and 2 months and speaks less than 15 words to date. At 18 months of age, she presented a

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classified seizure. The persistent pattern of seizures during temperature increases led to the diagnosis of epilepsy and as treatment, valoric acid and levetiracetam were started without improvement of the seizures.

In her last febrile episode, she presented a 10-minute seizure, which led to her admission for evaluation. On physical examination, she presented nasal width and low ear implantation and delayed neurodevelopment. Due to the clinical presentation of her epileptic events, a genetic study was requested, which reported SCN1A mutation associated with Dravet syndrome.

A CT scan of the head was performed, which was normal, as well as biometric tests, blood chemistry, ammonia and metabolic tests, all within normal limits.

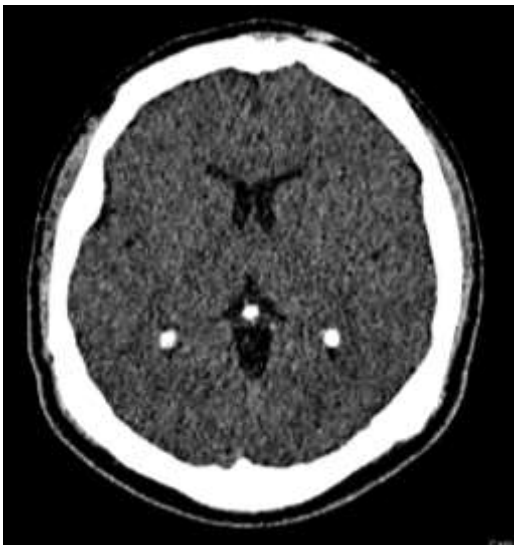

Figure 1.*Computed tomographyaxial section*

Normal brain, we observe normal frontal and parietal lobes, the density is homogeneous isodense, the visible basal ganglia do not show alterations, symmetrical ventricular system with calcified choroid plexuses (normal). Hyperdense cranial cap and finally the superficial soft tissues without alterations.

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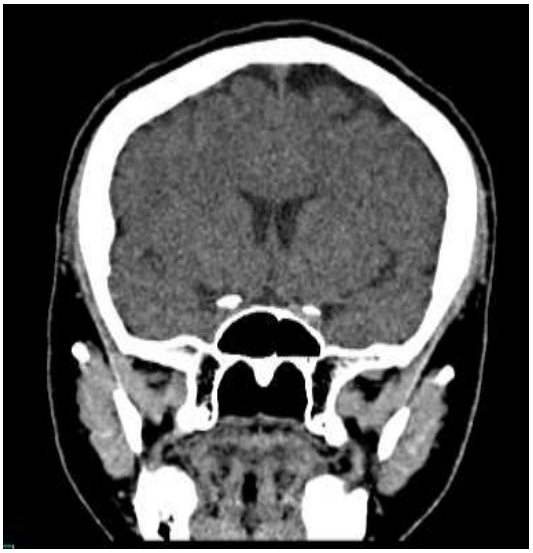

Figure 2.*Coronal section computed tomography*

Normal brain, we observe normal frontal lobe and temporal lobes. Central interhemispheric fissure. The ventricular system (lateral ventricles, third ventricle) are visible without alterations.

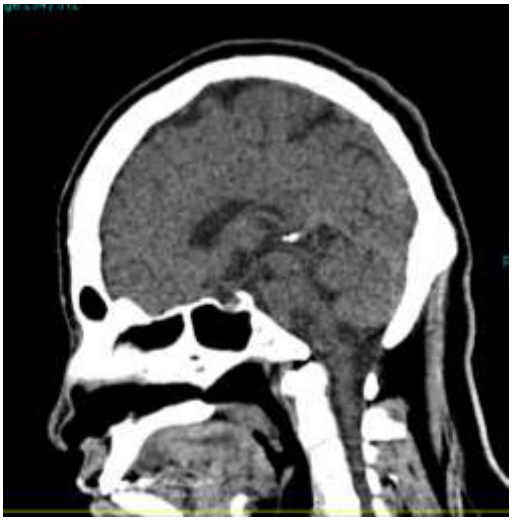

Figure 3.*Computed tomography sagittal section*

Normal brain, we observe normal frontal, parietal and occipital lobes. Corpus callosum located in the midline, cerebellum without alterations. Finally, we observe the brain stem with normal midbrain, pons and bulb with hypodense image in the pons as an occasional artifact in the posterior fossa.

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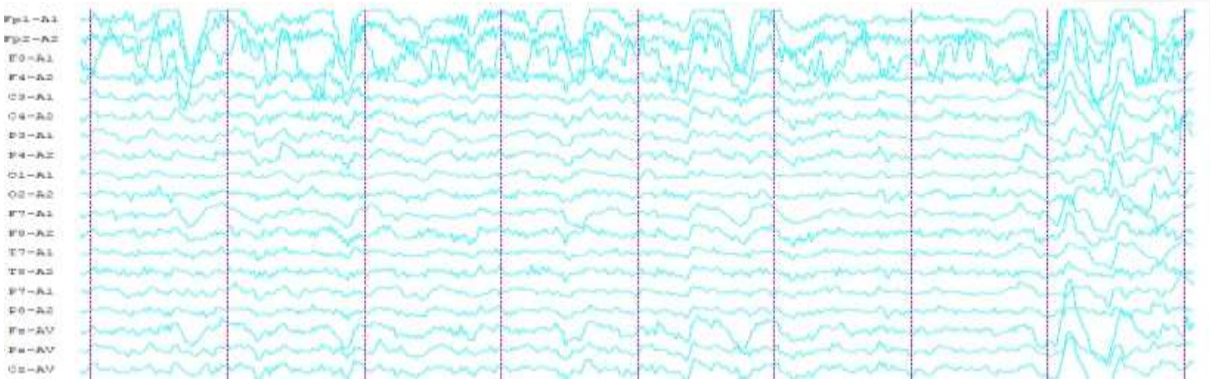

Figure 4.*Electroencephalogram*

The electroencephalogram reports slow baseline activity in the theta-delta range. Artifacts of frontal muscle contracture.

*Conclusion of the electroencephalogram:*signs of global brain dysfunction.

Discussion

A 3-year-and-8-month-old female patient presents a complex clinical picture characterized by recurrent seizure events triggered by febrile episodes. The suspicion of possible epilepsy, particularly of the Dravet type, arises due to the high frequency of seizures and the lack of response to current treatment with valproic acid and levetiracetam. The patient's developmental course provides additional relevant information, where atypical motor and language development was observed, with the onset of walking at 2 years and 2 months and limited verbal capacity to date. On physical examination, at the neurological level, the patient presents generalized hyporeflexia. These findings, combined with the clinical history, reinforce the suspicion of a specific epileptic syndrome. The decision to request a cranial tomography and a genetic study was essential to confirm the diagnosis and guide therapeutic management. The incorporation of topiramate in the treatment aims to improve the management of epileptic seizures, particularly in patients with DS.

The study by Pérez & Moreno (44) supports the description of Dravet syndrome (DS) as a severe epileptic encephalopathy that manifests in the first 12 months of life, with frequent crises triggered by fever and resistance to conventional treatments. Identified by Charlotte Dravet in 1978, this syndrome is illustrated by the case of a 4-year-old preschool girl with tonic-clonic seizures, cognitive delay, right hemiparesis and electroencephalographic alterations, without response to conventional treatments. Although a genetic study revealed de novo alterations in the SCN1A gene in the case presented by Pérez & Moreno(43)In the patient analyzed here, the lack of economic factors did not allow the genetic study to be carried out, but the initial suspicion of

Dravet syndrome is confirmed, since the clinical characteristics of the case presented coincide with the detailed description of this disease.

For their part, Suescún et al. also emphasize that Dravet syndrome, also known as severe myoclonic epilepsy of infancy, presents as a drug-resistant epileptic encephalopathy, typically beginning in the first 12 months of life. Its characteristics include epileptic seizures triggered by various factors, with febrile episodes being the most commonly associated. Due to its low frequency, the pathology is considered rare. The presented case of a 10-year-old boy with Dravet syndrome, in which a mutation in the SCN9 gene was evidenced through a genetic exome, highlights the importance of considering mutations in genes such as SCN9A, located on the same chromosome, which could influence the generation of this pathology in different ways.(44)The importance of a thorough evaluation and differential diagnosis in cases with similar clinical manifestations is emphasized. This highlights the need to consider other possible causes of the seizures and to rule out alternatives before confirming the diagnosis of Dravet syndrome. Genetic testing is important, however, as the patient's parents do not have the financial resources, it has not been possible to perform it.

Similarly, the study by Koppel et al. (10), from the year 2023, highlights this pathology as a severe epileptic encephalopathy, classified as unusual and with little medical knowledge, which makes its diagnosis difficult. The disease is linked to a modification in the SCN1A gene, the main encoder of the alpha 1 subunit of the sodium channel. A clinical history of a 6-month-old girl with a normal history is presented, who develops seizures after the last dose of the pentavalent vaccine, not attributable to this event. The difficulty in controlling seizures leads to genetic studies, demonstrating the importance of tools such as WES for an accurate diagnosis and appropriate treatment. The case highlights the underdiagnosis and inadequate treatment of Dravet syndrome, emphasizing the need for genetic tools and early intervention in order to improve the quality of life of patients.(9)This broadens the spectrum of possible seizure triggers by considering specific precipitating events, such as vaccine administration. This highlights the difficulty of the case and the importance of a thorough evaluation of the patient's medical history.

This syndrome is a severe epileptic encephalopathy that manifests in childhood. It is associated with variants of the SCN1A gene, generating prolonged seizures, febrile crises and myoclonus, resulting in significant impairment of cognitive and motor development. Despite a normal initial EEG, abnormal patterns are observed over time. The therapeutic approach focuses on minimizing triggers and using specific medications, although the prognosis remains challenging, with a notable risk of sudden death in epilepsy. Early identification and treatment of the condition are fundamental aspects to increase quality of life. This genetic disorder, known as Dravet Syndrome,

generally originates in the first six months of life, manifesting prolonged and recurrent febrile seizures, and can evolve into other types of epileptic seizures. The mutation in the SCN1A gene stands out as a common genetic marker in these patients, encoding a crucial subunit in the control of neuronal excitability through a sodium channel.(10,45).

One of the hallmarks of Dravet Syndrome is resistance to conventional anticonvulsant treatments, with many patients experiencing a lack of response to multiple drugs. In addition to seizures, affected individuals often exhibit delays in cognitive and motor development, as well as difficulties with speech and communication. The progression of the syndrome can result in significant cognitive disabilities and behavioral disturbances.(46).

The identification and determination of this pathology is based on clinical, genetic and electroencephalographic criteria, and genetic testing is recommended to confirm the presence of the SCN1A mutation. Therapeutic management seeks to control epileptic seizures and improve the patient's quality of life. However, since there is no definitive cure, personalized pharmacological strategies and support therapies are implemented, including cognitive and physical interventions.(47).

Current therapeutic approaches, such as anticonvulsant medications, ketogenic diet, and neurostimulation, have proven effective in reducing both the incidence and severity of seizures in affected patients. Close collaboration between family members, patients, and medical staff is essential to effectively manage the disease. Although there is no definitive treatment for this syndrome, medical advances continue to offer hope and therapeutic options to patients and their families.(19).

Regarding treatment, Galvis (48) points out in his study that he focused on assessing the clinical effectiveness and cost-effectiveness of cannabidiol (CBD) as an adjuvant compared to usual care in pediatric patients with Lennox Gastaut (LGS) and Dravet (DS) syndromes. The research is based on a Markov model with a 13-year horizon, using data from clinical and observational studies, as well as systematic reviews with meta-analysis. The results show that CBD, as an additional treatment, can prevent significantly more epileptic seizures than usual care, with a difference of 1,604 seizures avoided per 1,000 patients. Although the cost associated with the use of CBD is higher, the cost-effectiveness ratio indicates that CBD turns out to be a cost-effective strategy, especially if one is willing to pay a threshold equal to or greater than $10,600,000 COP for each crisis avoided.(5)Cannabidiol (CBD) is considered a potentially beneficial treatment option for improving epileptic seizures in Dravet syndrome. This opens up new therapeutic possibilities and emphasizes the importance of further research into the use of cannabinoids in this disease.

In summary, the discussion of the results highlights the importance of a comprehensive assessment and the need for a multidisciplinary approach to managing complex cases, such as the present one, where a deeper understanding of the diagnosis is sought and treatment is adjusted accordingly. As we advance in the understanding and treatment of severe epileptic disorders such as Dravet syndrome, consideration of innovative options, such as CBD, becomes critical to improving clinical outcomes and patient well-being.

Conclusions

- In conclusion, the case of a 3-year-and-8-month-old patient with recurrent seizures triggered by febrile episodes raises the possibility of an epileptic syndrome, possibly Dravet Syndrome. The lack of response to current treatment and clinical findings, such as atypical development and generalized hyporeflexia, reinforce the diagnostic suspicion. Genetic studies and a cranial tomography are essential to confirm the diagnosis and guide therapeutic management, including the implementation of topiramate.
- The analysis of the medical literature supports the description of Dravet Syndrome as a severe epileptic encephalopathy, with resistance to conventional treatments and a significant association with genetic alterations, especially in the SCN1A gene. The difficulty in diagnosis due to the rarity and complexity of the disease is highlighted in several studies, underlining the importance of genetic tools for accurate diagnosis and early management. Overall, the discussion highlights the need for a multidisciplinary and genetic approach to effectively understand and address Dravet Syndrome, a rare and challenging disease.

Conflict of interest

The authors declare that there is no conflict of interest in relation to the submitted article.

Authors' contribution statement

Author 1: I actively participated in the planning and design of the literature review. I also carried out a critical evaluation of the selected studies, analyzing both the methodological quality and the validity of the results.

Author 2: Significantly contributed to the interpretation and discussion of the findings obtained in the clinical case. He/she also played an important role in the writing and revision of the content of the manuscript.

Author 3: Provided valuable input by providing comments that improved the clarity and coherence of the work. Actively participated in the development of the results and conclusions of the study.

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