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Maple Syrup Urine Disease: About a Case

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Abstract

Qualitative study of a clinical case, maple syrup urine disease (MAOJA), inborn error of metabolism of branched-chain amino acids with accumulation of these, resulting in severe neonatal encephalopathy, which, not being diagnosed, it leads to the appearance of permanent neurological sequelae and death. A case is presented, a female patient, with EOJA diagnosed in her lactating period with the aim of analyzing the clinical manifestations, diagnosis and therapeutic behavior. He presented a variable clinic, with suspicion of other pathologies. Due to the clinical worsening and the "sweet" smell in the urine, a neonatal screening was performed, showing a total of isoleucine and valine above normal values, which confirmed the diagnosis. The patient presented severe neurological sequelae, physical retardation of 98%. It is concluded that the clinical manifestations of (EOJA) in the first days of life are crucial for early diagnosis, allowing family counseling through genetic studies. One of the non-invasive treatments that gradually helps stop the symptomatic progression of these patients is a low-protein diet and a special formula.

Keywords: *Urine, Maple, Leucine, Amino Acids.*

1. Introduction

According to BLACKBURN P, GASS J, Maple Syrup Urine Disease (EOJA), is a pathology where there is an autosomal recessive genetic alteration of branched amino acid metabolism. It is caused by variations at the level of the mitochondrial dehydrogenase complex of branched-chain keto acids (BCKDH), which is responsible for the second catabolic step in the degradation of leucine, isoleucine and valine. It is also known as branched-chain ketoaciduria or leucinosis, as defined by Sajeev M, et al. in their study (Blackburn et al., 2017; Sajeev et al., 2021). In his study Blackburn, he says that from the epidemiological point of view this disease worldwide is known for its low prevalence of 1: 290,000 newborns, being more frequent in English-speaking countries (Anglo-Saxons) with one case per 185,000 neonates and at the level of Latin America 1 case is known for every 60,000. Being a rare disease there is no record of statistical study in our country (Blackburn et al., 2017) In its classification you can find several types according to your clinic, such as: classic (severe),

intermediate or intermittent. It has been seen that newborns who have not undergone treatment can have a predictable course. For example, within the first twelve to twenty-four hours they present high concentrations of amino acids (leucine, isoleucine and valine present at the blood level), and the smell of maple syrup in earwax is already detectable (Strauss et al., 2020) When talking about hereditary disorders, it is known that they can produce inborn errors of protein metabolism due to the deficiency of enzymes or cofactors that lead to an accumulation of toxic metabolites and substrate deficiency. Clinically they present manifestations in the neonatal period with food intolerance, convulsions and encephalopathy that progress to coma (Jain et al., 2020).

BCAAs in blood and tissues in maple syrup-smelling urine disease induce neurological complications such as stereotyped movements, apnea, mental retardation, and demyelination. Metabolic encephalopathy comes to present as a complication cerebral edema. (Streck et al., 2021) Genetically this disease at conception, each sibling of an individual with the pathology has a 25% chance of being affected, a 50% chance of not being affected and being a carrier, and a 25% chance of not being affected and not being a carrier (Eduardo & Ana, 2021; Lanza & Montalvan, 2017). For the diagnosis of maple syrup-smelling urine disease, the patient's clinic is taken into account as the characteristic "sweet" smell that resembles maple syrup. The most important diagnostic test for MSUD is serum measurement of branched-chain amino acid concentrations (Leucine, Valine, and Isoleucine). Up to day 6 of extrauterine life, isoleucine levels are increased. Mutation analysis is an option in patients with MSUD to confirm the diagnosis, predict response to thiamine, and aid in prenatal diagnosis if future pregnancies are expected (Salazar, 2021; Lanza & Montalvan, 2017).

The treatment of this disease is recommended to use preparations free of BCAAs, taking into account that they can only be administered orally or enterally through a tube; There are special formulas that in the case of this pathology require that they have a low value of leucine. It is considered that the timely treatment is oral thiamine 100 – 300 mg / day L-valine, L-isoleucine. Using a mixture of BCAA-free amino acids through the use of parenteral nutrition is considered as a novel alternative in the treatment of acute decompensation of EOJA (Ugarte et al., 2018; Blanco et al., 2017). Also another alternative as a current treatment for leucinosis is liver transplantation. A recent study showed that this procedure is able to restore homeostasis and stop neurological effects, however, it cannot restore existing ones (Xu et al., 2020) OJA is a rare disease, which occurs in patients numerous complications, with a risk of acute metabolic decompensation (AMD), which can cause neurological deficits or death if it does not have immediate treatment (Tobin et al., 2021; Yıldız et al., 2020) One of the most important complications of the neonatal form, is a picture of severe and progressive neurological compromise, it can even also present neuropsychiatric manifestations, depression, anxiety disorders and attention deficit disorder (Ramírez et al., 2020; Pode et al., 2020) This research aimed to analyze the clinical manifestations, diagnosis and therapeutic behavior, before a case attended at the Health Center type B of Salcedo. As such, the clinical history was reviewed, a theoretical and methodological framework was designed to demonstrate the results.

2. Materials And Methods

The modality of the research was descriptive with a qualitative approach, since the study of a clinical case that was presented in an outpatient clinic at the Health Center type B of Salcedo was carried out, using both human and physical resources to facilitate future strategies aimed at the timely diagnosis of this disease. The instrument used was the patient's Clinical History.

3. Results and Discussion

Female patient, 4 days old, exclusively breastfeeding, mestizo, RN, born on January 22, 2009, in San Miguel – Salcedo, rural area, lives in her own home, has basic services. He lives with his two sisters and his parents.

CURRENT ILLNESS OF ADMISSION

The mother reports that her daughter at the time of discharge from a private clinic apparently does not present any alteration, on the fourth day she presents nausea that reaches vomiting on several occasions; of food content, accompanied by thermometrically proven fever, lethargy, which is why he

goes to this health home. Patient lives in rural area, in his own home, has all the basic services. He lives with his two sisters and his parents.

Personal pathological history: Delivery to term vaginal cephalus, without any complications. Vaccines received: BCG and Hepatitis
Family pathological history: HTN (Maternal mother and grandmother)
REGIONAL AND SYSTEM PHYSICAL EXAMINATION (POSITIVE)
Irritable patient, decreased crying, breast rejection, feverish.

Vitals:
Axillary temperature: 36.6 º C.
Heart rate: 125 bpm
Respiratory rate:40 RPM
SO2: 96% to the environment.

LEATHER AND FANERAS:
Skin: Turgor and elasticity preserved. Hot and humid. Normal looking faneras.
Head: Normocephalic. Anterior fontanelle convex, normal tension, not closed. Hypotonia of neck muscles.
Respiratory and Cardiovascular: Normal
ABDOMEN: Flat, soft, depressible, no discomfort on palpation, increased hydro-aerial noises.
NEUROLOGICAL EXAMINATION: Grasping reflex present, response to stimuli present and normal. Cervical hypotonia
PRESUMPTIVE DIAGNOSES

1. Neonatal sepsis
2. Viral meningitis

DEFINITIVE DIAGNOSIS

1. Maple syrup urine disease

Infantile paralysis as a diagnosis that occurred long-term

Checked: 25/01/2009
Newborn of female sex, four days old, is brought by her mother to the health home, for presenting for 24 hours, thermal rise, vomiting, accompanied by incoercible crying. Inadequate evolution, persistent lethargy, refusal to feed, and cervical hypotonia. Skull CT scan and lumbar puncture: normal. Admission to ICU for neonatal sepsis with VMA (artificial mechanical ventilation) and antibiotics; possible meningitis. Ventilated for 45 days, without clinical improvement, at the request of the family they decide to leave, even knowing the risks. Days later, in the emergency room, she was intubated and hospitalized again in pediatrics, administering oxygen by nasal cannula and fed by nasogastric tube. At approximately 15 days (endotracheal tube is removed).

At three months of birth comes the result of examinations, the amino acid profile – quantitative using as a method the spectrometry of MASSES in TADEM, where it was observed: Significant increase in the concentrations of the amino acids leucine (+ isoleucine) and valine (the methodology used does not separate leucine from isoeucine). With a value of 1810.0 mcmol/l (reference from 61.1 to 232.8 mcmol/l (Lanza & Montalvan, 2017; Salazar, 2021). In addition to significant decrease in alanine and discrete tyrosine. EOJA is diagnosed, according to criteria of (Strauss et al., 2020; Lanza & Montalvan, 2017; Salazar, 2021). Diet with low protein content is started, limited in leucine (60 – 90 mg / kg weight / day – 0.5 -0.8 mg / kcal / day, acute phase), then isoleucine and valine (the latter 80 – 120 mg / kg weight / day in the acute phase) and 40 – 50 mg / kg / weight / day. Protein requirements (3-4 g/kg body weight/day). Supplements of glutamine and alanine (250 mg/kg body weight/day each), and tyrosine, histidine and threonine, according to need and results of blood concentrations of amino acids (Ugarte et al., 2018).
Beta fatty acid oxidation tests, organic acid oxidation, urea cycle oxidation tests, normal.

08/03/2009

It continues with lethargy, refusal to feed, encephalopathy and abnormal odor of urine. Results of altered neonatal screening with high concentrations of amino acids. AoA is diagnosed (Lanza & Montalvan, 2017; Salazar, 2021). Dietary treatment is initiated (Blanco et al., 2017).

23/03/2009

Clinically, the patient is unable to move her upper or lower extremities, and her state of drowsiness persists (12)(13).
The results of the studies show a high concentration of isoleucine, valine in dried blood. Plasma amino acids are indicated, which yield increased values of the amino acids responsible for the EOJA (Lanza & Montalvan, 2017; Salazar, 2021).

07/04/2009

Amino acids continue to increase over time. Mass spectrometry screening results were received where an increase in leucine level of 2563.75 (normal range of 10 – 200), ornithine 954.10 (normal range of 0 – 117) and valine 496.51 (normal range of 43 – 243) was observed. Leucine and valine levels consistent with diagnosis of OOJA (Lanza & Montalvan, 2017; Salazar, 2021).
07/07/2010
Possible liver transplantation is suggested as a treatment option for OJA (Xu et al., 2020), but it is not achieved.

19/08/2010

Treatment with Complex Junior MSD was initiated(10). The patient continues with marked neurological deterioration, does not sit, does not crawl, barely moves hands and feet and responds to visual and auditory stimuli.
26/10/2011
Brain activity is tested, with an index of 30% to 70%. With an age-appropriate diagnosis of brain activity.

16/04/2012

It is continued with Complex junior MSD 30 grams (six measures), plus nutritional supplements (Ugarte et al., 2018; Blanco et al., 2017). Gastric button is placed due to loss of the suction reflex; Physiotherapy is started.
2015: Follow-up by a family doctor begins, in addition to psychotherapy, early stimulation and physiotherapy. Neurological deterioration continues. Disability 98% (Ramírez et al., 2020; Pode et al., 2020).
2016 – 2017: Spaced rehabilitation therapies are maintained. Irritable patient.
In 2018, no rehabilitation therapy is fulfilled.

In 2020, home control visits are maintained, pharmacological treatment is maintained. Maintains muscular hypotonia, epileptic picture, protein-caloric malnutrition, physical disability, infantile cerebral palsy (PCI). The neurological picture worsens markedly (Ramírez et al., 2020; Pode et al., 2020). At the beginning of 2021, the patient died, at the age of 16.

4. Conclusion

The clinical manifestations of the (EOJA) in the first days of life are crucial to make an early diagnosis, being an autosomal recessive hereditary disease, by genetic studies, allows counseling to the family. The diet low in protein and special formula is one of the non-invasive treatments that gradually helps to stop the symptomatic progression of these patients.

Conflict of interest:

The authors declare no conflict of interest.

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