Reporte de 5 casos con enfermedad de jarabe de arce en un periodo de 16 años. Tamiz metabólico ampliado, detección de errores innatos del metabolismo en el hospital para el niño poblano

Report of 5 cases with maple syrup disease over a period of 16 years. extended metabolic screening; comprehensive detection of inborn errors of metabolism in the hospital for child poblano

Juan Manuel Aparicio-Rodríguez
Benemérita Universidad de Puebla
jmapar@prodigy,net.mx

Resumen

Los Errores innatos del metabolismo (EIM) desde 1908 más frecuentes como fenilcetonuria, y galactosemia, así como albinismo, cistinuria y Porfiria y con una incidencia más rara Enfermedad de Orina con Olor de Jarabe de Arce (EOOJA) que se reporta en este estudio. Secundario a una deficiencia del complejo alfa-cetoacido deshidrogenasa (BCKDC), dando una alteración de los aminoácidos leucina, isoleucina y valina, originando productos tóxicos en sangre y orina.

Palabras clave: Errores innatos del metabolismo, jarabe de arce, proteína, enzima.

Abstract

The Inborn errors of metabolism (IEM) since 1908 frequently as phenylketonuria and galactosemia, and albinism, cystinuria and Porphyria and a rare incidence Odor Urine Disease Maple Syrup (MSUD) is reported in this study. Secondary to a deficiency of alpha-ketoacid dehydrogenase complex (BCKDC) giving an alteration of the amino acids leucine, isoleucine and valine, causing toxic blood and urine.

Key words: Inborn errors of metabolism, maple syrup, protein, enzyme.

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Introduction

The Inborn Errors of Metabolism (IEM) 2,3,4,5 are autosomal recessive diseases mostly. The alteration in a gene produces an enzyme defect, which leads to biochemical changes characteristic of every metabolic disease. Most inborn errors of metabolism occurs primarily in children, from the first hours of life, such is the importance of the results of neonatal screening and expanded 6,7,8,9. The symptoms are variable; desnutrición10,11, seizures and psychomotor or mental retardation. The disease maple syrup (MSUD) is caused by alterations in 3 essential amino acids, which means that the body does not produce and need to purchase food, leucine, isoleucine and valine, which damages the central nervous system and most tissues in general Table 2 the importance of the alteration of the three essential amino acids lies in the different functions in humans 12,13,14,15, 16.

Valine 18, Figure 1 is part of the genetic code and is found in high concentration in the muscles is very important for its function and keep the body in good condition.
Leucine 18, Figure 2 is the most abundant amino acid of the three branched chain amino acids (valine and isoleucine) and are used only during exercise, besides being a third of the protein in muscle tissue. Also part of the genetic code and is involved in the formation and repair of muscle tissue; helps regulate blood sugar levels. This amino acid is altered during aging, which causes an imbalance in the production of proteins.

Regarding the Isoleucine 18, Figure 3, its structure is similar to valine and leucine amino acids and belongs to the BCAA. It is very important in fevers, trauma or stress. It is essential for human nutrition, because it regulates blood sugar levels, aids in muscle repair and is required for the formation of hemoglobin. After exercise helps repair muscles, aids in blood clotting and after metabolism, can be converted into lipids or carbohydrates.

Some EIM, besides endangering the lives of patients, may be the wrong musculoskeletal system including craniofacial development, which is important to be considered within the general consultation pediatrics and pediatric dentistry.

Materials and methods.

Metabolic studies in 2370 patients were performed with different EIM. 5 of them with maple syrup disease, including patient study of 14 days of life. The studies were carried out taking into account national and international parameters. An expanded metabolic profile Figure 4, qualitative and quantitative study of blood and urine to detect alterations in amino acids, organic acids and acylcarnitines was collected. The ages of the patients ranged from newborn rated 5 years old.

RESULTS.

The metabolic screening in 2370 patients was conducted over a period of 16 years. A total of 102 patients had metabolic abnormalities (4.3%) Table 1, grouped into four categories; 15 defective in mucopolysaccharides, 43 carb and 2 mitochondrial diseases 42 had some disorder in amino acid 5 with Maple Syrup, of whom died, as did the patient 24 days presented in this study, which began with difficulty their diet with high malnutrition and Figure 5 gastrostomy performed to ensure their nutritional intake, also present problems breathing so an operator coupled with serious deterioration in their neurological status with constant monitoring respirator Figure 6, dehydration and infection is widespread use in the dermis and organic septicemia Figures 7, 8.

DISCUSSION.

Some of the patients were treated in a timely manner with development until now normal, however some of them as in the case of the two patients with hyperlysinemia Table 1 were hospitalized in a coma at the intensive care unit without a definitive diagnosis metabolic screening to be performed, with poor prognosis. Patients with maple syrup disease had a progressive deterioration all, although the nutritional management was completely changed by the Department of Nutrition. This deterioration is caused by a genetic defect in the metabolism of amino acid of these three essential importance for living; 12,13,14,15,16,17

BCAA leucine, isoleucine and valine accumulation of these chemicals in the blood. In its most severe form, MSUD can damage the brain by severe sepsis as in the case of the patient with severe vascular problems and discoloration of the dermis Figures 7.8, coupled with periods of fever or lack of food a long time, and this patient was used gastrostomy Figure 5, as nutritional support. This series of functional and metabolic changes are secondary to deficiency of essential amino acids, since as mentioned above valine 18, Figure 1 is part of the genetic code and is found in high concentration in the muscles is very important for its function and thus maintain in good condition the body and must be consumed in animal protein red meat, poultry, eggs, dairy and fish-legumes and nuts and a good combination of food is needed to get the essential amino acids and maintain in good state agency.

Leucine 18, Figure 2 is the most abundant amino acid of the three branched chain amino acids (valine and isoleucine) and are used only during exercise, besides being a third of the protein in muscle tissue. Also part of the genetic code and is involved in the formation and repair of muscle tissue; helps regulate blood sugar levels. This amino acid is altered during aging, which causes an imbalance in the production of proteins, a fact that causes the loss of muscle mass. It has a beneficial effect on post-surgical patients. Besides protecting the muscles, acts as fuel in high stress training. Foods that provide leucine are animal proteins such as meat, fish, eggs and milk.

Regarding the Isoleucine 18, Figure 3, its structure is similar to valine and leucine amino acids and belongs to the BCAA. It is very important in fevers, trauma or stress. It is essential for human nutrition, because it regulates blood sugar levels, aids in muscle repair and is required for the formation of hemoglobin. After exercise helps repair muscles, aids in blood clotting and after metabolism, can be converted into lipids or carbohydrates. It is one of the eight essential amino acids to the body, is part of the genetic code and an integral part of muscle tissue. Isoleucine needs humans, must be ingested through the diet and are found in animal proteins such as meat, fish, dairy and eggs and vegetable proteins such as beans, grains and some nuts. A low protein diet with isoleucine deficiency causes headaches, depression, fatigue and irritability.

Early detection of EIM 1.2, 3,4,5 in pediatric patients is very important as well as the initial treatment of an EIM As in the case of the 5 patients that have evolved in a torpid form a

fatal outcome. Figures 7.8 Which is important to reflect on the importance of 6,7,9 neonatal metabolic screening should be mandatory in every newborn patient. This type of EIM is considered an emergency and pediatric neonatología8 to provide the patient an early, timely treatment and thus ensure a better quality of life.

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FIGURES AND TABLES

Figure 1 Valine is part of the genetic code and is found in high concentration in the muscles is very important for its function and keep the body in good condition. http://es.wikipedia.org/wiki/Valina.

Figure 2 Leucine is part of the genetic code and is involved in the formation and repair of muscle tissue; helps regulate blood sugar levels. This amino acid is altered during aging, which causes an imbalance in the production of proteins, a fact that causes the loss of muscle mass. http://es.wikipedia.org/wiki/Leucina.

Figure 3. Isoleucine is part of the genetic code and an integral part of muscle tissue, belongs to the BCAA. It is very important in fevers, trauma or stress. It is essential for human nutrition, because it regulates blood sugar levels, aids in muscle repair and is required for the formation of hemoglobin. http://es.wikipedia.org/wiki/Isoleucina.

Figure 4 Metabolic Sieve gel electrophoresis performed in a patient with maple syrup showing positive patterns for this disease.

Figure 5. lack of swallowing the patient start with malnutrition from lack of food for a long time, as in this patient gastrostomy was used as nutritional support.

Figure 6 The patient had respiratory problems since its automatic hospitalization coupled with what a serious deterioration in his neurological status with constant monitoring respirator use.

Figure 7 In its most severe form, MSUD can damage the brain by severe sepsis as in the case of the patient with severe problems in the vascularization and dehydration and generalized infection in the dermis coloring with ectodermal changes with periods of relapsing fever and generalized sepsis.

Figure 8 The patient had severe problems vascularization starting in upper limbs and discoloration of the dermis with organ failure.

Table 1 Metabolic Screen in 2370 patients (1994-2010) with a total of 102 patients with abnormal (4.3%). Five of them with maple syrup disease.

Table 2 Some of the key EIM found in the Hospital for Poblano child, clinical and biochemical abnormalities, including Maple Syrup Disease reported in this study.

TABLE 1.

Amino Acids	MPS	Carbohydrates	mitocondriales
42	**15**	**43**	**2**
7 cistinuria	8 Hurler	1 Gucogenosis	1 acetil COA tiolasa mitocondrial
8 fenilcetonuria	2 Hunter	9 Galactosemia	1 cadena respiratoria mitocondrial
4 s de fanconi	5 Morquio	33Glucosuria	
4 tirosinemia			
2 hiperlisinemia			
5 jarabe de Arce			
1 argininemia			
1 hiperalaninemia			
10 homocistinuria.			

TABLE 2. Disease symptoms Major Alteration Biochemistry

Alterations of amino acids:		
Cistinuria	**Kidney stones. Increased urinary excretion of cystine, lysine, arginine and ornithine. Defienciente and buccal bone calcification.**	**Decreased tubular reabsorption of dibasic amino acids (lysine, arginine, ornithine) and cystine**
Fenilcetonuria	**Vomiting, mental retardation, hipopimentación, dental crowding organs.**	**Enzyme phenylalanine Rivosiltransferasa**
Síndrome de Fanconi	**Stunting. Skeletal and dental deformities fever, dehydration, acidosis. In adults: glycosuria, aminoaciduria, hypokalemia, uremia**	**Impaired renal transport mechanism of glucose, phosphate, amino acids, less marked for water and potassium**

	and bleeding gums.	
Tirosinemia	**Urinary excretion of acid p-hydroxyphenylpyruvic**	**Deficiency hydroxyphenylpyruvic p-oxidase**
Hiperlisinemia	**Neurological damage, seizures, vomiting, coma and caries.**	**Increased amino acid lysine.**
Jarabe de Arce	**The urine has a smell like syrup Maple, vomiting, refusal to eat a potentially lethal neurological damage.**	**Branched chain amino acids valine, leucine and isoleucine.**
Hiperglicinemia	**A severe psychomotor mental retardation, seizures and drowsiness that accumulates in biological fluids especially in the CSF. Little wear of tooth organs.**	**Due to a congenital metabolic deficiency glycine in the oxidation of glycine by a D-aminooxidase causes the glyoxylate.**
Homocistinuria	**Mental retardation, lens dislocation, skeletal abnormalities, and a tendency to thromboembolic episodes.**	**Deficiency synthase beta cistionina above.**

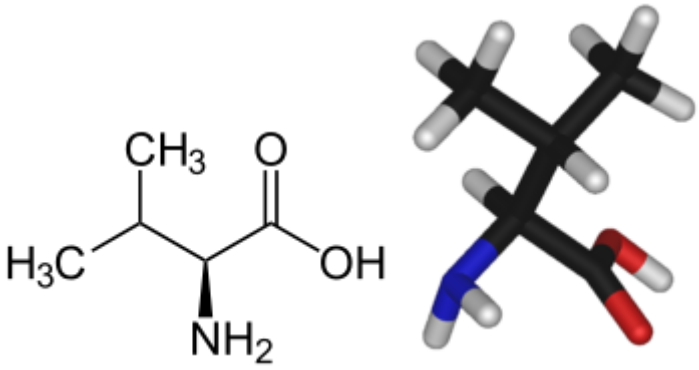

FIGURE 1. Valina.

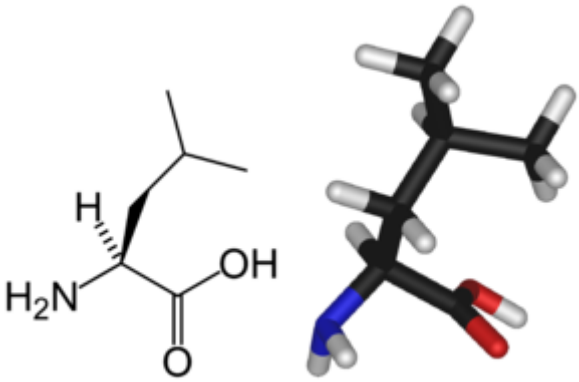

FIGURE 2. Leucina.

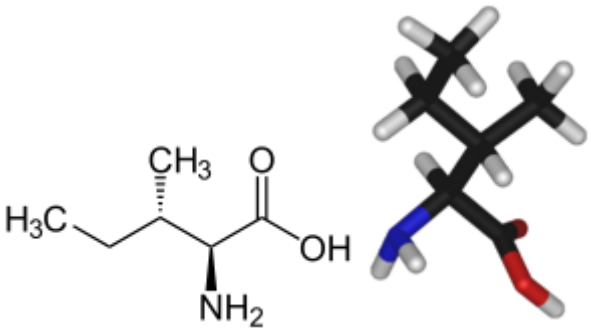

FIGURE 3. Isoleucina.

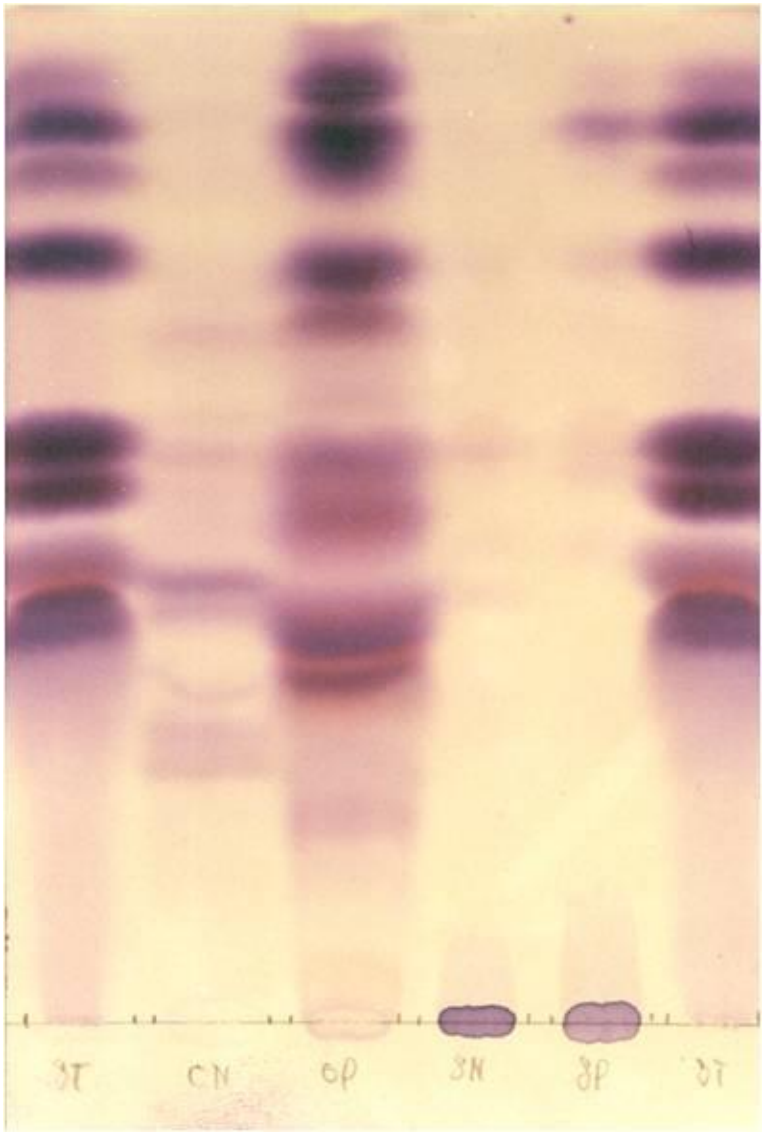

FIGURE 4.

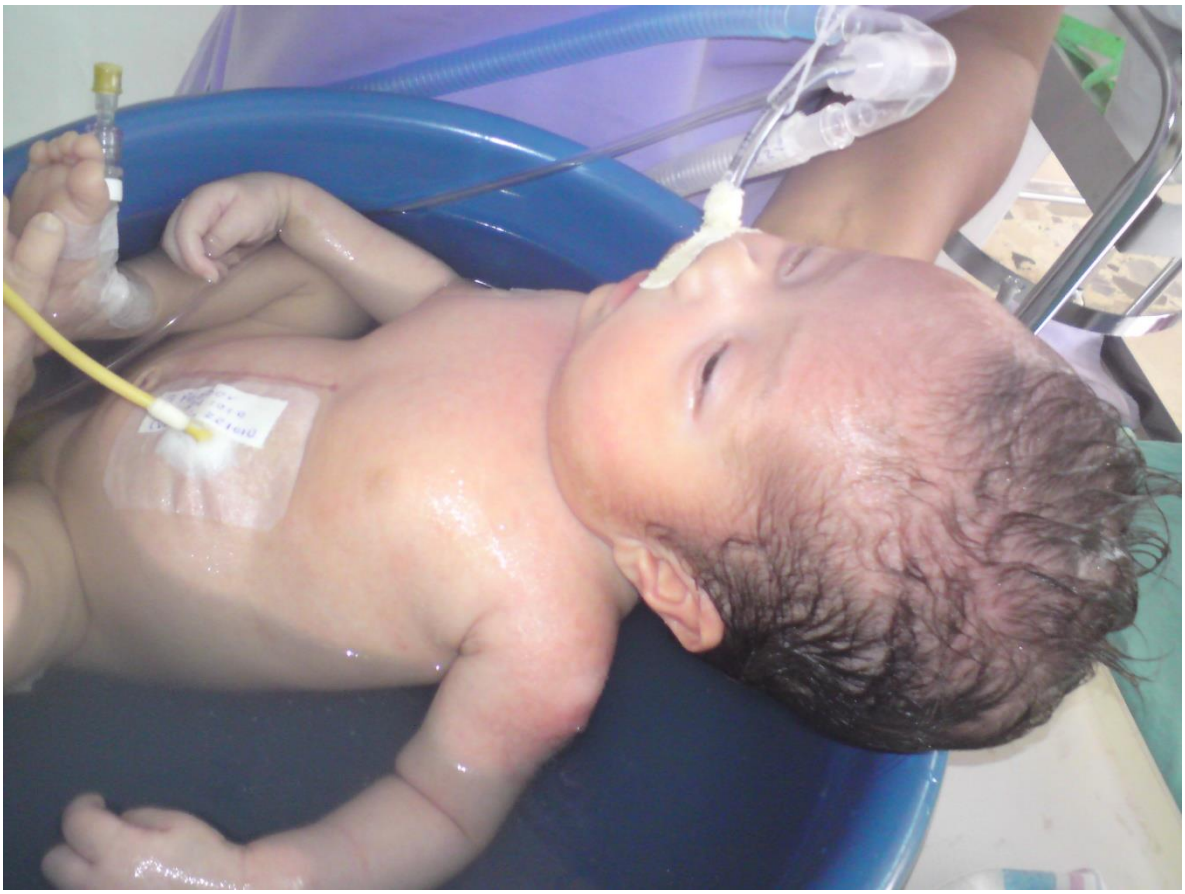

FIGURE 5.

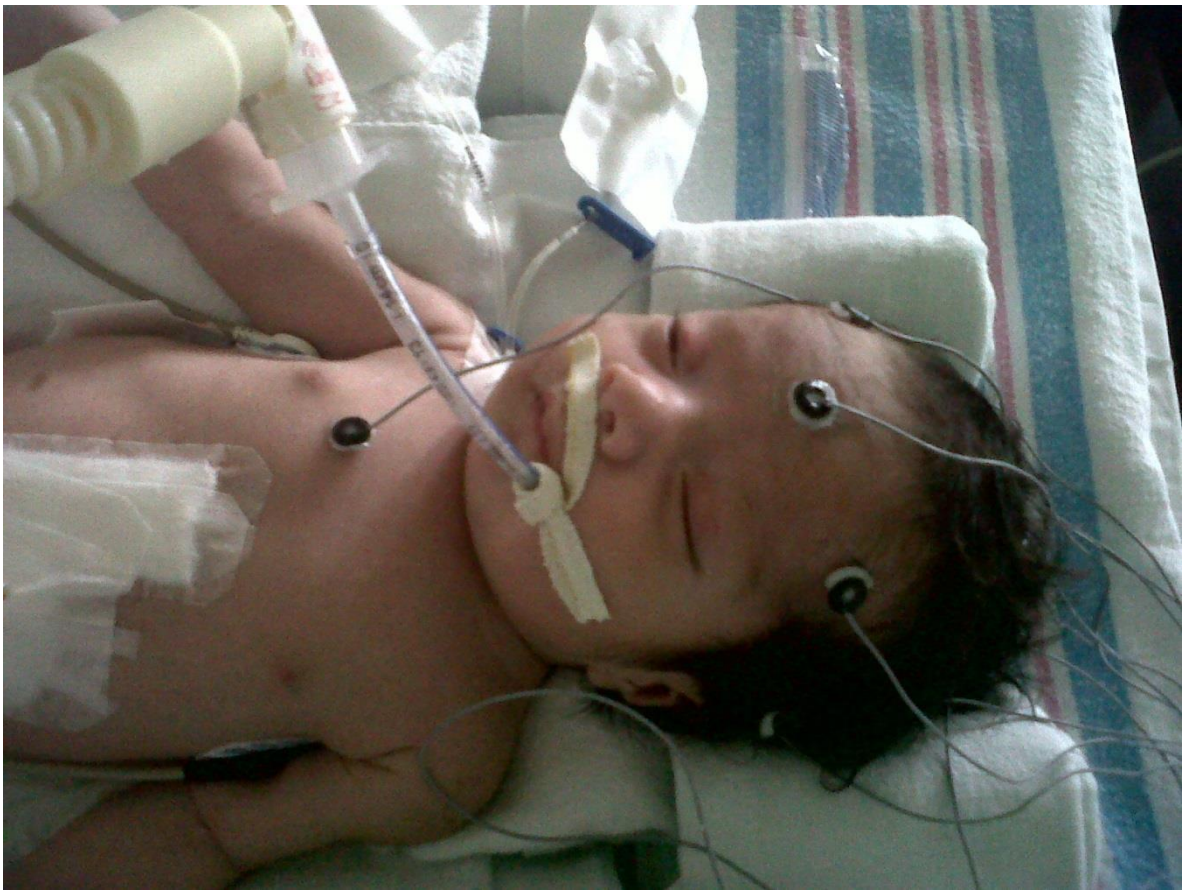

FIGURE 6.

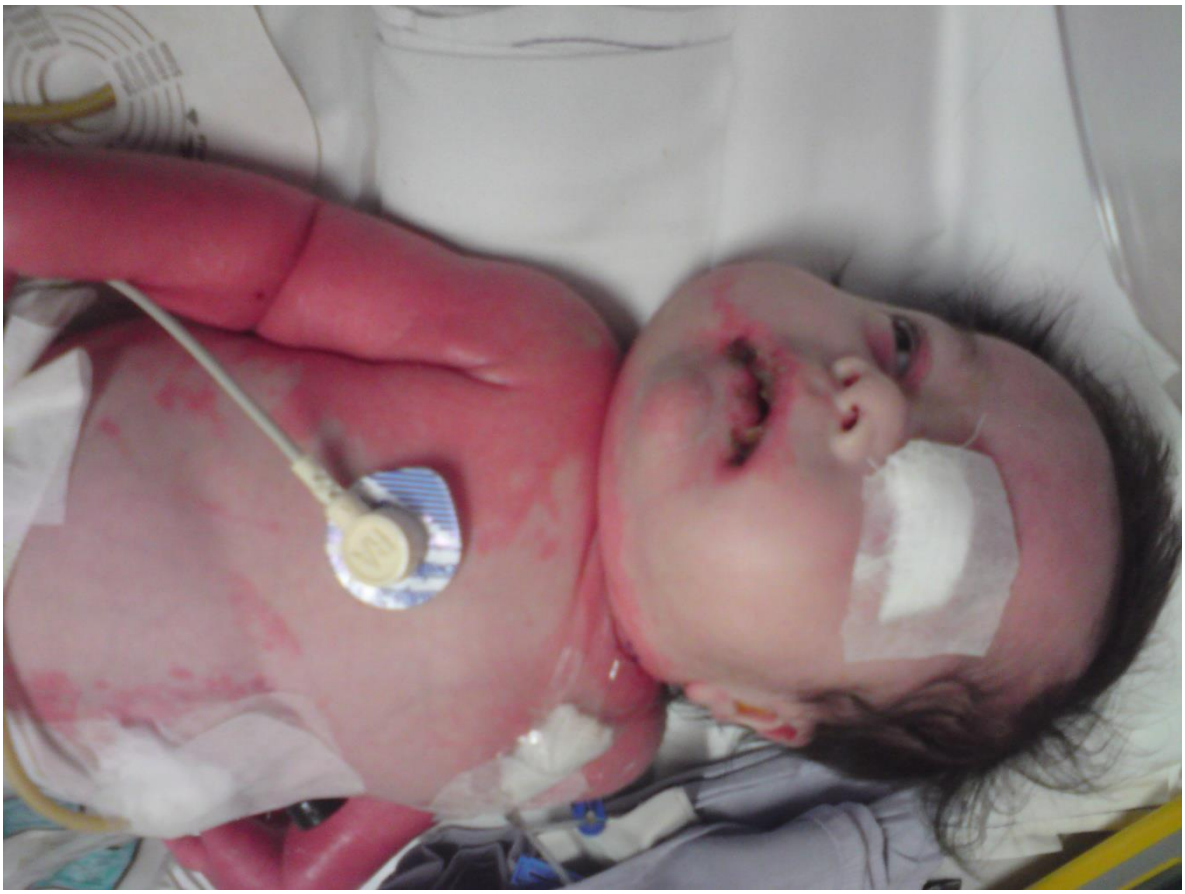

FIGURE 7.

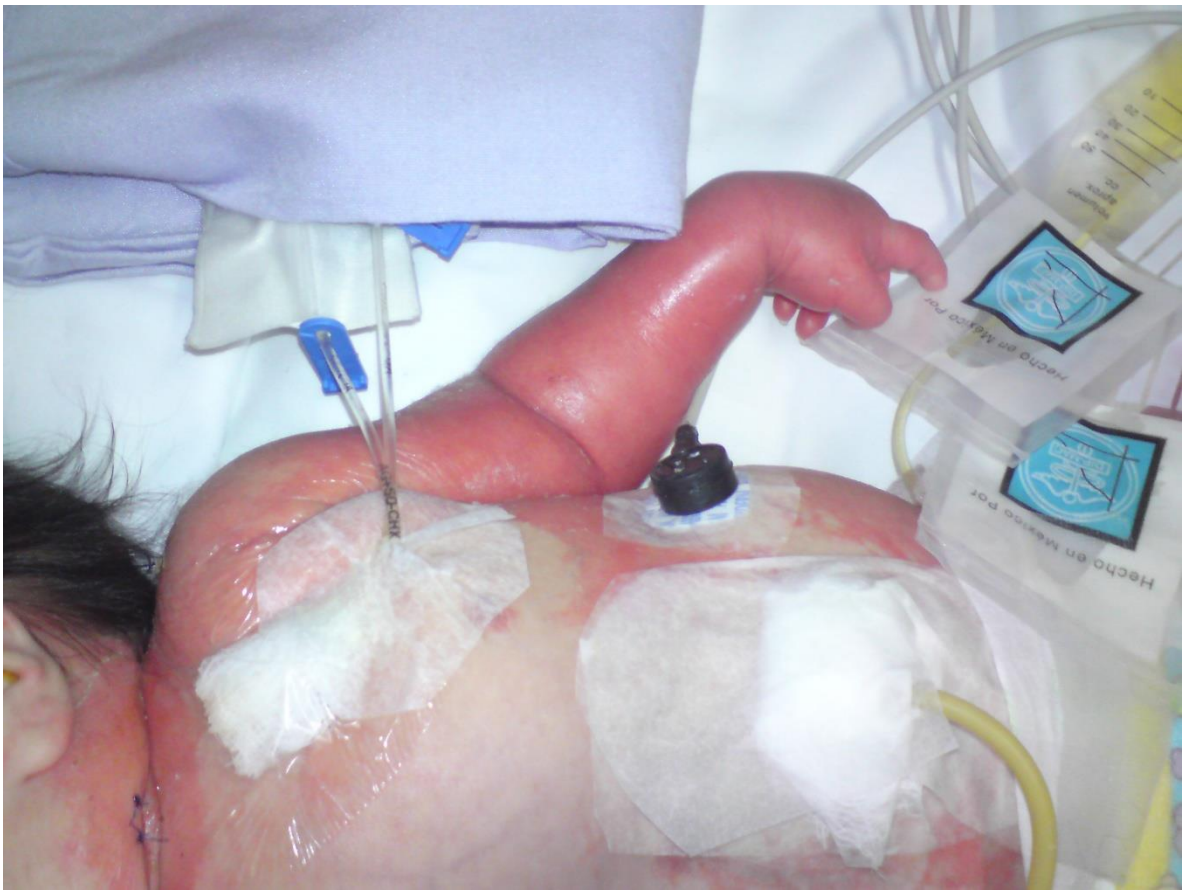

FIGURE 8.