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CONGENITAL HYPERINSULINISM – CASE REPORT

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Abstract: **Goal:** To describe the symptoms, diagnostic investigation and clinical management of a case of persistent neonatal hypoglycemia in Manaus, Amazonas. **Methods:** The proposed study is an observational and descriptive case report, developed in a private hospital in Manaus, started in October 2022. The instruments used for data collection were anamnesis and physical examination in the period in which the patient The patient remained hospitalized in the aforementioned hospital unit - both in the neonatal intensive care unit (neonatal ICU) and in the Clinical Nursing, through the review of the medical record. The observation and discussion of the case in the multidisciplinary meetings of the service were also part of the data acquisition. The completion of the information collection occurred through the acquisition of secondary data with continuous review of the electronic medical record and photographic record of the diagnostic methods to which the patient was submitted and bibliographic review. All the records and information obtained were duly explained and requested from the patient's mother, who by mutual agreement and without profit, signed an informed consent (ICF). Experience report: Reinforce, through a case report, the importance of clinical manifestations and complementary tests in the investigation of neonatal hypoglycemia in a child from the Western Amazon and describe the treatment established and the recommended clinical follow-up. Conclusion: Neonatal hypoglycemia can have a multifactorial origin and, if it is not properly identified and treated, it can have consequences on the child's neuropsychomotor development. Early diagnosis and proper management are essential, since they improve survival and avoid sequelae to the patient.

Keywords: Neonatal hypoglycemia, Congenital hyperinsulinism, Pediatrics.

INTRODUCTION

Hyperinsulinemic hypoglycemia (HH) is characterized by a group of clinical, morphological and genetic changes that occur with hypoglycemia, which is attributed to inadequate and unregulated insulin secretion by pancreatic β cells. It is the most frequent cause of persistent hypoglycemia in newborns (NB) and infants. Patients with HH are at significantly greater risk of permanent brain damage secondary to the metabolic actions of insulin (DEMIRBILEK et al., 2017; DEMIRBILEK and HUSSAIN, 2017).

Insulin acts by transporting glucose to tissues and inhibits endogenous glucose production by inhibiting glycolysis and gluconeogenesis. Consequently, this leads to a reduction in serum glucose levels. It also acts by inhibiting the release of fatty acids and the production of ketone bodies, which are the main alternative sources of energy for neurons in situations of hypoglycemia. Thus, it is essential that the diagnosis and proper treatment of this condition take place as soon as possible, in order to avoid the neurological complications that are potentially associated (DEMIRBILEK et al., 2017).

Neonatal hypoglycemia is classified into two groups: transient (lasting from a few hours to 3 days) and persistent (lasting longer than 3 days). In some situations, such as SGA NB (small for gestational age) or LGA (large for gestational age), congenital heart disease, polycythemia, sepsis, low food acceptance, transient hypoglycemia can last for a few weeks, being confused with persistent hypoglycemia (SBP, 2022; LIBERATORE JUNIOR and MARTINELLI JUNIOR, 2011).

The clinical presentation of HH is usually variable, from mild and nonspecific symptoms of hypoglycemia (lethargy, irritability, hyporexia) to severe symptoms (apnea, convulsions, coma). Other risk factors are perinatal asphyxia, intrauterine growth

restriction, maternal diabetes mellitus, genetic syndromes (Beckwith-Wiedemann syndrome) or metabolic conditions (congenital disorders of DCG glycosylation) (DEMIRBILEK et al., 2017).

METHODS

The proposed study is a case report, observational and descriptive, developed at Hospital Samel, started in October 2022. The instruments used to collect information were anamnesis and physical examination during the period in which the patient remained hospitalized. at Hospital Samel, in Manaus, Amazonas - both in the neonatal intensive care unit (neonatal ICU) and in the pediatric ward, through review of medical records. Observation and discussion of the case in the service's multidisciplinary meetings were also part of data acquisition. The completion of information collection was due to the acquisition of secondary data with continuous review of the electronic medical record and photographic record of the diagnostic methods to which the patient was submitted and literature review. All records and information obtained were duly explained and requested from the patient's mother, who by mutual agreement and non-profit signed a free and informed consent form (TCLE).

CASE REPORT

Patient H.A.S.V, 3 days old, female, born and raised in Manaus (Amazonas), admitted to a private hospital on May 10, 2022, with maternal report that since discharge with 48 hours of life, the daughter had had episodes frequent episodes of regurgitation followed by choking, drowsiness, difficulty breastfeeding, in addition to low colostrum production by the mother. Clinical evaluation was performed with anamnesis and physical examination, in addition to initial complementary tests. On physical examination, the child was in regular general condition, atypical facial features, hypoactive, reactive to handling, hydrated, flushed, eupneic, afebrile, without lymph node enlargement, without cardiovascular or pulmonary alterations, physical examination of the abdomen without alterations, typical female genitalia. Initial capillary blood glucose was 35mg/dL, confirmed by hypoglycemia with plasma glucose of 30mg/dL. Other laboratory tests also showed hyperbilirubinemia (Table 1). Chest X-ray (05/10/2022) without alterations. Negative admission blood culture.

HEMOGLOBIN	20,8 g/dL
HEMATOCRIT	58,1%
LEUKOCYTES	13.490 µL
SEGMENTED	65,1%
LYMPHOCYTES	24,9%
STICKS	0%
PLATELETS	172.000 µL
SODIUM	134 mmol/L
POTASSIUM	5,3 mmol/L
GLUCOSE	30 mg/dL
TOTAL BILIRUBIN	18 mg/dL
RETICULOCYTES	0,2%
C-REACTIVE PROTEIN	1,0 mg/dL

TABLE 1 - ADMISSION LABORATORY EXAMINATIONS (05/10/2022).

Source: Electronic medical record (Tasy System).

After initial measures of glucose correction and hospitalization, the patient maintained episodes of hypoglycemia (plasma glucose 28 mg/dL), even receiving diet through an orogastric tube on a regular basis, in addition to presenting hypoactivity, acrocyanosis, dehydration, apneas and drops in oxygen saturation. He was transferred to the neonatal ICU for better clinical support and diagnostic

investigation.

In the past pathological history, the mother denied previous surgeries, hospitalizations and allergies. Daughter of healthy parents, no consanguinity report, complete vaccination history. In the neonatal history, the patient was classified as full-term NB (FTN), gestational age 39 weeks, adequate for gestational age (AGA), born by emergency cesarean section due to ruptured water for more than 24 hours and induction failure. Birth weight: 3240 grams, length 50 cm, head circumference 32 cm; maternal age 29 years, mother G2P0A1, mother's blood type O+, NB blood type A+, 12 prenatal consultations performed, pregnancy uneventful, no report of urinary tract infection or gestational diabetes, serology for TORCHS negative, culture for negative GBS (4/6/22). She was born well, cried soon after birth, amniotic fluid clear and without lumps, Apgar score 9/10/10, no need for resuscitation maneuvers. After the birth, she was sent to rooming-in, where she underwent the neonatal screening and infectious risk exams, all without alterations. Clinically, the patient had difficulty breastfeeding; she was discharged after 48 hours of life with guidance and supplementation with artificial milk formula if necessary.

Her hospitalization in the neonatal ICU lasted 54 days, where she maintained frequent episodes of hypoglycemia. During some episodes of hypoglycemia, she also developed convulsive crises. Diagnosed with late-onset sepsis, she received culture-guided antibiotic therapy, progressing with improvement. After that, she developed respiratory distress requiring invasive ventilatory support with orotracheal intubation for one day (05/21 to 05/22).

Diagnostic investigation was initiated at 10 days of life due to persistent hypoglycemia, even using intravenous glucose with high VIG (glucose infusion rate), in addition to diet. With the main risk factors for hypoglycemia ruled out, the hypothesis of congenital hyperinsulinism was suggested; critical sample collection was then scheduled during a hypoglycemic event, with plasma glucose below 50 mg/dL (gasometry, lactate, insulin, c-peptide, beta hydroxybutyrate, free fatty acids, acylcarnitine profile, ammonia, amino acid profile, cortisol, GH, urine summary, TGO, TGP, GGT, alkaline phosphatase, urea, creatinine, uric acid) in addition to genetic panel examination. During hospitalization, 2 insulin quantification tests were performed during episodes of hypoglycemia, with the following values: 1st sample (05/20/22): 0.9 microUI/mL; 2nd sample (01/06/22): 1.4 microUI/mL, values that confirm the hypothesis of congenital hyperinsulinism. Other tests performed on the critical sample with normal results.

During hospitalization in the neonatal ICU, other tests were performed, such as: cerebrospinal fluid (05/21/22): normal. Echocardiogram (05/21/22): patent foramen ovale, slight turbulence of the pulmonary and aortic trunk. Echocardiogram (06/21/22): presence of patent foramen ovale without hemodynamic repercussion, persistence of ductus arteriosus in closure, mild pulmonary trunk stenosis, without other alterations. Transfontanel ultrasonography (05/23/22): normal. Viral panel (5/24/22): negative. Electroencephalogram (05/30/22): normal. Full abdomen ultrasound (06/21/22): normal. Ocular fundoscopy (06/29/22): normal.

At 27 days of life, the patient continued to have recurrent episodes of hypoglycemia, even when using high VIG; she was awaiting genetic panel results for treatable diseases. Treatment with diazoxide was started on 06/16/22, initially at a dose of 5 mg/kg/day, but with no satisfactory response. Progressively adjusted dose and dosages up to 20 mg/kg/day, but the patient still had frequent

episodes of hypoglycemia, requiring high levels of intravenous glucose for correction. Concomitant with the use of diazoxide, she started hydrochlorothiazide at a dose of 1 mg / kg / day every 12 hours. After clinical stabilization, the infant was discharged from the ICU on 07/02/22, at 1 month and 27 days of life, using diazoxide at a dose of 25 mg/ kg/day and intravenous hydration with VIG 7.0, in addition to glucagon for rescue from hypoglycemia.

On 07/04/22, 2 days after discharge from the ICU, the infant presents a new clinical instability and evolves with severe hypoglycemia, requiring readmission to the ICU. He continued with the need for intravenous hydration with high VIG (VIG 7), frequent corrections with glucose boluses and diet volume adjustment (initiated soy-based formula on 07/03/22). During this period, a therapeutic test with glucagon had been performed, which responded well with increased blood glucose. The child remained stable, without signs of infection, on room air, evolving with clinical improvement, being discharged from the ICU on 07/18/22 to maintain follow-up in the pediatric ward.

During hospitalization in a pediatric ward, the result of the molecular neonatal screening (cheek test) collected on 06/24/22 was received, with a normal result. The infant remained stable, eupneic, hydrated, tolerating an oral diet with soy formula, using diazoxide at the maximum recommended dose and intravenous hydration with moderate VIG (6.5 mg/kg/min), being monitored by a multidisciplinary team (pediatrics, endocrinopediatrics, medical genetics, physiotherapy, nursing, nutrition). Even with diazoxide at the maximum dose, the infant did not have satisfactory blood glucose levels, tending to frequent hypoglycemic episodes. Decided to start Octreotide on 07/30/22, second-line drug in the treatment of hyperinsulinism, in continuous intravenous infusion with variable dose between 0.08-0.3 mcg/kg/h, with withdrawal of parenteral glucose on 31/ 07/22. Medication was well tolerated by the patient, subsequently Octreotide was adjusted for subcutaneous injection at a dose of 2 mcg/kg/day divided every 6 hours. The infant evolved with good glycemic control, with satisfactory development and growth, receiving an oral diet with soy formula 60 ml every 3 hours and breast milk on demand.

On 08/22/22, the infant developed acutely (3 days) with focal myoclonic paroxysms in the left upper limb lasting less than 1 minute, without Jacksonian gait, without change in interaction with the environment, without fever, feeding difficulties or encephalopathy, which occurred even with the use of high-dose phenobarbital. An electroencephalogram was performed (08/24/22): disorganized baseline activity, without focal paroxysms. Head CT (08/26/22): within normal limits. Associated with levetiracetam initially at a dose of 7 mg/ kg every 12 hours, then adjusted to 10 mg/kg every 12 hours and subsequently withdrawn from phenobarbital. After these adjustments, the patient evolved without new episodes of myoclonus, maintaining stable blood glucose levels.

The infant evolved satisfactorily from an endocrinological point of view, with a favorable response in glycemic control, without new hypoglycemic episodes, seizures or clinical instability after starting Octreotide. An intravenous prescription was initially made, later adjusted to the subcutaneous route, with transition to the intramuscular route to assess the possibility of hospital discharge and outpatient follow-up. Started on 08/28/22 Octreotide Lar Acetate (Sandostatin Lar ampoule 20 mg/2 ml) intramuscularly, after issuing medical reports to the Central de Medicamentos do Amazonas (CEMA)

requesting the medication. Gradual weaning of the subcutaneous dose was performed and transition to the application of Octreotide at a dose of 0.5 mg/kg intramuscularly every 28 days, with normalization of capillary glycemia. He was discharged from the hospital on 09/10/22 with prescriptions, guidelines and referrals to a pediatrician, pediatric endocrinologist, neuropediatrician and physiotherapist.

DISCUSSION

Neonatal hypoglycemia is an individualized condition where the plasma glucose concentration is low enough to determine signs and/or symptoms of cerebral dysfunction. In symptomatic neonates, hypoglycemia is defined according to limits that may vary between different guidelines and that still do not have a consensus. In newborns up to 48 hours of life, it is determined by blood glucose below 47 mg/dl according to the American Academy of Pediatrics (AAP) and 50 mg/dl according to the Pediatric Endocrine Society (PES); in newborns with more than 48 hours of life, the results are conflicting, although values below 60 mg/dl are accepted; in newborns with more than 72 hours of life, values below 70 mg/dl according to the AAP and PES (SBP, 2022).

Newborns with symptomatic hypoglycemia may evolve with clinical findings ranging from mild to severe. Among the mild ones, abnormal crying, agitation, tremors, irritability, pallor, cyanosis, hypothermia or diaphoresis are observed (SBP, 2022). Severe symptoms include lethargy, respiratory failure, apnea, seizures, hemodynamic instability, cardiorespiratory arrest and coma (DEMIRBILEK et al., 2017; SBP, 2022). The patient presented in this study presents severe symptoms of the disease from the first moment, in addition to poor response to corrections with intravenous glucose.

There are several factors that can cause hypoglycemia in the neonatal period, and these can be divided into conditions related to the mother or the newborn (SBP, 2022; LIBERATORE JUNIOR and MARTINELLI JUNIOR, 2011). Among maternal causes, the following stand out: gestational diabetes, preeclampsia, use of beta-blockers, use of tocolytics or oral antidiabetics by the pregnant woman, family history of neonatal hypoglycemia, report of previous macrosomic NB (SBP, 2022). Among the causes related to the NB, the following can be mentioned: prematurity, SGA or LGA NB, intrauterine growth retardation (IUGR), children of diabetic mothers, perinatal asphyxia, genetic syndromes, among others (SBP, 2022).

During pregnancy, the fetus continuously receives glucose across the placenta through facilitated diffusion, a transporter-mediated process from the maternal circulation. In labor and delivery, secretion of glucocorticoids and catecholamines elevate fetal blood glucose concentrations. Although the supply of glucose is essential for survival, the total amount of glucose in the bloodstream can provide energy for a short period of time to the brain; however, this organ demands a constant supply of glucose, since it cannot synthesize or store it for more than a few minutes. Thus, the regulation of serum glucose concentrations is critical for survival after birth. Several metabolic pathways are involved in this process (glycogenolysis, gluconeogenesis, oxidation of mitochondrial fatty acids and ketogenesis), in addition to the participation of different hormones (glucagon, epinephrine, cortisol and growth hormone) (SBP, 2022).

In the first 48 postnatal hours, many neonates may develop hypoglycemia; however, it is due to the process of adapting to extrauterine life (SBP, 2022; RODRIGUES, COLLI and CZEPIELEWSKI, 2007). Clinically significant neonatal hypoglycemia reflects

an imbalance between the supply and use of glucose and other alternative fuels, and can result from numerous inefficient regulatory mechanisms (SBP, 2022).

Neonatal hypoglycemia is classified into 2 groups: transient (lasting from hours to 3 days) and persistent (lasting longer than 3 days) (SBP, 2022; LIBERATORE JUNIOR and MARTINELLI JUNIOR, 2011). About 50% of cases of neonatal hypoglycemia are classified as transient and asymptomatic, 15% transient symptomatic, 35% associated with other diseases and only 2% are persistent or recurrent (SBP, 2022).

Congenital hyperinsulinism (CH) is a rare disease, characterized by a group of clinical, genetic and morphological disorders that occur with inappropriate insulin secretion by pancreatic β cells (DEMIRBILEK et al., 2017; ROŽENKOVÁ et al., 2015); affects about 1 in every 30,000 to 50,000 live births (SBP, 2022), but in some isolated communities where founder mutations have been reported, and in populations with high rates of consanguinity, the incidence can increase to approximately 1 in every 3,000 live births (HEWAT, JOHNSON and FLANAGAN, 2022). It is the most common cause of persistent and severe neonatal hypoglycemia in early childhood (BANERJEE et al., 2018; SBP, 2022). Hypoglycemia can start in the neonatal period or during the first year of life; a finding that suggests the diagnosis is the need for high glucose infusion rates (SBP, 2022). It is a serious situation, with high morbidity and mortality and a significant risk of hypoglycemic seizures that can cause irreversible brain damage (BANERJEE et al., 2018; SBP, 2022).

Patients with CH may have a variable clinical phenotype, ranging from asymptomatic hypoglycemia, mild disease responsive to drugs or, in severe forms, unresponsive to pharmacological therapy and requiring surgical intervention (DEMIRBILEK et al., 2017). Regarding histology, CH can be classified into 3 subgroups: diffuse, focal and atypical (DEMIRBILEK et al., 2017). Differentiation of the histological subtype can determine therapeutic success, since partial (in focal forms) or total (diffuse or atypical forms) pancreatectomy may be required.

The diagnosis is made through clinical analysis (signs and symptoms presented by the patient) associated with complementary tests that detect inappropriate insulin secretion and hypoglycemia (SOUSA, 2020). Such tests include serum glucose dosage, gasometry, insulin, C-peptide, lactate, beta-hydroxybutyrate, free fatty acids, acylcarnitine profile, ammonia, amino acids and type 1 urine, requiring the collection of these tests in the presence of hypoglycemia (critical sample), (SBP, 2022; SOUSA, 2020).

Several mutations related to CH are known, so far, they have been described in 9 different genes: inactivating mutations of the ABCC8 and KCNJ11 genes on chromosome 11p15.1 (ROSENFELD et al., 2019); activating mutations of the GCK, GLUD1 and HADH genes (SHAD); SLC16A1 (MCT-1) mutations; UCP2 mutations; mutations of the HNF4A and HNF1A genes, congenital disorders of glycosylation and type 1 tyrosinemia (DEMIRBILEK et al., 2017; SBP, 2022). It may also be related to genetic syndromes: Beckwith-Wiedemann syndrome (SBW), Sotos, Perlman, Simpson-Golabi-Behmel, Patau, Costello, Usher, Timothy, Kabuki, Trisomy 13, Turner mosaic, among others (SBP, 202; ROSENFELD et al., 2019; LIBERATORE JUNIOR and MARTINELLI JUNIOR, 2011). Mutations of the ABCC8 and KCNJ11 genes are responsible for about 50% of cases of permanent CH, and of these about 80% do not respond to treatment with diazoxide (SBP, 2022).

The goal of initial treatment in CH is to

stabilize plasma glucose levels and achieve normoglycemia. This can be achieved by administering additional dextrose, but administration of oral dextrose is rarely effective in preventing severe hypoglycaemia; in most cases it is necessary to administer high levels of dextrose intravenously through a central venous catheter. Early therapy with glucagon was also beneficial, as it could control blood glucose and reduce dependence on large volumes of liquid, reducing fluid overload and complications such as pulmonary edema, heart failure and hydroelectrolytic disorders. Glucagon can be administered intramuscularly in solutions diluted with saline solution or intravenously associated with dextrose when continuously needed. These infusions are carried out in the short term, in doses ranging between 2 and 20 mcg/kg/h to reach normoglycemia, while waiting for the start of specific treatment, such as diazoxide (BANERJEE et al., 2018).

Diazoxide is a Katp channel agonist, being the first choice for the definitive treatment of patients with CH (BANERJEE et al., 2018; DEMIRBILEK and HUSSAIN, 2017). Diazoxide is usually effective in all forms of CH where the Katp channels are intact, but children with severe, neonatal forms, recessive or even dominant mutations of the Katp channel (mutations in the ABCC8/KCNJ11 genes) do not respond to treatment (DEMIRBILEK et al., 2017; BANERJEE et al., 2018; DEMIRBILEK and HUSSAIN, 2017). Diazoxide works by binding to the SUR1 subunit of the Katp channel. Therefore, it requires a functionally intact Katp channel. The response to diazoxide has been important for molecular genetic analysis, differential diagnosis and CH management strategies (DEMIRBILEK and HUSSAIN, 2017).

The initial dose of diazoxide is 5 mg/kg/day, in 3 divided doses that can be increased to a maximum dose of 15-20 mg/kg/day. Drug response criteria include age-adjusted fasting tolerance, ability to maintain normoglycemia, and normal eating plan. Diazoxide has a number of side effects that require careful monitoring; in the acute phase, the most serious side effect that limits the use of the medication is water retention, heart failure and hydroelectrolytic imbalance. This side effect can be circumvented with the use of thiazide diuretics (hydrochlorothiazide) in addition to restricting fluid intake in the neonatal period to up to 150 ml/kg/day, aiming to reduce pulmonary overload (BANERJEE et al., 2018, DEMIRBILEK and HUSSAIN, 2017). In the chronic phase, diazoxide can cause excess body hair, usually at doses greater than 5 mg/kg/day. About 25% of children with CH are partially or totally insensitive to diazoxide treatment, which may generate the need for treatment with second-line medications, such as octreotide (BANERJEE et al., 2018).

Octreotide is a long-acting synthetic amino acid analogue of somatostatin that inhibits insulin. Used as a second-line treatment, it works by binding to somatostatin receptors 2 and 5 (SSTR 2 and SSTR5); activation of SSTR5 decreases the promoter activity of the insulin gene, inhibiting calcium mobilization and acetylcholine activity (BANERJEE et al., 2018; DEMIRBILEK and HUSSAIN, 2017). Somatostatin also inhibits the Kap channel which leads to a reduction in insulin secretion. The recommended initial dose is 5 µg/kg/day, administered subcutaneously or in continuous intravenous infusion, at intervals of 6-8 hours, with a maximum dose of 30-35 µg/kgday (DEMIRBILEK and HUSSAIN, 2017). The first response to octreotide administration is usually hyperglycemia, followed by a decrease in the effect in the first 24 to 48 hours (tachyphylaxis), and dose adjustment may be necessary to maintain normoglycemia (DEMIRBILEK et al., 2017). Some expected side effects are anorexia, nausea, abdominal

pain, necrotizing enterocolitis, elevation of liver transaminases; however, recent studies that evaluated the long-term effect of octreotide in children with CH showed little clinical relevance in the linear growth of these patients (DEMIRBILEK et al., 2017). Monitoring of serum concentration is recommended for dose titration, in order to avoid low efficacy and reduce side effects, reaching optimal doses to ensure greater efficacy and safety for the patient (DEMIRBILEK and HUSSAIN, 2017).

A drawback of conventional octreotide therapy is the need for a high number of daily applications; this can become an obstacle to good adherence to treatment (DEMIRBILEK and HUSSAIN, 2017). An alternative was then developed with the monthly application of long-acting somatostatin analogues (LAR, octreotide, lanreotide) (DEMIRBILEK and HUSSAIN, 2017; SBP, 2022). Long-acting octreotides (LAR) are formulated with biodegradable microspheres, which increases the half-life of the medication, with the advantage of being administered once every 28 days. This positively impacted the management of CH in children, increasing adherence to treatment and improving their quality of life (DEMIRBILEK and HUSSAIN, 2017). The patient in this study initially used conventional therapy with octreotide, with good response, and was discharged with a prescription for LAR-octreotide, maintaining normoglycemia and good adherence to treatment.

Surgical treatment may be indicated in HC when there is no satisfactory response to drug therapy, or when the genetic study shows mutations in paternal heterozygosity in ABCC8 or KCNJ11 (SBP, 2022). Ideally, a CT-PET Scan with Fluor 18 is performed before the procedure to identify focal lesions; in the presence of a focal lesion, partial pancreatectomy is indicated, but this test is not available in Brazil (SBP, 2022). Thus, subtotal or total pancreatectomy is indicated in most cases where the drug response is unfavorable (SCOTT ADZICK, 2020; SBP, 2022).

CONCLUSION

Hypoglycemia is the most frequent metabolic disorder in neonatology, and can be classified as transient or persistent. Of the persistent neonatal hypoglycemias, the most prevalent is caused by congenital hyperinsulinism, which must have its diagnosis and appropriate treatment instituted immediately, in order to avoid neurological complications in patients and allow them a better quality of life. The patient in the case report had the diagnosis made respecting the most current criteria, including collection of critical samples in the presence of hypoglycemia. The therapy performed has been proving to be effective so far. The definitive etiological diagnosis, however, requires tests that are still unavailable in Brazil.

FINANCING

The study received no funding.

CONFLICTS OF INTERESTS

The authors declare that there are no conflicts of interest.

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