Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria
ISSN-Online: 2236-6814

Submitted on: 09/12/2021
Approved on: 10/26/2021

CASE REPORT

Congenital hypothyroidism diagnosed on the sixth day of life: a case report.

Douglas Rafael Ertel[1,2], Aldo Roberto Ferrini Filho[1,2], Ludmila de Oliveira Jaime Sales[1,2], Dayana Carla de Oliveira[1,2], Carlos Alberto Moreno Zaconeta[1,2]

Keywords:
Congenital hypothyroidism, Neonatal screening, Intellectual disability.

Abstract

Introduction - Congenital hypothyroidism results from insufficient secretion of thyroid hormones, which are related to the maturation of the central nervous system, being the main cause of preventable intellectual disability in childhood. The diagnosis can be suspected from the neonatal screening test, revealing its importance, since most cases are asymptomatic or oligosymptomatic at birth with nonspecific manifestations, as well as the classic manifestations become evident only later, causing neurological damage. **Objective** - describe a clinical case of a patient diagnosed with congenital hypothyroidism on the sixth day of life, screened through the neonatal screening test, with subsequent laboratory confirmation, highlighting points of diagnosis, treatment and clinical follow-up, avoiding the progression of late diagnosis. **Case report** - male patient, born through normal delivery without complications, who developed asymptomatic hypoglycemia at the first hours of life, treatment resistant. The patient presented alterations compatible with congenital hypothyroidism in the neonatal screening test, with subsequent confirmation through laboratory tests. Thyroglobulin replacement was started on the seventh day of life, with progressive improvement in hypoglycemia and favorable clinical evolution throughout the first months of life. **Conclusion** - Congenital hypothyroidism is the main cause of preventable intellectual disability in childhood, it must be diagnosed as early as possible, demonstrating the importance of neonatal screening tools. After the institution of appropriate treatment and clinical follow-up, the evolution is favorable, avoiding the drastic progression of late diagnosis.

[1] Hospital Materno-Infantil de Brasília, Programa de Residência Médica em Pediatria, Neonatologia - Brasília - Distrito Federal - Brasil.
[2] Escola Superior de Ciências da Saúde, Secretaria de Saúde do Distrito Federal, Governo do Distrito Federal - Brasília - Distrito Federal - Brasil.

Correspondence to:
Douglas Rafael Ertel.
Hospital Materno Infantil de Brasília.Setor de Rádio e TV Norte (SRTVN) – 701 Norte – Via W5 Norte, lote D CEP: 70.719-040. E-mail: dr.ertel@hotmail.com

Resid Pediatr. 2023;13(4).
DOI: 10.25060/residpediatr-2023.v13n4-725

This work is licensed under a Creative Commons Attribution 4.0 International License.

INTRODUCTION

Congenital hypothyroidism (CH) is characterized by insufficient secretion of thyroid hormones thyroxine (T4) and triiodothyronine (T3), which are involved in the physiology of organs and systems and in the maturation of the central nervous system (CNS). CH is the main cause of preventable intellectual disability in childhood. It is most common congenital metabolic endocrine disorder, with a prevalence between 1:1,500-1:4,000 live births. Females are affected twice as often as males, and children with Down Syndrome are at increased risk of presenting the disease[1,2].

The diagnosis of CH is difficult because the majority of cases are asymptomatic or oligosymptomatic at birth, with non-specific alterations such as constipation, prolonged jaundice, lethargy, mottled skin and cold extremities, which may not appear initially, demonstrating the importance of neonatal screening for CH.[1,3] The typical manifestations of CH (cretinoid facies, growth and mental retardation, and neurological disorders such as ataxia, incoordination, strabismus, choreiform movements and sensorineural hearing loss) become evident over the course of the first months of life, when treatment is no longer as effective, since the critical period in which the formation of the CNS relies on hormones starts in fetal life and extends to the age of two years.[1]

Most of the children diagnosed and treated from neonatal screening achieve adequate physical and intellectual development, in what may be described as one of the most important medical achievements of the 20th century. The first blood sample for screening tests must be collected between three and five days after birth, when the physiological peak in thyroid-stimulating hormone (TSH) levels has ceased, thus preventing false-positive results. TSH cutoff values may vary according to where the screening test is applied. The Brazilian Neonatal Screening Program recommends a TSH cutoff value of 10 mIU/l[1,4,5,6].

Neonatal screening tests are not confirmatory. After a change is identified, clinical evaluation and measurement of serum concentrations of TSH and total T4 (TT4) or free T4 (FT4) are required until the second week of life. TSH values above 10 µU/mL and low FT4 or TT4 confirm the diagnosis. Children with TSH levels between 6 and 10 µU/mL and normal TT4/FT4 levels should be monitored and tested again a week later.[1,7,8,9]

CH is categorized as primary (PCH) when alterations affect the thyroid gland; secondary when the pituitary gland is affected; and tertiary when the hypothalamus is affected. PCH can be caused by thyroid dysgenesis (athyreosis, thyroid hypoplasia or thyroid ectopia), and in 15% of cases it results from thyroid dyshormonogenesis (defects in hormone synthesis). PCH can also be transient (5-10% of the cases) when the mother takes antithyroid medication, the mother or the infant is exposed to iodinated agents, and maternal TSH receptor blocking antibodies pass through the placenta, among other causes.[1,3,4,10]

This report was approved by the Ethics and Research Committee of the Escola Superior de Ciências da Saúde (ESCS/FEPECS) and awarded certificate 48092121.3.0000.553 based on substantiated opinion 4.822.531. The study was carried out at the Hospital Materno Infantil de Brasília, an institution managed by the Secretary of Health of the Federal District, Government of the Federal District. Patient guardians signed informed consent forms and allowed the use of images from the patients in this article.

CASE REPORT

A male infant was born at term (38 weeks and four days) in good clinical condition without the need for resuscitation. His mother had untreated gestational diabetes and was prescribed prepartum insulin therapy. The infant was delivered via a cesarean section because his mother had been diagnosed with HELLP Syndrome. His measurements at birth were as follows: weight 3895g; height 51cm; and head circumference 34.5cm. Since he was born to a diabetic mother who needed insulin therapy and was categorized as large for gestational age, glucose monitoring was prescribed.

In the first hours after birth, the infant developed asymptomatic hypoglycemia (glucose 21mg/dL), which did not resolve with oral supply of breast milk. He was transferred to the intensive care unit (ICU) and prescribed glucose, delivered initially at an infusion rate of 5.5 mg/kg/min and later increased to 11 mg/kg/min; hydrocortisone (10mg/kg/day) was added to the prescription within the first days after birth.

Neonatal screening tests performed 48 hours after birth revealed CH (TSH 42.10 µU/ml); serum levels of TSH were elevated (78.8mcUI/mL, reference value 0.35 to 4.94µU/mL) and T4L serum levels were normal (1.28ng/dL, RV 0.7 to 1.48ng/dL). Two additional screening samples were collected (five and 11 days after birth), which supported the tentative diagnosis. The patient was diagnosed with congenital hypothyroidism and treatment with levothyroxine 10 mcg/kg/day was started six days after birth, with subsequent improvement in glucose levels and removal of corticosteroids and cessation of glucose infusion, without complications.

Thyroid ultrasound scans showed a gland with reduced size for age, without other alterations (Figures 1A, 1B and 1C). The echocardiogram showed mild biventricular hypertrophy, pulmonary hypertension with a fetal pattern and a patent foramen ovale. Complete ultrasound of the abdomen, kidneys and urinary tract showed no changes.

A - Global view of the thyroid gland, with an estimated volume of 0.19 mL; B - Left thyroid lobe measuring 12 x 2 x 5 mm; C - Right thyroid lobe measuring 12 x 3 x 5 mm;

The infant was discharged from the ICU and sent to rooming-in after his blood sugar levels normalized. He did not develop complications and was discharged from hospital on exclusive breastfeeding and a prescription of levothyroxine 10mcg/kg/day. The patient was prescribed follow-up care at a specialized center as recommended by the Brazilian Society of Pediatrics. He gained weight and height and showed adequate global development (Figure 2A and 2B; Table 1).



Figure 1. Thyroid ultrasound scans showing glandular tissue in topical anatomy, with smaller size for age.
A - Global view of the thyroid gland, with an estimated volume of 0.19 mL; **B** - Left thyroid lobe measuring 12 x 2 x 5 mm; **C** - Right thyroid lobe measuring 12 x 3 x 5 mm;.

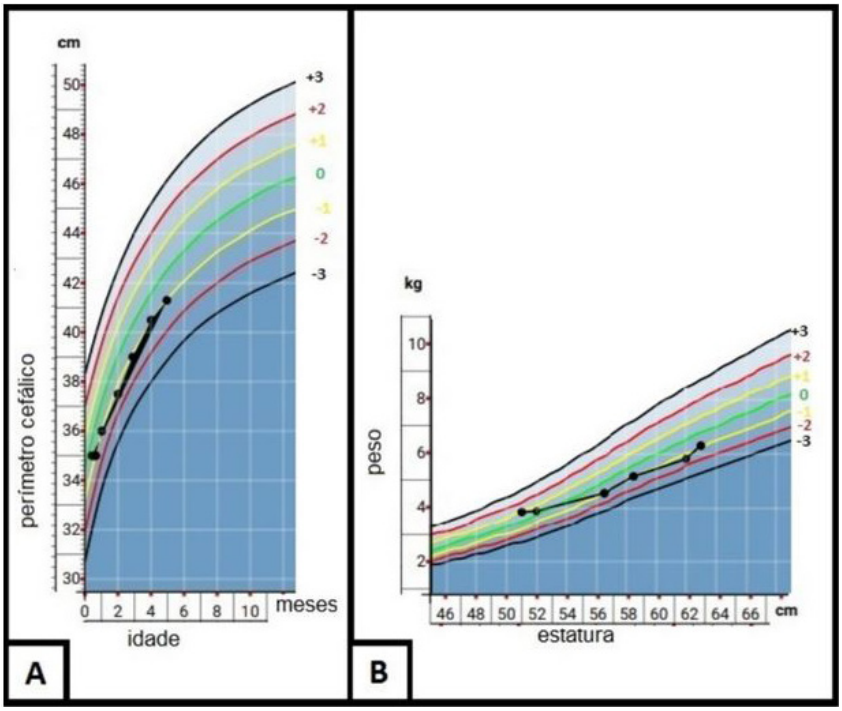


Figure 2. Head circumference and height and weight charts from birth to six months of age.
A - Head circumference in the first six months of life, based on charts from the World Health Organization (WHO), in Z-score. **B** – Height and weight in the first six months of life, based on charts from the World Health Organization (WHO), in Z-score.

DISCUSSION

This article describes the case of a male newborn with no complications at birth, who developed asymptomatic hypoglycemia within hours of birth, did not improve after glucose infusion and corticosteroid therapy, and was subsequently diagnosed with CH.

The low prevalence of signs and symptoms of disease hinders the diagnosis of HC. Individuals with prolonged jaundice, transient hypothermia, a large fontanelle, weak sucking or respiratory discomfort during feedings must be suspected. Classic signs and symptoms only become evident after a few months of life, which may delay diagnosis and treatment and cause irreversible damage to the CNS[1,2,3].

The heel prick test, performed 48 hours after birth in the patient described in this article, showed results suggestive of CH (42.10 µU/ml - RV: less than 10.0 µU/ml), along with increased serum levels of TSH – 78.8mcUI/mL (RV: 0.35 to 4.94µU/mL) and normal T4L levels – 1.28ng/dL (RV: 0.7 to 1. 48ng/dL), which supported the diagnosis of CH and warranted treatment with levothyroxine (10mcg/kg/day), with subsequent improvement of blood glucose levels.

Ultrasound examination can identify the absence of or volume changes in the thyroid gland, which help to elucidate the etiology of CH. Ultrasound scans should be performed as early as possible. Initiation of treatment must not be delayed if ultrasound examination is not available. In such cases, etiological investigation should be postponed until three years after birth, at which point hormone replacement therapy can be briefly discontinued without harming normal global development. The patient in question had a small thyroid gland for his age (0.35 mL, hypoplasia considered), which supported a diagnosis of primary CH[1,2,12,13,14].

Table 1. Global development levels based on the Denver Developmental Screening Test (Translated and adapted from the Denver II Test[11]).

Development monitoring sheet						
Development Milestones	Age (months)					
(expected response)	1	2	3	4	5	6
Startles to voice/sound (Moro reflex)	P					
Turns head in supine position	P					
Follows face	A	P				
Cries out of distress	P					
Gazes and follows object within the field of vision	A	P				
Chin up in prone position	A	P				
Coos and smiles spontaneously	NV	A	A	P		
Starts to tell day from night	NV	A	P			
Posture: moves from a lateral to a midline position	NV	A	A	P		
When in prone position, raises and holds the chin up bearing weight on the forearms	NV	A	A	A	P	P
Emits sounds – babbles	NV	A	A	A	P	P
Counts on the help of other people, but does not remain passive	NV	NV	A	A	P	P
Rolls front to back	NV	NV	NV	A	A	P
When lifted by the arms, helps maintain position with body	NV	NV	NV	A	A	P
Orients head in the direction of a voice or sound	NV	NV	NV	P	P	P
Recognizes when spoken to	NV	NV	NV	NV	A	A
Sit – no support	NV	NV	NV	NV	A	A
Holds and transfers objects hand to hand	NV	NV	NV	NV	A	A
Responds directly to familiar and unknown faces	NV	NV	NV	NV	NV	A
Imitates small gestures and games	NV	NV	NV	NV	NV	A

NV – development milestone not verified; A – development milestone absent in physical examination; P – development milestone present in physical examination; age at which development milestone is expected to show.

Around 10% of the patients with CH have other associated congenital anomalies, including cardiac and digestive tract anomalies, trisomy disorders, and urogenital tract and CNS malformations. Furthermore, up to 20% of the children with CH may have hearing loss.[1] Our patient was examined for such conditions and had cardiac alterations without clinical repercussions.

Treatment for CH must be initiated before 14 days of life. When started early, treatment may substantially decrease the negative impact of serious conditions.[1] Since our patient was promptly diagnosed, treatment was initiated six days after birth. The goal of drug therapy is to normalize T4 levels within about two weeks and TSH levels within a month. The most commonly used medication is levothyroxine, at an initial dose of 10 to 15µg/kg/day.[2]

Patient management and potential dose adjustments are based on physical examination, weight gain and global development assessment, in addition to serial T4/T4L and TSH measurements, carried out every one to two months during the first six months of life, and thereafter every two to three months until the age of three years, when levels are measured every six months or yearly. The objective of treatment is to ensure adequate growth and normal global development for the age and genetic potential, while avoiding excessive treatment for a prolonged period, which could cause craniosynostosis and mood disorders.1,2,8,10,

A study carried out in 2000 investigated patients with different degrees of CH and found that individuals with low T4 and high TSH levels had worse results in cognitive tests during the first year of life.[6] Our patient was monitored at the outpatient pediatrics service and achieved adequate development and growth.

CONCLUSION

CH is a disease that is difficult to diagnose based on clinical signs and symptoms. Neonatal screening plays a key role in diagnosis and initiation of treatment within 14 days of birth. Treatment includes careful patient management to avoid the natural progression of the disease, which can cause irreparable neurological damage, while minimizing potential impacts on patient quality of life and ensuring patients can become productive and healthy individuals in adult life.

BIBLIOGRAPHIC REFERENCES:

1. Sociedade Brasileira de Pediatria, Departamento Científico de Endocrinologia. Hipotireoidismo Congênito: Triagem Neonatal. Porto Alegre: SBP, 2018.
2. Rose SR, Brown RS, Foley T, Kaplowitz PB, Kaye CI, Sundararajan S, et al. . Update of Newborn Screening and Therapy for Congenital Hypothyroidism. Ped. 2006 jun;117(6):2290–303.
3. Neto Coelho JR, Nascimento ML, Guerra-Júnior G: Doenças da tireoide. In: Burns DAR, Campos Junior D, Silva LR, Borges WG (org.). Tratado de Pediatria. 4 ed. São Paulo: Sociedade Brasileira de Pediatria, 2017;1:675-80.
4. Fisher DA. Disorders of the thyroid in the newborn and infant. In: Sperling MA. Pediatric Endocrinology. 4nd. Philadelphia: Elsevier Saunders; 2014. p186-208.

5. worldwide view of strategies. Best Pract Res Clin Endocrinol Metab. 2014;28(2):175–87
6. Nascimento ML. Situação atual da triagem neonatal para hipotireoidismo congênito: críticas e perspectivas. Arq Bras Endocrinol Metab. 2011;55(8):528–33.
7. Elmlinger MW, Kühnel W, Lambrecht HG, Ranke MB. Reference intervals from birth to adulthood for serum thyroxine (T4), triiodothyronine (T3), free T3, free T4, thyroxine binding globulin (TBG) and thyrotropin (TSH). Clin Chem Lab Med. 2001;39(10):973-9
8. LaFranchi SH. Approach to the diagnosis and treatment of neonatal hypothyroidism. J Clin Endocrinol Metab. 2011;96(10):2959-67
9. Bongers-Schokking JJ, Koot HM, Wiersma D, Verkerk PH, de Muinch Keizer-Schrama SMPF. Influence of timing and dose of thyroid hormone replacement on development in infants with congenital hypothyroidism. J Pediatr. 2000; 136:292-7
10. Maciel LMZ, Kimura ET, Nogueira CR, Mazeto GMFS, Magalhães PKR, Nascimento ML, et al. Congenital hypothyroidism: recommendations of the Thyroid Department of the Brazilian Society of Endocrinology and Metabolism. Arq Bras Endocrinol Metabol. 2013;57(3):184–92.
11. Frankenburg WK, Dodds J, Archer P, Shapiro H, Bresnick B. The Denver II: a major revision and restandardization of the Denver Developmental Screening Test. Ped. 1992;89:91-7.
12. Eugster EA, LeMay D, Zerin JM, Pescovitz OH. Definitive diagnosis in children with congenital hypothyroidism. J Pediatr. 2004;144(5):643-7.
13. Souza LRMF, Sedassari NA, Dias EL, et al. Ultrasound measurement of thyroid volume in euthyroid children under 3 years of age. Radiol Bras. [online]. 2021;54(2):94-8.
14. Gruters A, Krude H. Update on the management of congenital hypothyroidism. Horm Res. 2007;68 Suppl 5:107-11.