



## OPEN ACCESS

## EDITED BY

Rodolfo A. Rey,  
Centro de Investigaciones Endocrinológicas  
"Dr. César Bergadá" (CEDIE) CONICET—FEI—  
División de Endocrinología, Hospital de Niños  
Ricardo Gutiérrez, Argentina

## REVIEWED BY

Agnieszka Lecka-Ambroziak,  
Institute of Mother and Child, Poland  
Francisca Grob,  
Pontificia Universidad Católica de Chile, Chile

## \*CORRESPONDENCE

Mireia Tirado-Capistros  
✉ mtirado@santpau.cat

RECEIVED 05 February 2024

ACCEPTED 29 April 2024

PUBLISHED 22 May 2024

## CITATION

Català L, Casas J, Yeh S, Josa-Eritja M, Tirado-  
Capistros M, Moliner E and Carreras G (2024)  
Unusual congenital goiter due to maternal  
Hashimoto thyroiditis: a case report.  
Front. Pediatr. 12:1348431.  
doi: 10.3389/fped.2024.1348431

## COPYRIGHT

© 2024 Català, Casas, Yeh, Josa-Eritja,  
Tirado-Capistros, Moliner and Carreras. This is  
an open-access article distributed under the  
terms of the [Creative Commons Attribution  
License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or  
reproduction in other forums is permitted,  
provided the original author(s) and the  
copyright owner(s) are credited and that the  
original publication in this journal is cited, in  
accordance with accepted academic practice.  
No use, distribution or reproduction is  
permitted which does not comply with  
these terms.

# Unusual congenital goiter due to maternal Hashimoto thyroiditis: a case report

Laura Català<sup>1</sup>, Judit Casas<sup>1</sup>, Sean Yeh<sup>1</sup>, Maria Josa-Eritja<sup>1,2,3</sup>,  
Mireia Tirado-Capistros<sup>1,2,3\*</sup>, Elisenda Moliner<sup>1,2,3</sup> and  
Gemma Carreras<sup>1,2,3</sup>

<sup>1</sup>Department of Pediatrics, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, <sup>2</sup>Institut de Recerca Biomèdica - IIB Sant Pau, Barcelona, Spain, <sup>3</sup>Department of Pediatrics, Obstetrics and Gynecology, and Preventive Medicine and Public Health, Universitat Autònoma de Barcelona, Bellaterra, Spain

Congenital hypothyroidism (CH) is the most common cause of endocrinopathy in the newborn. Its incidence lies between 1 in 3,000 and 1 in 2,000. However, congenital goiter is a rare form of presentation. Hypothyroidism secondary to autoimmune etiology is extremely rare, with an incidence of 1:84,700–1:31,000 newborns. Anti-thyroid peroxidase antibodies (TPOAb) are able to cross the placenta but rarely induce hypothyroidism in the newborn, much less goiter. A case of congenital goiter in a male newborn secondary to maternal high TPOAb levels is reported. The mother was diagnosed of Hashimoto thyroiditis prior to the pregnancy. At birth, a grade 3 goiter was detected in the newborn. Laboratory testings revealed hypothyroidism with free thyroxine of 7.6 pmol/L, thyroid-stimulating hormone of 108 mUI/L and high TPOAb levels. Treatment with Levothyroxine was started the second day of life with progressive thyroid function normalization. Neurological development has been normal until the date.

## KEYWORDS

goiter, hypothyroidism, autoantibodies, newborn, congenital hypothyroidism (CH)

## 1 Introduction

Normal thyroid function during childhood is an essential condition for proper growth and neurodevelopment. Congenital hypothyroidism (CH) is the most common cause of endocrinopathy in the newborn, with an incidence between 1 in 3,000 and 1 in 2,000 (1). It is also considered one of the most common preventable causes of intellectual disability. In addition, most patients with congenital hypothyroidism will not present clinical symptoms at birth or this will be non-specific. Neonatal screening programs were established in the 1970s and are available in 30% of countries worldwide (predominantly developed countries). Congenital hypothyroidism is due to thyroid hormone (TH) defect and can be classified as: primary (thyroidal), central (hypothalamo-pituitary axis) and peripheral. Another classification is: permanent or transient, as well as isolated or syndromic (2). The early treatment of CH is of vital importance for neurological development, starting supplementation with adequate doses of Levothyroxine (T4) as soon as CH is detected, preferably in the first two weeks of life (1).

Congenital goiter is a rare condition produced by multiple causes such as dyshormonogenesis, transplacental passage of maternal antibodies, maternal ingestion of antithyroid drugs, activating mutations of the TSH receptor, or congenital syndromes (3). Depending on the etiology, goiter can be associated to hypothyroidism, hyperthyroidism or normal thyroid function. Once the goiter is detected, management will depend on the thyroid function and its etiology.



FIGURE 1  
Congenital goiter detected at birth.

Transient CH due to autoimmune etiology is extremely rare, with an incidence of 1:84.700–1:31.000 newborns (4). Hashimoto's thyroiditis (TH), also known as chronic lymphocytic thyroiditis, is a thyroid autoimmune disease and it's the most prevalent thyroid pathology in women of childbearing age. Anti-thyroid peroxidase antibodies (TPOAb) are able to cross the placenta but rarely induce hypothyroidism in the newborn, much less goiter (5).

Due to its extremely rare presentation we present a case of congenital goiter secondary to maternal Hashimoto's thyroiditis.

## 2 Case description

We present a case of congenital goiter in a male term newborn secondary to maternal high TPOAb levels.

The mother was a 27-year-old healthy woman and was diagnosed of Hashimoto's thyroiditis 4 years prior to the pregnancy, with positive TPOAb levels (>1,000U/L, external lab test) with normal thyroid function. She presented 3 years prior to the pregnancy subclinical hypothyroidism that did not undergo treatment. Further on, no more thyroid function tests were conducted.

No history of hypothyroidism was reported in the parents' family. The pregnancy progressed without complications. It was the mother's first pregnancy, with no prior history of miscarriages. She tested negative for syphilis, hepatitis B, hepatitis C, and human immunodeficiency virus (HIV), and was immune to toxoplasma and rubella. Prenatal ultrasounds revealed no morphological abnormalities, except for an initial suspicion of aortic coarctation, which was later ruled out. Additionally, the thyroid gland and fetal vitals were found to be normal. There were no reported maternal infections during pregnancy, and she tested negative for group B streptococcus. The baby was delivered at 40 + 0 weeks gestation with APGAR scores of 7/8/8.

Mild distress was noted at birth, which resolved within the first few hours of life.

At birth, a grade 3 goiter was detected (see Figure 1) in the newborn, non-obstructive and apparently asymptomatic.

## 3 Diagnostic, treatment and follow-up

Given the early detection of the goiter, laboratory testings were conducted in the first day of life, revealing hypothyroidism with free thyroxine of 7.6 pmol/L (reference range for newborn 10–26 pmol/L) and thyroid-stimulating hormone of 108mUI/l (<10 mUI/L in neonates). A thyroid ultrasound (US) was performed the second day of life, showing diffusely enlarged thyroid in both its lobes and the thyroid isthmus. The echostructure appeared homogeneous without nodules or intraparenchymal lesions and the doppler study showed normal vascularization. The estimated size was of 5.76 cm<sup>3</sup> [normal size in neonates 0.63 ± 0.2 cm<sup>3</sup> (6)].

A scintigraphy was performed to rule out dysmorphogenesis (7), revealing homogeneous uptake of the radiotracer, which was Technetium-99 m pertechnetate, with no evidence of ectopic thyroid tissue or nodules. The observed pattern was indicative of a diffuse goiter.

Treatment with Levothyroxine 15 mcg/kg/day was started the second day of life.

In the etiological study iodine deficiency was ruled out and negative genetic test result was obtained (clinical exome sequencing with human phenotype ontology directed analysis related to goiter, dysmorphogenesis and hypothyroidism, including 105 genes). Thyroid autoimmunity was analyzed on the newborn, with high level of TPOAb: 1,842,5 UI/ml (normal <100 UI/ml) with negative anti-thyroglobulin (TgAb) and anti-thyroid hormone receptor antibodies (TSHrAb). Also the mother was studied, remaining euthyroid but presenting at that moment high TPOAb levels (6,500 UI/ml), confirming the diagnosis of hypothyroidism by maternal Hashimoto disease. The mother was referred to the endocrinology department and has been followed-up regularly.

The patient's clinical course showed favorable progression, characterized by gradual normalization of thyroid hormone levels and complete resolution of the goiter within the first month of life. Due to communication issues, the hospital did not receive the positive newborn screening results for congenital hypothyroidism (CH) until the patient was three weeks old and had already begun treatment.

Our patient underwent regular thyroid function assessments every 3–4 weeks. During this period, the dosage of levothyroxine was gradually reduced by 50% until the substitution therapy was discontinued at three months of age (Table 1). At the time of discontinuation, the patient's thyroid function values were as follows: TSH 0.82 pmol/L and T4 16 mUI/L. Current guidelines recommend initial laboratory follow-up evaluations 1–2 weeks after initiating LT4 treatment, with subsequent evaluations every 2 weeks until normalization of TSH levels. Once TSH levels are within the target range, the optimal frequency of follow-up can be extended to every 1–3 months.

TABLE 1 Treatment adjustment according to thyroid hormone levels.

Newborn age	12 h of life	2 days of life	5 days of life	20 days of life	48 days of life	2 months and 10 days	3 months	4 months	8 months	1 year
TSH levels (mU/L)	108	23.3	3.08	0.24	0.16	0.27	0.82	0.84	1.06	3
Reference values (-2 SD to +2 SD) (18):	2.43–24.03	1.4–13.1	0.6–6.82	0.58–5.57	0.58–5.57	0.58–5.57	0.58–5.57	0.58–5.57	0.58–5.57	0.57–5.54
Free-T4 Levels (pmol/L)	7.6	9.5	17.4	20.4	18.6	16.9	16.0	14.7	15.0	18.4
Reference values (-2 SD to +2 SD) (18):	12.12–56.54	12.12–56.54	12.32–42.54	12.81–44.33	12.81–44.33	13.41–36.83	13.41–36.83	13.82–31.39	13.82–31.39	14.14–28.22
Levothyroxine dosage (µg/kg/day)		15	15	10.5	6	3	End of treatment	No treatment needed	No treatment needed	No treatment needed

SD, standard deviation.

A follow-up ultrasound was conducted at three months of age: it showed significant volume reduction. Monitoring of thyroid peroxidase antibodies (TPOAb) was not conducted during treatment, as the primary objective was to achieve euthyroidism and authors have not reported a relation between TPOAb levels and thyroid function (8).

Notably, the patient did not exhibit any clinical signs of hypothyroidism prior to treatment initiation, and neurological development has remained normal to date (currently at three years of age).

## 4 Discussion

### 4.1 Congenital hythyroidism

CH poses a significant health concern due to its potential for adverse neurological outcomes if left undetected and untreated. The condition often presents with nonspecific or absent clinical manifestations at birth, attributed in part to the trans-placental transfer of maternal thyroid hormones, leading to missed diagnoses in up to 95% of cases (9).

The etiology of congenital hypothyroidism (CH) often dictates its clinical course, determining whether hypothyroidism is transient or permanent and whether it is primary, secondary, or peripheral. In iodine-sufficient regions, thyroid dysgenesis accounts for approximately 85% of CH cases, while dyshormonogenesis typically explains 10%–15% of cases. Less common causes include maternal autoimmune thyroid disease.

### 4.2 Newborn screening (NBS) and diagnose

NBS for CH is imperative for timely detection and intervention. The primary goal of NBS is to identify all forms of primary CH, ranging from mild to severe presentations (1). Thyrotropin (TSH) measurement emerges as the most sensitive screening tool for primary CH. However, it's crucial to recognize that NBS alone may not completely eliminate the risk of false negatives, and it does not detect central CH, emphasizing the need for clinical vigilance and consideration of hypothyroidism in the presence of relevant symptoms (10).

Since 1982, congenital hypothyroidism (CH) has been tested in all newborns born in Spain, with the primary strategy focusing on newborns' TSH levels to detect primary hypothyroidism. If TSH levels exceed the 99th percentile, the result is considered positive, with newborns having TSH levels >20 uUI/ml requiring immediate diagnosis and treatment. Conversely, positive screenings with TSH levels <20 uUI/ml will need to be retested before 15 days of life (11).

It is important to emphasize the importance of a thorough physical examination in order to detect alterations in the thyroid gland early. The examination of the thyroid in the newborn will be carried out with the baby in the supine position and cervical hyperextension, although the goiter size can be overestimated in some cases.

In accordance with current guidelines regarding congenital hypothyroidism, it is advised that either ultrasonography (US),

scintigraphy, or a combination of both modalities be employed for diagnostic evaluation in neonates (1). In our clinical scenario, initial assessment utilized ultrasonography due to its accessibility. However, it is widely acknowledged that scintigraphy is the most accurate diagnostic test for determining the etiology of CH, especially in case of thyroid dysgenesis. Our approach integrated both thyroid ultrasonography and scintigraphy, facilitating the acquisition of high-resolution anatomical and functional insights.

### 4.3 Maternal autoimmune thyroid disease

Maternal autoimmune thyroid disease presents unique considerations in the context of CH. The prevalence of autoimmune hypothyroidism or Hashimoto disease, and autoimmune hyperthyroidism or Graves disease in women are approximately 0.3% and 0.5%, respectively but CH secondary to autoimmune etiology is extremely rare, with an incidence of 1:84.700–1:31.000 newborns (12). Evidence suggests that pregnant women with autoimmune thyroid disease should undergo strict thyroid function control and therapy has to be initiated if hypothyroidism is detected (13).

Our case is exceptional since several authors agree that despite TPOAb being able to cross the placenta, it does not usually influence fetal or neonatal thyroid function (14, 15). According to Marín et al. study, most offspring of mothers with Hashimoto's thyroiditis had normal thyroid function with the most frequent alteration being high TSH with normal T4 levels. They only report one premature baby with persistent hyperthyrotropinemia that required replacement therapy with levothyroxine (16).

In cases of maternal hypothyroidism or hyperthyroidism, systematic thyroid function screening in newborns is recommended, including LT4 and TSH. However, if maternal thyroid function remains normal during pregnancy, routine neonatal thyroid blood testing may not be warranted, and regular NBS may be sufficient, similar to standard procedures for other newborns. Additionally, whereas congenital goiter can be observed in autoimmune hyperthyroidism, it is exceptionally rare in autoimmune hypothyroidism. In our particular case, despite the mother remaining euthyroid, neonatal screening wouldn't have been indicated. However, once goiter was detected, considering the maternal medical history, autoimmune etiology should have been prioritized, highlighting the importance of clinical judgment in such cases and the need for further research to guide modifications in current screening guidelines.

### 4.4 Treatment and prognosis

Early initiation of levothyroxine treatment is paramount for optimizing neurological outcomes in infants with CH (17). Adverse effects of long-term levothyroxine treatment are rare when appropriately prescribed. The recommended initial dosage is 10–15 mcg/kg/day, with adjustments based on the severity of hypothyroidism (1).

The goal of L-T4 treatment is to support normal neurocognitive development and growth. Dose adjustments of hormone supplementation are recommended until the recovery of the thyroid axis is verified, which in some cases can be delayed for up to 3 years. Subsequently, a close follow-up with analytical determinations will be necessary in the event of the slightest suspicion of recurrence of hypothyroidism (8). With proper management, hypothyroidism secondary to maternal autoimmune disease typically resolves within 3–5 months as maternal antibodies dissipate, leading to a positive long-term prognosis.

In conclusion, the management of congenital hypothyroidism secondary to maternal autoimmune disease necessitates an early detection and proper endocrinologist management. CH secondary to TPOAb still needs to be properly evaluated and characterized. With vigilant clinical care and adherence to established guidelines, the prognosis for infants with CH is promising, emphasizing the importance of ongoing monitoring and support.

## Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

## Ethics statement

Written informed consent was obtained from the minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

## Author contributions

LC: Writing – original draft. JC: Writing – original draft. SY: Writing – original draft. MJ-E: Writing – review & editing. MT-C: Writing – review & editing. EM: Writing – review & editing. GC: Writing – review & editing.

## Funding

The author(s) declare that no financial support was received for the research, authorship, and/or publication of this article.

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated

organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

## References

- van Trotsenburg P, Stoupa A, Léger J, Rohrer T, Peters C, Fugazzola L, et al. Congenital hypothyroidism: a 2020–2021 consensus guidelines update—an ENDO-European reference network initiative endorsed by the European society for pediatric endocrinology and the European society for endocrinology. *Thyroid*. (2021) 31(3):387–419. doi: 10.1089/thy.2020.0333
- Stoupa A, Kariyawasam D, Carré A, Polak M. Update of thyroid developmental genes. *Endocrinol Metab Clin North Am*. (2016) 45(2):243–54. doi: 10.1016/j.ecl.2016.01.007
- Salim FA, Varma SK. Congenital hypothyroidism and the importance of universal newborn screening. *Indian J Pediatr*. (2014) 81(1):53–7. doi: 10.1007/s12098-013-1299-x
- Mengreli C, Maniati-Christidi M, Kanaka-Gantenbein C, Girginoudis P, Vagenakis AG, Dacou-Voutetakis C. Transient congenital hypothyroidism due to maternal autoimmune thyroid disease. *Hormones (Athens)*. (2003) 2(2):113–9. doi: 10.14310/horm.2002.1190
- van Trotsenburg ASP. Management of neonates born to mothers with thyroid dysfunction, and points for attention during pregnancy. *Best Pract Res Clin Endocrinol Metab*. (2020) 34(4):101437. doi: 10.1016/j.beem.2020.101437
- González M, González CP, Sanabria A. Determinación ecográfica del volumen normal de la glándula tiroidea en una población pediátrica de Bogotá, Colombia. *Biomedica*. (2006) 26(1):95–100. doi: 10.7705/biomedica.v26i1.1398
- Karakoc-Aydiner E, Turan S, Akpınar I, Dede F, Isgüven P, Adal E, et al. Pitfalls in the diagnosis of thyroid dysgenesis by thyroid ultrasonography and scintigraphy. *Eur J Endocrinol*. (2012) 166(1):43–8. doi: 10.1530/EJE-11-0140
- Rovelli R, Vigone MC, Giovanettoni C, Passoni A, Maina L, Corrias A, et al. Newborn of mothers affected by autoimmune thyroiditis: the importance of thyroid function monitoring in the first months of life. *Ital J Pediatr*. (2010) 36:24. doi: 10.1186/1824-7288-36-24
- Rastogi MV, LaFranchi SH. Congenital hypothyroidism. *Orphanet J Rare Dis*. (2010) 5:17. doi: 10.1186/1750-1172-5-17
- Rose SR, Wassner AJ, Wintergerst KA, Yayah-Jones NH, Hopkin RJ, Chuang J, et al. Congenital hypothyroidism: screening and management. *Pediatrics*. (2023) 151(1):e2022060419. doi: 10.1542/peds.2022-060419
- Grupo de trabajo de protocolos de cribado neonatal de la Ponencia de cribado poblacional. *Protocolo de Cribado Neonatal del Hipotiroidismo Congénito*. Madrid: Ministerio de Sanidad (2021). Available online at: [https://www.sanidad.gob.es/areas/promocionPrevencion/cribado/docs/CribadoNeonatal\\_HipotiroidismoCongenito.pdf](https://www.sanidad.gob.es/areas/promocionPrevencion/cribado/docs/CribadoNeonatal_HipotiroidismoCongenito.pdf)
- Lazarus JH, Mestman JH. Thyroid disorders during pregnancy and postpartum. In: Braverman LE, Cooper DS, editors. *Werner & Ingbar's the Thyroid: A Fundamental and Clinical Text* 10th ed. Philadelphia: Lippincott Williams & Wilkins (2013). p. 815e35.
- Alexander EK, Pearce EN, Brent GA, Brown RS, Chen H, Dosiou C, et al. 2017 guidelines of the American thyroid association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid*. (2017) 27(3):315–89. doi: 10.1089/thy.2016.0457
- Seror J, Amand G, Guibourdenche J, Ceccaldi PF, Luton D. Anti-TPO antibodies diffusion through the placental barrier during pregnancy. *PLoS ONE*. (2014) 9(1):e84647. doi: 10.1371/journal.pone.0084647
- Banakar MK, Formosa M. Serum thyroid function tests in neonates of mothers with thyroid disease. *Indian J Pediatr*. (2011) 78(7):870–3. doi: 10.1007/s12098-010-0337-1
- Marín Uruña SI, Infante López ME, Samaniego Fernández CM, Montejo Vicente MM, Escribano García C, Izquierdo Caballero R, et al. Follow-up of infants born to mothers with autoimmune thyroid disease: what should not be screened? *Endocrinol Diabetes Nutr (Engl Ed)*. (2020) 67(3):172–8. doi: 10.1016/j.endinu.2019.05.008
- Léger J, Olivieri A, Donaldson M, Torresani T, Krude H, van Vliet G, et al. European society for paediatric endocrinology consensus guidelines on screening, diagnosis, and management of congenital hypothyroidism. *J Clin Endocrinol Metab*. (2014) 99(2):363–84. doi: 10.1210/jc.2013-1891
- Lem AJ, de Rijke YB, van Toor H, de Ridder MA, Visser TJ, Hokken-Koelega AC. Serum thyroid hormone levels in healthy children from birth to adulthood and in short children born small for gestational age. *J Clin Endocrinol Metab*. (2012) 97(9):3170–8. doi: 10.1210/jc.2012-1759