Residência RP Pediátrica
Publicação Oficial da Sociedade Brasileira de Pediatria

Submitted on: 08/04/2022
Approved on: 11/30/2022

CASE REPORT

A case of autoimmune hypothyroidism causing growth and neurodevelopment delay in early childhood

Cecilia Gomes Pereira[1], Francisca Dias Freitas[1], Sara Nogueira Machado[1], Vânia Oliveira[2], Filipe Costa[2], Carla Meireles[1]

Keywords:
Body Weight Changes, Thyroiditis, Autoimmune, Hashimoto Disease.

Abstract

A previously healthy 4 and a half year old boy presented to primary health care consultation. Due to red flags in the neurodevelopment evaluation, autism spectrum disorder is suspected and the child was oriented to child psychiatry. Seven months later, he is evaluated once again and, in addition to worsening neurodevelopmental delay and poor school performance, growth retardation is noted, as well as exponential weight gain. Prader Willi syndrome is suspected and the patient was referred to the pediatricians consultation. An analytical study was performed showing an exponentially elevated TSH (>750 mUI/L) associated with a decreased free T4 (0.24 ng/dL). A radiograph of the hand and fist revealed mineral bone age around two years and eight months. The autoimmune study revealed positive antithyroid peroxidase antibodies and antithyroglobulin antibodies and the diagnosis of autoimmune hypothyroidism was established. Levothyroxine was initiated with clinical improvement and return to linear growth. However, cognitive impairment was still present. Autoimmune thyroiditis is the most common cause of acquired hypothyroidism in pediatric age, although it is rare under the age of three. This condition, if not treated in a timely manner, can cause adult height loss and delayed neurodevelopment. The presented case illustrates the importance of including thyroid function in the study of children with growth retardation and unexplained weight gain. Changes in behavior and school performance should also alert to this diagnosis.

[1] Hospital Senhora da Oliveira, Serviço de Pediatria - Guimarães - Guimaraes - Portugal.
[2] S. Nicolau Family Health Unit, ACES Alto Ave - Guimarães - Guimaraes - Portugal.

Correspondence to:
Cecilia Gomes Pereira.
Hospital Senhora da Oliveira. R. dos Cutileiros 114, Creixomil, Portugal. E-mail: ceciliapereira@hospitaldeguimaraes.min-saude.pt

Resid Pediatr. 2024;14(2).
DOI: 10.25060/residpediatr-2024.v14n2-934

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

INTRODUCTION

Autoimmune hypothyroidism is the most common cause of acquired hypothyroidism in pediatric age, with an estimated prevalence of 1 to 2% with a 4:1 female predominance[1]. In developed countries, is the most common cause of goiter and acquired hypothyroidism in children and adolescents in iodine-sufficient areas of the world. In approximately 50% of cases, there is a positive family history of autoimmune thyroid disease[1-3]. The incidence of this disorder increases with age. However, it is rare before the age of three[2]. The diagnosis of autoimmune hypothyroidism is based on clinical history, physical examination, radiologic data, and evaluation of thyroid function[4,5].

CASE REPORT

A previously healthy 4-and-a-half-year-old boy, son of a mother with type 1 diabetes and autoimmune hypothyroidism, presented to primary care consultation with complaints of otalgia. When evaluated, poor eye contact and absence of speech were noted. When was asked about the child's usual behavior, the mother reported a normal neurodevelopment until the age of three, when the child began to show progressive behavioral changes, adding that his kindergarten teacher had expressed concerns about the child's behavior eight months ago. The mother described that an extremely shy and calm child, who interacted poorly with other children and family members, and had very few communication skills, spending most of his time in the sofa. She also mentioned difficulty climbing stairs and running, loss of appetite, and snoring. Given the child's behavior and neurodevelopment red flags, autism spectrum disorder was suspected, and the boy was referred to child psychiatry specialist.

Seven months later, the boy presented again to his primary care physician for routine consultation. Besides the worsening of previous complaints, the child's growth charts revealed a weight gain of approximately 15 kg in the last year with percentile crossover and a velocity of growth of 2.5 cm/year, also with percentile crossover (Fig. 1).

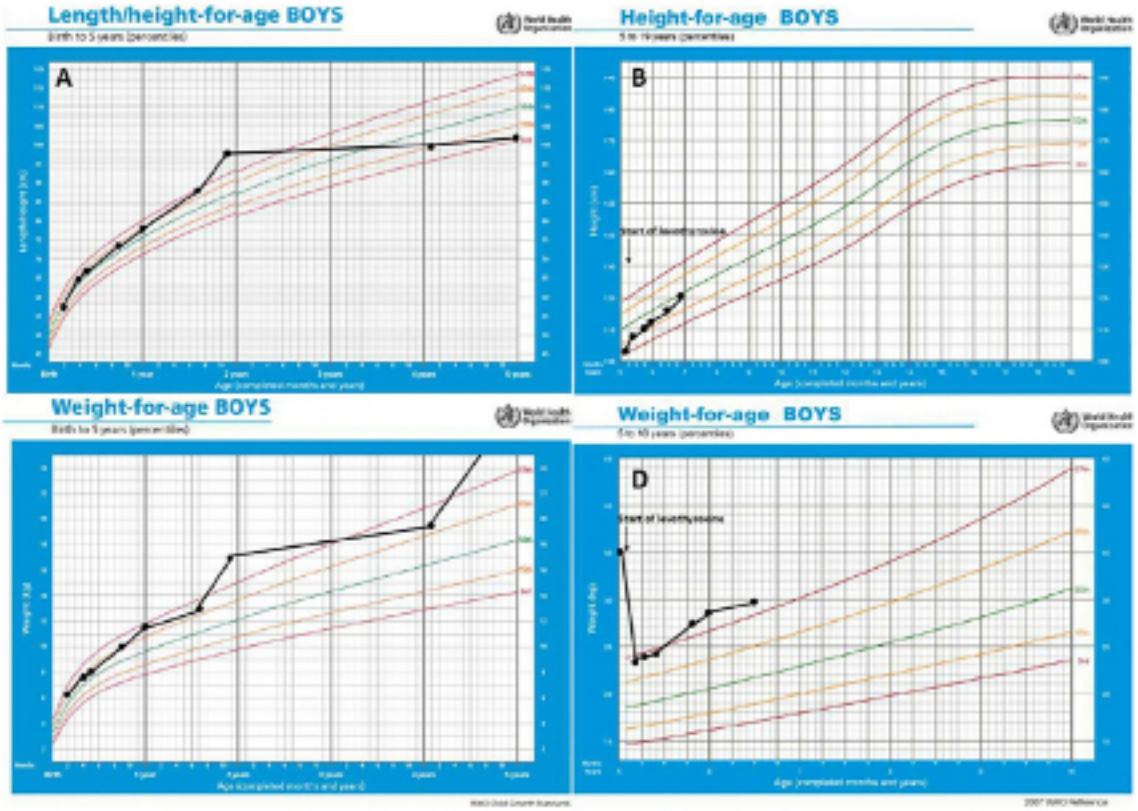


Figure 1. A and B: Child stature-for-age curve. Linear growth curve reveals a crossing of percentiles from upper 97th percentile to the 3th percentile prior to levothyroxine initiation; **C and D**. Weight curve shows excessive weight gain and subsequent weight loss after levothyroxine.

On physical examination (Fig. 2), the child was lethargic, apathetic, and with easy fatigue. He had an endomorphic biotype, with a winged neck, almond-shaped eyes, thin upper lip, and small hands and feet. The hair was scarce and thin. No other relevant findings were registered, including goiter. Given the apparent neurodevelopment delay and compatible physical changes, the suspicion of Prader Willi syndrome was raised and the child was referred to pediatrics consultation. Additional testing revealed an extremely elevated Thyroid-Stimulating Hormone (TSH) (>750 mUI/L, N 0,56-5,41 mIU/L) associated with a decreased free thyroxine (free T4) (0,24 ng/dL, N 1,08-1,93 ng/dL). There was also elevated total cholesterol (TC) (300 mg/dL) and high low-density lipoprotein cholesterol (LDL-C) (217 mg/dL).



Figure 2. A and B: Endomorphic biotype prior to the initiation of levothyroxine therapy.

Celiac disease screening was negative, and Insulin Growth Factor 1 was normal for his age (74 ng/mL). Further analytical study was unremarkable. A radiograph of the hand and fist revealed mineral bone age around two years and eight months (chronological age of 5 years and 1 month).

The child was started on levothyroxine 1,4 ug/kg/day, with gradual dose increasing until 3,1 ug/kg/dia. The auto-immune study revealed positive antithyroid peroxidase antibodies (TPOAb) (>4000 IU/mL) and antithyroglobulin antibodies (TgAb) (>600 IU/mL), establishing the diagnosis of autoimmune thyroiditis. Thyroid ultrasound showed a thyroid gland with irregular contour and parenchymal changes consistent with thyroiditis. Five months after starting therapy, there was a significant clinical improvement, with better performance in motor and social skills and reduced snoring. In addition, the child lost 12 kg and resumed linear growth (9 cm/year), with increased capillary density (Fig. 3). TSH and FT4 values were corrected to normal values (TSH 0,980 mU/L, FT4 1,08 ng/dL).



Figure 3. A and B: Appearance of the child after initiation of therapy, with weight loss, thickening and increased capillary density.

The absence of developmental delay up to the age of 3 years, the significant clinical improvement after the start of treatment, as well as the return to linear growth associated with significant weight loss, allowed the hypothesis of Prader-Willi syndrome to be ruled out.

Although there was a significant clinical and analytical improvement, the boy continues follow up in child psychiatry consultation for developmental delay, with special focus in language skills (scores 68 - extremely low - in the Wechsler Preschool and Primary Scale of Intelligence).

DISCUSSION

The authors describe the case of a preschool child with a 2-year history of growth retardation, exponential weight gain, and neurobehavioral changes caused by a hypothyroidism.

Goiter is the most frequent physical finding of autoimmune hypothyroidism. Clinical manifestations are variable and include neurodevelopmental and physical anomalies. However, children are often asymptomatic[3,6]. Neurodevelopmental anomalies include lethargy, impaired memory, inability to concentrate, poor school performance, and slow speech. Symptoms include fatigability, somnolence, cold intolerance, constipation, and decreased appetite. Physical examination can reveal slight weight gain, delayed puberty, pallor, puffy face, dry skin, coarse hair, hair loss, brittle nails, bradycardia, decreased systolic blood pressure,

increased diastolic blood pressure, delayed relaxation of deep tendon reflexes, ataxia, non-pitting oedema, muscle weakness, and pseudohypertrophy of muscles[3,6]. Our patient's clinical presentation was somewhat similar to that what is described in the literature (lethargy, easy fatigue, behavioral changes, brittle hair). However, weight gain was more marked than would be expected for the disorder[5,7], probably caused by the myxedema and the prolonged time of symptomatology. The absence of goiter, so frequent in this condition[3], may have been a factor in delaying the diagnosis. The absence of goiter may happen in cases of severe and rapid autoimmune-mediated destruction of the thyroid[4].

On initial assessment in primary health care, the hypothesis of a Prader-Willi Syndrome was raised. The significant weight gain in pre-school age, impaired growth and neurodevelopment delay corroborated this hypothesis. Besides that, Prader-Willi Syndrome can also be associated with hypothyroidism and other endocrinological comorbidities. However, this syndrome usually is associated with intrauterine-growth restriction, hypotonia in early age and difficulty feeding with or without failure thriving in the first year of life, which was not described in the personal history of the presented child. In addition to that, in the reported case a significant clinical improvement was noted after initiating levothyroxine, which is highly against the diagnosis of Prader-Willi syndrome, allowing this diagnosis to be excluded[8].

Thyroid hormones have a crucial role in the growth and development of the skeleton. Therefore, some patients may present with declining growth velocity, which often results in short stature. The onset of hypothyroidism in childhood is insidious. Often, the diagnosis is made because of the detection of a goiter on a routine exam or because oge growth delay that it may be present for several years before other symptoms occur[1,6,7,9]. This is more frequent in severe and prolonged hypothyroidism (TSH typically >100 mUI/L) and there is usually concomitant bone age (BA) delay and, for the majority of patients, decreased final adult height.[4] In the described case, the analytical findings associated to BA evaluation are suggestive of prolonged disease evolution, with onset prior to 3 years old. The late diagnosis may have severe consequences for the development of the patient, not only in growth, but also neurocognitive. Thyroid hormones also play an essential role in neurological development, particularly through the first 3 years of life. An onset after this age is less expected to cause neurodevelopment delay[2,3,7]. The early onset present in our case can justify the child's poor neurocognitive performance.

Early diagnosis and treatment are crucial in pediatric age, especially in early age, to preserve final height and ensure normal cognitive and neurologic development[3,6].

Analytical diagnosis of hypothyroidism is made by an elevated TSH. The diagnosis of autoimmune thyroiditis relies on the demonstration of circulating TPOAb (present in 85 to 90% of children) and TgAb (present in 30 to 50% of children), however about 5% of the patients have no measurable thyroid antibodies. In cases where no antibodies are identified, thyroid ultrasound is essential to make the diagnosis[5,10,11]. Levothyroxine is the standard treatment and necessary doses tend to decrease with age[6].

This case illustrates the importance of including thyroid function in the initial evaluation of a child with growth deceleration and weight gain. This diagnosis must be considered even in the absence of other classic symptoms of hypothyroidism[10]. In our patient, percentile crossing, and weight gain were important clues to the diagnosis. In children, in addition to classic signs and symptoms of hypothyroidism, changes in academic performance and behavior are a complementary sign of thyroid dysfunction, although rare at diagnosis. As so, adequate treatment is expected to improve social skills[10].

Timely diagnosis and subsequent treatment are also crucial to improving quality of life and intellectual development, as the absence of treatment can cause permanent changes in the central nervous system[7]. Therefore, clinicians, from pediatricians to primary care providers, must be aware of the signs and symptoms of hypothyroidism in children to achieve an early diagnosis, especially in younger ages.

REFERENCES

1. anley P, Lord K, Bauer AJ. Thyroid Disorders in Children and Adolescents: A Review. JAMA Pediatr. 2016;170(10):1008-19. DOI: https://doi.org/10.1001/jamapediatrics.2016.0486.
2. Wassner AJ. Pediatric Hypothyroidism: Diagnosis and Treatment. Paediatr Drugs. 2017;19(4):291-301. DOI: https://doi.org/10.1007/s40272-017-0238-0.
3. Leung AKC, Leung AAC. Evaluation and management of the child with hypothyroidism. World J Pediatr. 2019;15(2):124-34. DOI: https://doi.org/10.1007/s12519-019-00230-w.
4. Bauer AJ, Wassner AJ. Thyroid hormone therapy in congenital hypothyroidism and pediatric hypothyroidism. Endocrine. 2019;66(1):51-62. DOI: https://doi.org/10.1007/s12020-019-02024-6.
5. de Vries L, Bulvik S, Phillip M. Chronic autoimmune thyroiditis in children and adolescents: at presentation and during long-term follow-up. Arch Dis Child. 2009;94(1):33-7. DOI: https://doi.org/10.1136/adc.2007.134841.
6. Alarcon G, Figueredo V, Tarkoff J. Thyroid Disorders. Pediatr Rev. 2021;42(11):604-18. DOI: https://doi.org/10.1542/pir.2020-001420.
7. Segni M. Disorders of the Thyroid Gland in Infancy, Childhood and Adolescence. In: Feingold KR, Anawalt B, Blackman MR, Boyce A, Chorousus G, Corpas E, et al., eds. Endotext. South Dartmouth (MA): MDText.com, Inc.; 2017.
8. Butler MG, Miller JL, Forster JL. Prader-Willi Syndrome - Clinical Genetics, Diagnosis and Treatment Approaches: An Update. Curr Pediatr Rev. 2019;15(4):207-44. DOI: https://doi.org/10.2174/1573396315666190716120925.

9. Gutch M, Philip R, Philip R, Toms A, Saran S, Gupta KK. Skeletal manifestations of juvenile hypothyroidism and the impact of treatment on skeletal system. Indian J Endocrinol Metab. 2013;17(Suppl 1):S181-3. DOI: https://doi.org/10.4103/2230-8210.119565.

10. Schumaker T, Censani M. Growth Failure and Excessive Weight Gain in a 10 Years Old Male With Obesity: Approach to Diagnosis, Management, and Treatment of Acquired Hypothyroidism. Front Pediatr. 2018;6:166. DOI: https://doi.org/10.3389/fped.2018.00166.

11. Rotondi M, Martinis L, Coperchini F, Pignatti P, Pirali B, Ghilotti S, et al. Serum negative autoimmune thyroiditis displays a milder clinical picture compared with classic Hashimoto's thyroiditis. Eur J Endocrinol. 2014;171(1):31-6. DOI: https://doi.org/10.1530/EJE-14-0147.