THE TREATMENT OF AUTOIMMUNE THYROIDITIS IN ADOLESCENT– A CONTINUOUS CHALLENGE

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Abstract

Background: Autoimmune thyroiditis is the most frequent thyroid disorder in pediatric age, especially in females and puberty. ***Aim:*** The authors wanted to present the case of an adolescent girl diagnosed with autoimmune thyroiditis, describing all the difficulty encountered in the management of this pathology. ***Case presentation:*** We reported the case of 11 years old girl adolescent who was presented in 2011 into the Department of Endocrinology of " Louis Turcanu" Children Emergency Hospital, Timisoara for a tumor localized in the anterior neck. Her psychical examination revealed a well-developed adolescent, with enlarged and non-tender thyroid gland (stage II). Her laboratory assessment revealed thyroid-stimulating hormone level elevated and free thyroxine level suppressed with anti-thyroid peroxidase antibody and anti-thyroglobulin antibody increased. The patient was diagnosed with autoimmune thyroiditis with hypothyroidism and goiter and she initiated thyroid hormone replacement therapy at a dose of 25 µg/day. She remained euthyroid on a stable dose of Euthyrox without recurrences and normal growth and sexual development. In January 2013, the clinical examination was normal except the presence of dysphonia and an increased goiter. All the thyroid parameters were modified while the thyroid ultrasound identified multiples hypoechogenities in both thyroid lobes. The results of MRI and scintigraphy evaluations described a thyroid gland with increased size and decreased function, characteristic to the Hashimoto's thyroiditis. The cause of this thyroid dysfunction was the inappropriate administration of the hormonal treatment (at 12 o'clock, postprandial). ***Conclusions:*** The hormonal replacement therapy of hypothyroidism associated with autoimmune thyroid is permanent and should be monitoring although involve adolescents. The poor compliance to the hormone substitution is an important cause of treatment failure.

Key words: adolescent, autoimmune thyroiditis, hypothyroidism

Background

Autoimmune thyroid disease (ATD) is the most common autoimmune condition, affecting approximately 2% of the female population and 0.2% of the male population with its prevalence peaks in adulthood . It represents the most common etiology of acquired thyroid dysfunction (hypothyroidism) in pediatrics and the most common autoimmune disease in all ages, with a prevalence of 1.3 - 3.4% in children, depending on geographic location, type of study and gender of patients ATD is more common in females and usually occurs in early to mid-puberty .

The term thyroiditis is defined as evidence of "intrathyroidal lymphocytic infiltration" with or without follicular damage. Two types of AT (also defined as chronic lymphocytic thyroiditis) are causes of persistent hypothyroidism: Hashimoto's disease (goitrous form) and atrophic thyroiditis (nongoitrous form). Both are characterized by circulating thyroid autoantibodies and different degrees of thyroid dysfunction, differing only by the presence or absence of goiter. Transient thyroiditis seems to be a variant presentation of AT. It is characterized by an autoimmune-mediated lymphocytic inflammation of the thyroid gland resulting in a destructive thyroiditis with release of thyroid hormone and transient hyperthyroidism, frequently followed by a hypothyroid phase and full recovery.

Aim of study

The authors aimed to present the case of an adolescent girl diagnosed with autoimmune thyroiditis, describing all the difficulty encountered in the management of this pathology.

Case presentation

We reported the case of 11 years old girl adolescent who presented in 2011 into the Department of Endocrinology of Children Emergency Hospital, Timisoara for a tumor localized in the anterior neck. This has been observed since two months before medical presentation and it has been growing since then. She has no family history of endocrine or autoimmune disease.

Her psychical examination revealed a well-developed, well-nourished adolescent in no apparent distress. She had a normal blood pressure level of 110/68 mmHg and her pulse was increased (110 beats/minute). There was no lid lag or proptosis. Her thyroid gland was enlarged (stage II) and was non-tender at palpation. There was no cervical lymphadenopathy or appendicular tremor. The remainder of her physical examination was within normal limits. Her anthropometric data at the hospital admission are presented below.

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Chronological age=11 years and 1 month	Real weight=39kg	Real height=147 cm
Age-for-height=11 years and 9 months	Weight-for-height=46kg	Height-for-age=142±6.93 cm
	BMI=18.05 kg/m^2 (50th -75th percentiles)	Z score= +0.72

Tabel no. 1: Anthropometric measures at the diagnosis moment

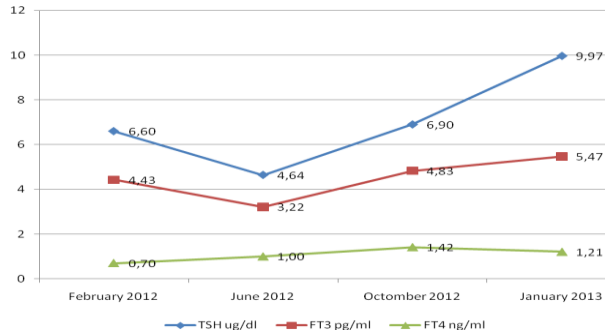

Figure no.1 Evolution in time of the values of thyroid hormones

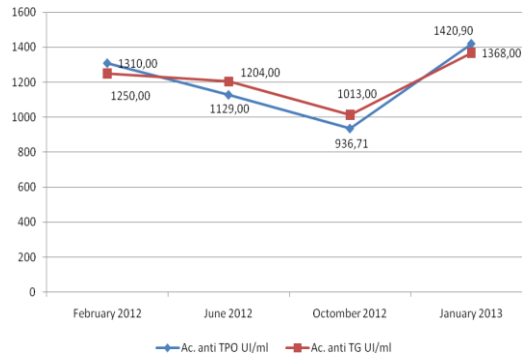

Figure no2. Evolution of the thyroid antibodies

Chronological age=12 years and 11 months	Real weight=47kg	Real height=157 cm
Age-for-height=13 years and 3 months	Weight-for-height=50 kg	Height-for-age= 155.74 ± 6.60 cm
	BMI=19.10kg/m^2 (50th -75th percentiles)	Z score= + 0.19

Tabel no 2: Anthropometric measurement in January 2013

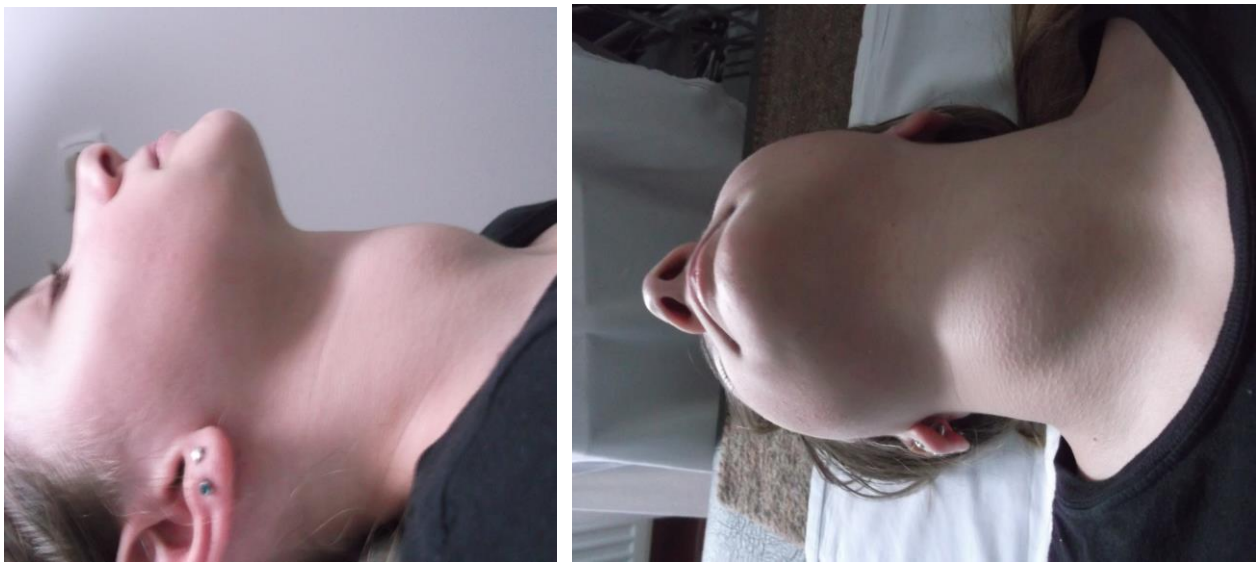

Figure 3 Clinical aspects of the increased goiter

Her laboratory assessment revealed normal blood counts, electrolytes, lipid profile and liver and kidney function. Her serum thyroid-stimulating hormone (TSH) level was elevated at 6.80μg/dl (normal range 2.9 to 4.2 μg/dl) and her free thyroxine level was suppressed at 0.82 pg/ml (normal range, 0.90 to 6.8 pg/dl). The FT3 level was within normal range. An anti-thyroid peroxidase antibody (anti TPO) was elevated at 1228.9 UI/ml (normal, <5.6 UI/ml), and the serum anti-thyroglobulin antibody (anti TG) was increased at 1260 UI/ml (normal, <34 UI/ml).

The cardiologic consult revealed the present of tachycardia and a minor form of right bundle- branch block. No association with another autoimmune disease was encountered.

The patient was diagnosed with autoimmune thyroiditis with hypothyroidism and goiter. Therefore, given the combination of her laboratory parameters and clinical signs, the decision was made to initiate thyroid hormone replacement therapy at a dose of 25 μg/day with Euthyrox administered in the morning, at least 20 min before eating or ingestion anything. This dose normalized the serum TSH and free thyroxine values. The patient was clinical and biological (TSH, FT3, FT4, anti TPO and anti TG) evaluated every 3-4 months. She has remained euthyroid on a stable dose of Euthyrox for over 6 months without recurrences, normal growth and sexual development.

During her last visits in our department, it impresses the elevations of the values of her thyroid hormones and antibodies as described in the figures below (Figure no.1, Figure no.2). This fact was followed by the increasing of the dose of the substitution hormone (from 25 μg/day up to 50μg/day).

In January 2013, she came to the hospital for the periodical evaluation. Her anthropometric measures (table no. 2) were according to the tables and percentiles for age and sex and the clinical examination was normal except the fact that she was still dysphonic with cough and her goiter was increased (Figure no 3).

The ENTT examination (indirect laryngoscopy) revealed the presence of free space glottis with vocal cords slightly thickened and congested but mobile with phonation and respiration. This was suggestive for a severe episode of laryngitis.

All the thyroid parameters were modified. TSH level was increased at 9.97μg/dl (normal range 0.53 to 3.59 μg/dl) and all thyroid hormones were free suppressed: FT3 at 5.47 pg/ml (normal range, 35 to 77 pg/dl) and FT4 at 12.15 ng/dl (normal range, 12-20.6 ng/dl). The anti-thyroid peroxidase antibody was elevated at 1420.9 UI/ml (normal, <5.6 UI/ml) while the serum anti-thyroglobulin antibody (anti TG) was normal. The thyroid ultrasound showed an increased volume of thyroid gland and identified multiples hypoechogenities in both thyroid lobes.

In order to exclude the presence of malignant nodes and to elucidate the cause of goiter enlarger, MRI examination and thyroid scintigraphy were performed. The magnetic resonance (Figure 5,6) imagistic examination described the presence of thyroid gland increased in size overall with the right thyroid lobe = 2.3/1.9/6.3 cm, the left thyroid lobe = 2/1.6/5.7 while the pyramidal lobe = 0.7/1.3/2 cm, isthmus=1 cm, gadophil and homogeneous tissue, without focal lesions. Several nodular formations (one nodule posterior to the carotid artery, 1 cm dimension, in the right part and 3 nodules localized between the trachea and the common carotid artery, maxim 8 mm dimension in the left part) were identified lower to the thyroid lobes and paratracheal. They were visible in T1, T2 isosignal, homogeneous and gadophil.

A thyroid scintigraphy (figure 7) was performed after she stopped the hormone substitution and described a decreased function of thyroid and a diffuse capture.

The results of these imagistic evaluations described a thyroid gland with increased size and decreased function, characteristic to the Hashimoto's thyroiditis. The nodular formations described at MRI were considered as cervical lymphadenopathy secondary to the laryngitis.

The cause of this goiter enlargement and thyroid hormone abnormalities was the poor compliance to the hormone substitution. The adolescent admitted the fact she took her treatment every day around 12 o'clock

Discussions and conclusions

The case presented nicely illustrates a typical case of an autoimmune thyroiditis with goiter and hypothyroidism due to glandular dysfunction in a teenager. Optimal quantities of thyroid hormone substituted are critical to neurodevelopment and growth in a child diagnosed with autoimmune thyroiditis. Once biochemical euthyroidism has been achieved, TSH can be monitored every 4–6 months in the growing child and yearly up to the attainment of final height. Also, growth and sexual development in these patients should be followed systematically as in any pediatric patient, because they may be deranged. Similar to other endocrine causes of growth failure, linear growth is compromised to a greater degree than weight gain, and the bone age is delayed . In the case presented, the teenager had a normal height gain (from 147 cm up to 157 cm), with a growth velocity of approximately 5 cm/year.

Typically, hypothyroidism induces pubertal delay. Medical literature had reported cases of pseudoprecocious puberty induced by hypothyroidism and manifested as testicular enlargement in boys, breast development, and/or vaginal bleeding in girls . Clinically, it may vary from true precocity by the absence of accelerated bone maturation and linear growth. Our teenager girl had a normal sexual development with menarche installation at 12 years and 3 months.

One problem frequent identified, especially in the adolescents is the poor compliance to the hormone substitution. This is an important cause of treatment failure. FT4 should be measured when it is suspected. A serum TSH greater than twice normal, with a concomitant normal FT4 level, suggests intermittent omission of the medication. It should be administered at least 20 min before eating or ingestion of any medication. The girl presented considered that it was not so important the period of day when Euthyrox was administered. Also she was passing through a difficult period in her life, which marked her because her parents divorced.

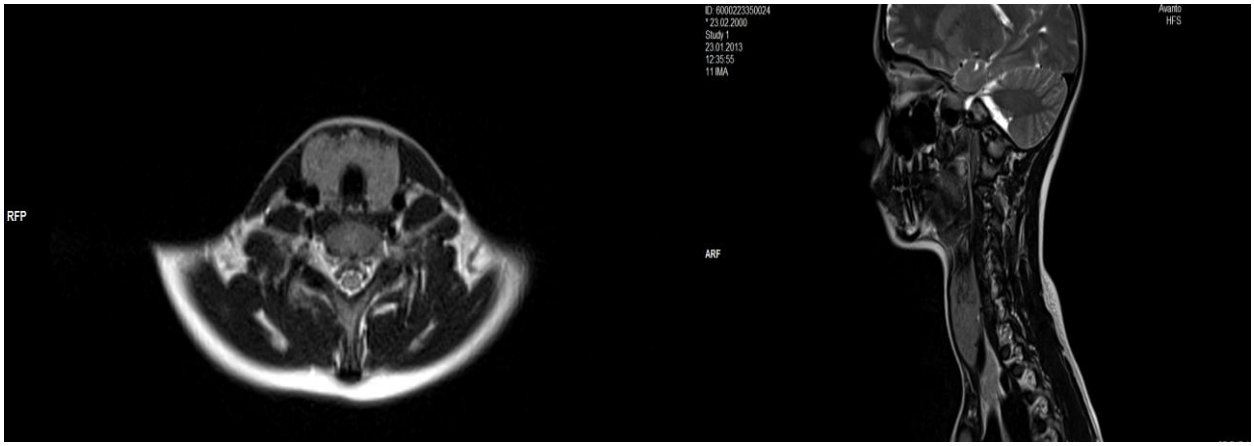

Figure 5, 6 Thyroid MRI image

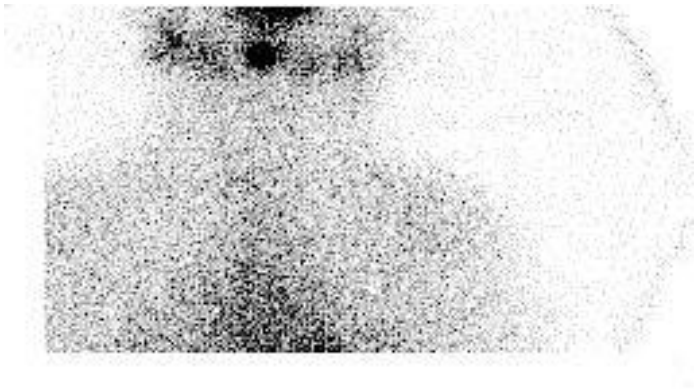

Figure 7 Thyroid scintigraphy aspect

Parents of children with autoimmune thyroiditis should be advised that the hypothyroidism is likely to be permanent and monitoring of thyroid function for all patients should be lifelong although they are adolescents. This is a difficult period when they want to be independent, they believe they know everything, they think they are able to do without any help from the adults.

Also as a physician we have to keep in mind that there are a variety of conditions (phenylketonurie, cystic fibrosis, cirrhosis, and mucosal diseases of the small bowel, bypass and small bowel resection) or drugs (calcium and iron supplements, sucralfate, potassium binding resins, antacids drugs containing aluminium) may alter thyroid hormone requirements .

The hormone dose replacement should be adapted always according to the values of thyroid hormones. It is important to elucidate the cause of a sudden increased of the dose of therapy and sometimes imagistic investigations are required.

It is important to remember that thyroid nodules are more often malignant in adolescent than in adults. A recent study published analyzed the relationship between autoimmune thyroiditis, cancer, and thyroid nodules in a large case series of paediatric patients. Thyroid nodules were found in 115 of 365 patients with autoimmune thyroiditis (31.5%), more frequent presented as a solitary nodule (60.0%) palpable at clinical examination and confirmed by ultrasonography. On histologic examination after total thyroidectom, papillary carcinoma was detected with exhibiting lymph node metastasis. The prevalence of male sex among patients with cancer was greater than that among patients with autoimmune thyroiditis. When it is even a little suspicion of malignant cancer exist, imagistic evolutions should be performed.

References:

204. P. Saravanan and C. M. Dayan, "Thyroid autoantibodies," Endocrinology and Metabolism Clinics of North America, vol. 30, no. 2, pp. 315–337, 2001.

205. I. Hunter, S. A. Greene, T. M. MacDonald, and A. D. Morris, "Prevalence and aetiology of hypothyroidism in the young," Archives of Disease in Childhood, vol. 83, no. 3, pp. 207–210, 2000.

206. A. Chiesa, L. Gru ˜ neiro de Papendieck, A. Keselman, J. J. Heinrich, and C. Bergad ´ a, "Final height in long-term primary hypothyroid children," Journal of Pediatric Endocrinology and Metabolism, vol. 11, no. 1, pp. 51–58, 1998.
207. Cabrera SM, DiMeglio LA, Eugster EA Incidence and characteristics of pseudoprecocious puberty because of severe primary hypothyroidism. J Pediatr. 2013 Mar;162(3):637-9.
208. Marco Cappa, Carla Bizzarri, and Francesca Crea. Autoimmune Thyroid Diseases in Children of Thyroid Research Journal Volume 2011, Article ID 675703.
209. A. Corrias, A. Mussa, F. Baronio et al., "Diagnostic features of thyroid nodules in pediatrics," Archives of Pediatrics and Adolescent Medicine, vol. 164, no. 8, pp. 714–719, 2010.

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