Rapid Changes of Thyroid Function in a Young Woman with Autoimmune Thyroid Disease

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Significance of the Study

- Hashimoto's thyroiditis and Graves' disease share several pathogenetic features, while a transition between the entities is possible. We present the case of a patient with an unusually rapid transition from hyperthyroidism to hypothyroidism and vice versa within just a few weeks.

Keywords

Hashimoto's thyroiditis · Graves' disease · Hashitoxicosis ·
Case report

Abstract

Objective: A conversion from Hashimoto's thyroiditis to Graves' disease and vice versa leads to diagnostic and therapeutic challenges. **Clinical Presentation and Intervention:** A 30-year-old female presented with overt hyperthyroidism and negative thyroid-stimulating hormone receptor antibodies (TRAbs). Since hashitoxicosis was assumed, the patient was treated with propranolol. Within the next few weeks, the patient developed severe overt hypothyroidism, which was treated with levothyroxine. However, after several more weeks, she presented with overt hyperthyroidism once again, this time showing elevated TRAbs. **Conclusion:** We suggest educating patients and physicians to recognize changes in thyroid function and close monitoring of unclear cases of overt hyperthyroidism.

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Background

Hashimoto's thyroiditis (HT) and Graves' disease (GD) are the two most common forms of autoimmune thyroid disorders [1]. While the major autoantibodies in HT are directed against thyroid peroxidase (TPO) and thyroglobulin (Tg), a hallmark of GD is the detection of thyroid-stimulating hormone (TSH) receptor antibodies (TRAbs), even though TPO and Tg antibodies can also be found in approximately 70% of GD patients. However, TRAbs are only rarely detected in HT patients [2]. Usually, HT requires thyroid hormone replacement therapy with levothyroxine (LT) if certain conditions; e.g., overt hypothyroidism, are present [3]. In patients with GD, beta-adrenergic blocking agents can be used to ameliorate symptoms of hyperthyroidism, while three effective causal treatment options exist: antithyroid drugs, radioactive iodine therapy, and thyroidectomy [4].

Even though HT and GD have long been considered two different entities, a conversion from HT to GD can

Fig. 1. Sonographic study of the thyroid gland at the patient's first visit (**a**) and after conversion to overt hyperthyroidism (**b**). Right thyroid lobe, transverse axis (1); left thyroid lobe, transverse axis (2); right thyroid lobe, sagittal axis (3); left thyroid lobe, sagittal axis (4).

be observed in some rare cases. While the pathophysiological background of this conversion is not yet entirely clear, several reports on the topic have been published [5–7]. As rapid changes in thyroid function may be observed, such cases often lead to diagnostic and therapeutic challenges.

We present the case of a 30-year-old female with autoimmune thyroid disease and a particularly rapid change in thyroid function that fluctuated from hyperthyroidism to hypothyroidism and vice versa within just a few months.

Case Report

In April 2017, a 30-year-old female patient presented at the endocrine outpatient department of the Medical University of Graz, Austria, for further evaluation of overt hyperthyroidism found during a routine check by her primary care physician. She complained of tachycardia, weight loss, and anxiety. Ten years earlier, the patient was on thyroid hormone replacement therapy for a short period but has not received any thyroid-specific medication since then. No concomitant diseases were reported.

Sonographic examination revealed a thyroid gland with normal vascularization and without any nodular or cystic lesions (Fig. 1). Laboratory parameters showed a suppressed TSH with slightly elevated free triiodothyronine (FT3; 6.7 pmol/L with a reference range of 3.0–6.3) and normal free thyroxine (FT4). Both

TPO and Tg antibodies were elevated, while TRAbs were within the normal range. Assuming hashitoxicosis with hyperthyroidism, the patient received symptomatic therapy with propranolol and was discharged with an appointment for routine follow-up after approximately 3 weeks.

During the following 2 weeks, the patient presented at our emergency unit twice due to ongoing tachycardia and new onset of chest pain and dyspnea. Possible differential diagnoses of acute coronary syndrome, pulmonary embolism, or pneumothorax were ruled out by biochemical examinations as well as imaging studies (echocardiography, chest X-ray).

When the patient returned to the endocrine outpatient department 4 weeks after her first visit, biochemical tests revealed a normal thyroid function with TSH in the lower normal range (0.20 μ U/mL, reference range 0.10–4.00; FT3 and FT4 within the reference range). However, within the next 4 weeks, the patient developed severe overt hypothyroidism with markedly elevated TSH (100.90 μ U/mL) and decreased FT4 (6.2 pmol/L, reference range 9.5–24.0). Therefore, thyroid hormone replacement therapy with 25 μ g of LT daily was initiated. The comparatively low dose of LT was chosen in view of the patient's clinical presentation with tachycardia and palpitations while also considering the recent low or low-to-normal serum concentrations of TSH. Until this point, the patient was treated with propranolol alone and did not receive any thyroid-specific medication, in particular no thionamides.

Within the following weeks, the patient experienced recurrent tachycardia and chest pain. After about 5 weeks, biochemical tests revealed overt hyperthyroidism once again. At this time, TRAbs were markedly elevated (234.4 U/L, reference range 0–15.0), while TPO and Tg antibodies increased even further. Consequently, thyreostatic therapy with methimazol was started (beginning with 10

Table 1. Progression of several thyroid-related parameters, CRP, liver transaminases, and thyroid-related therapy

	Reference range	April 26	April 29	May 2	May 24	June 27	July 27	August 9	August 18	August 23	August 29	September 6	September 8	October 3	October 17
TSH, $\mu\text{U/mL}$	0.10–4.00	0.00		0.00	0.20	100.90	0.22	0.02	0.03	0.01	0.00	0.01	0.02	0.00	0.01
FT4, pmol/L	9.5–24.0	16.3		16.4	11.9	6.2	19.2	23.9	24.8	21.9	15.3	11.5	10.7	17.3	16.1
FT3, pmol/L	3.0–6.3	6.7		6.2	4.5	3.4	7.8	10.6	13.0	10.6	6.7	5.8	5.6	7.2	6.4
TPO antibodies, U/mL	≤ 60	432						768		746	705			443	
TRAbs, U/L	≤ 15	1.5						234.4		340.4	195.7	272.1		211.3	
Tg antibodies, U/mL	≤ 60	1,045						>3,000		>3,000	>3,000				
Tg, ng/mL	≤ 30	1.24						0.34							
CRP, mg/L	≤ 5		1.3												
AST, U/L	≤ 30		24					32				22	22		30
ALT, U/L	≤ 35		43					52				43	37		56
Therapy															

TSH, thyroid-stimulating hormone; FT4, free thyroxine; FT3, free triiodothyronine; TPO antibodies, thyroid peroxidase antibodies; TRAbs, thyroid-stimulating hormone receptor antibodies; Tg, thyroglobulin; CRP, C-reactive protein; AST, aspartate transaminase; ALT, alanine transaminase. Therapy: continuous arrow = symptomatic therapy with propranolol; bold arrow = levothyroxine; discontinuous arrow = methimazole.

mg daily), while LT was discontinued earlier. At that time, thyroid sonography showed a hypoechoic organ with significantly elevated vascularization (Fig. 1). Thyroid scintigraphy revealed a diffusely increased uptake of technetium-99m across the entire organ, resulting in an increased total uptake of 10%.

As of February 2018, the patient is still on therapy with methimazole at a reduced dose. Serum concentrations of free thyroid hormones significantly decreased to the normal range, while clinical symptoms ameliorated. During the whole observation period, there were no clinical signs of endocrine orbitopathy or ophthalmopathy.

Table 1 depicts the progression of biochemical parameters as well as therapeutic interventions from April to October 2017.

Discussion

While the severity and rate of fluctuation in thyroid function as in our case are exceptionally rare, similar cases with conversion from GD to HT or vice versa have been reported in the literature [5–7]. Thus, the existence of such entities needs to be considered by clinicians treating patients with autoimmune thyroid disease, while patients should be educated to recognize possible changes in thyroid function. Furthermore, unclear or typical cases of overt hyperthyroidism warrant close biochemical and clinical monitoring until a definite diagnosis can be made.

However, in some cases, the differential diagnosis of hyperthyroidism can be challenging. In our case, sonographic thyroid studies and TRAb within the reference range initially argued against the presence of GD. Due to the spontaneous normalization of TSH and the free thyroid hormones over the following weeks, radioactive iodine or technetium uptake measurements were initially not performed. As seen in our patient, a relatively higher increase in FT3 when compared to FT4 as well as an in-

creased FT3/FT4 ratio may be indicative of prevalent GD [8]. However, as Doppler studies did not reveal increased vascularization, and both TPO and Tg antibodies were positive, hashitoxicosis was initially assumed as the cause for hyperthyroidism. After the rapid conversion to overt hypothyroidism, our patient developed overt hyperthyroidism for a second time, this time showing typically elevated TRAbs and increased vascularization in color-coded Doppler imaging, compatible with GD.

The pathophysiologic background for the conversion from HD to GD is still not entirely understood. Nevertheless, functionally heterogeneous TRAbs exist in both entities; stimulating TRAbs activate the TSH receptor leading to hyperthyroidism, while blocking TRAbs occupy the receptor, hereby causing hypothyroidism [9]. A conversion or quantitative change from blocking to stimulating subtypes, or vice versa, could possibly explain the transformation from one autoimmune thyroid disorder to the other. Indeed, in a study conducted in patients with either blocking or stimulating TRAbs over the course of 10 years, the authors reported a disappearance or change of TRAb subtype in some of the study subjects [10].

Conclusion

We present the case of a 30-year-old Austrian female patient with unusually rapid conversion from overt hyperthyroidism to overt hypothyroidism and vice versa within only a few weeks. Despite the rarity of such extreme cases, we suggest educating patients to recognize symptoms of changes in thyroid function as well as close clinical and biochemical monitoring of unclear cases of overt hyperthyroidism.

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