

Asymptomatic course of overt primary hypothyroidism with a very high peak systolic velocity of the superior thyroid arteries: A case report

Andrey V. Ushakov

From Head, Department of Medicine, Ushakov Thyroid Clinic, Moscow, Russia

ABSTRACT

This study reports the case of a 59-year-old woman with asymptomatic overt hypothyroidism who presented with signs of increased thyroid exertion involving the autonomic nervous system. These signs included significantly increased peak systolic velocity (PSV) of the superior thyroid arteries (STA) and moderately increased blood flow intensity. The findings suggest an increase in the rate of thyroxine deiodination and the sufficiency of free triiodothyronine (FT3) for the functional needs of the body. The absence of typical symptoms of hypothyroidism may depend on the sufficiency of FT3 in the serum and additional nonhormonal circumstances. Hence, FT3 should always be measured in addition to thyroid-stimulating hormone and free thyroxine levels. When Doppler ultrasound is used, the intensity of blood flow and PSV-STA from both sides should be determined to assess the magnitude of thyroid exertion. Probably, PSV-STA may not be an absolute criterion for the diagnosis of Graves' disease.

Key words: Autonomic nervous system, Doppler, Graves' disease, Hyperthyroidism, Hypothyroidism, Thyroid ultrasound

The clinical manifestations of hypothyroidism differ in patients that can range from life-threatening symptoms to no symptoms. Therefore, hypothyroidism is determined based on biochemical parameters [1]. The presence of the excessive thyroid-stimulating hormone (TSH) in the serum is the main criterion for the diagnosis of hypothyroidism. The combination of increased levels of TSH above the normal range with a deficiency of free thyroxine (FT4) is commonly classified as overt or clinical hypothyroidism [2]. This classification does not take into account the amount of free triiodothyronine (FT3), the most important calorogenic hormone in the body. In contrast to the subclinical type of hypothyroidism (excess TSH and normal FT4 levels), with overt hypothyroidism, various symptoms are usually determined, which are associated with thyroid hormone metabolism [2,3]. Therefore, this type of hypothyroidism is called clinical hypothyroidism. However, combining laboratory parameters and disease symptoms/signs may not be feasible in hypothyroidism because although characteristic symptoms are often detected in subclinical hypothyroidism, they may be absent in overt (clinical) hypothyroidism [4].


Studying such important features of hypothyroidism manifestations in its different types will help us determine the essence of the pathogenesis of the disease. However, despite the

cases of asymptomatic patients with overt hypothyroidism in clinical practice, clinical descriptions of such cases are scarce in the literature. Therefore, this study reports a typical case of an asymptomatic patient with overt hypothyroidism and evaluates the key laboratory and ultrasound findings.

CASE REPORT

A 59-year-old woman (164 cm, 67 kg) visited our clinic for examination and consultation. Upon being asked, she reported feeling all right. She had no complaints except for semicough in the morning, which she had become accustomed to. Common symptoms of hypothyroidism (fatigue, drowsiness, dry skin, depression, deterioration of thinking abilities, hair loss, etc.) were absent. There were no problems with the abdomen or hypochondrium, and she had no relevant medical history. The bowel movement was regular with formed stool. She fell asleep around 11 p.m.–12 a.m. and woke up at 07:30 a.m., feeling satisfied. She could cope with her position as a chief accountant and had not experienced difficulties when walking and climbing several floors; her body did not get cold, and she did not feel the need to warm up (in the shower or otherwise).

The patient first noticed a slight increase in the size of her thyroid gland in 2002 but sought no medical help because she did not feel sick. In 2020, the thyroid gland became more protruded, which made her consider consulting a physician. She visited

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Correspondence to: Ushakov Andrey Valerievich, Ushakov Thyroid Clinic, Perervinsky Boulevard 15, Corp. 1, Moscow, Russia. E-mail: docthyroid@gmail.com

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our hospital for a diagnosis only at the end of 2021. The patient had never used any hormonal drugs (levothyroxine) nor had she been on any medications. She was not aware of any cases of hypothyroidism and goiter among her relatives. Among the possible causes of hypothyroidism, long-term mental overstrain owing to work responsibilities was noteworthy.

External examination revealed no signs of hypothyroidism or any other pathology. The patient's skin was of normal color with normal elasticity. The density of hair in the main area on the head, as well as on eyebrows and eyelashes, was sufficient. Her tongue was clean and of normal form, without any pathological signs. She adequately responded to the questions asked. Her blood pressure was 113/75 mmHg and the pulse rate was 67 bpm.

Serological analysis revealed a TSH level of 38.2 (0.4–4.0) mIU/L, an FT4 level of 3.5 (7.7–14.2) pmol/L, an FT3 level of 4.5 (3.8–6.8) pmol/L, an anti-thyroid peroxidase antibody (anti-TPO Abs) level of 8,977.8 (0.0–6.6) IU/mL, an anti-thyroglobulin autoantibody level of 28.5 (0.0–4.0) IU/mL, an erythrocyte count of $4.50 (3.92\text{--}5.08) \times 10^{12}/\text{L}$, and a hemoglobin level of 141 (119–146) g/L. The iodine level in the urine was 200 (100–250) mcg/L.

Ultrasound examination revealed an increase in the volume of the thyroid gland to 82.5 mL (42 dex + 40.5 sin), signs of moderate to significantly pronounced stromal swelling spread throughout the gland, moderately noticeable intralobular tissue destruction, moderate lymphocytic infiltration, minor stromal fibrosis, minor intralobular regeneration, and several small nodes of a reparative nature ("white knight" [5]). The parenchyma, which appeared to be homogenous to varying degrees, comprised approximately 80–85% (Fig. 1a and b). The intensity of blood flow in the two lobes of the thyroid gland in the Doppler energy mode was enhanced moderately (Fig. 1c–f). The peak systolic velocity (PSV) of blood flow in the superior thyroid arteries (STA) was 83.5 cm/s on the right and 146.5 cm/s on the left (Fig. 1g and h).

The blood PSV in the common carotid arteries at the STA level was 80 cm/s on the right and 75.2 cm/s on the left.

DISCUSSION

The asymptomatic course of overt hypothyroidism is insufficiently represented in the literature. A literature search revealed sporadic publications on this topic. When describing the course of this pathophysiology, the previous studies have not really focused on the level of FT3, ultrasound pattern of the thyroid gland in the Doppler mode, and PSV of the thyroid arteries. Furthermore, the reason behind the absence of symptoms in overt hypothyroidism has not been analyzed [6].

One of the key features of the disease course in our patient was the absence of the typical hypothyroidism symptoms associated with a deficiency of thyroid hormones in the body. An outwardly noticeable goiter was the only sign that made the patient seek medical help (goiter may be observed with any type of thyroid hormone metabolism). For the patient, a significant increase in the TSH and anti-TPO Ab levels in November 2021 was unexpected and alarming.

What could be the reason for such an asymptomatic course in overt hypothyroidism? In addition to the absence of symptoms, two additional key signs of the disease are noteworthy: normal FT3 level and increased blood flow intensity and PSV-STA in the Doppler mode. The main hormone produced from the thyroid gland is thyroxine (T4). However, triiodothyronine (T3) is the main hormone consumed by the body; most of T3 is produced from T4 through deiodination. The deiodination process may have varying rates, which might be enhanced with the increase in the assimilation of T3 in the body [7]. The ratio between the normal level of FT3 and a significant decrease in FT4 indicated an increased rate of T4 deiodination. In addition, the serum level of FT3, occupying the 23rd percentile of the reference range, represented not only the

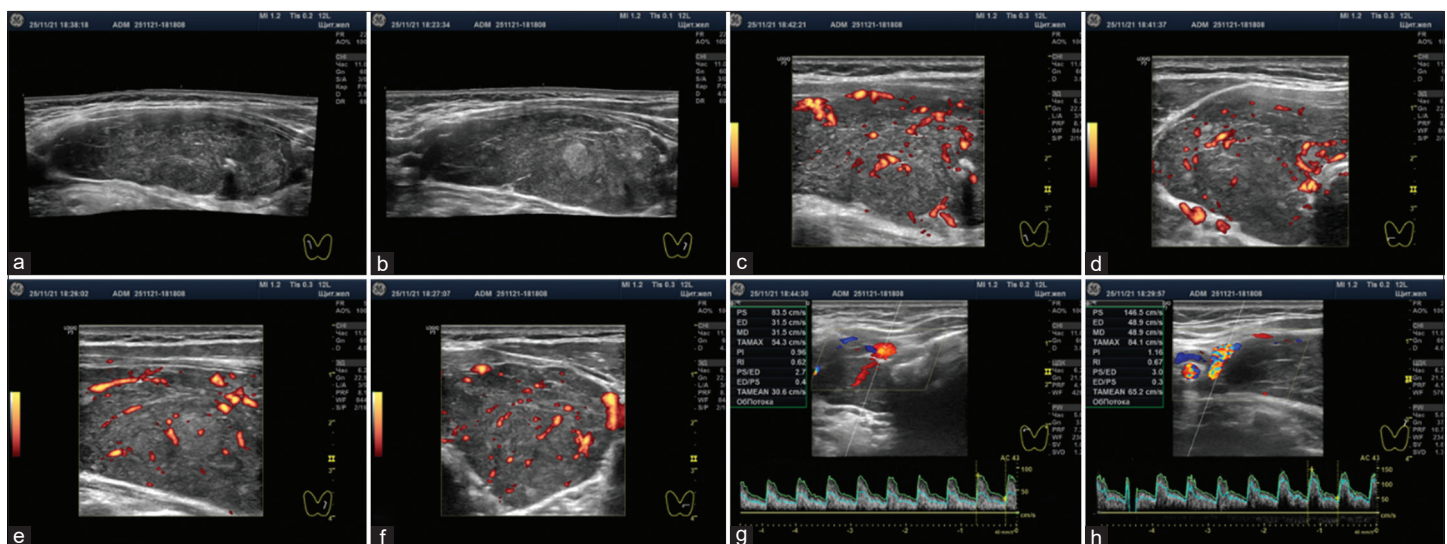


Figure 1: Ultrasound data. (a and b) Panoramic images of the right and left lobes of the thyroid gland in the longitudinal projection; (c and d) Images of the right lobe of the thyroid gland in transverse and longitudinal projections in the Doppler energy mode; (e and f) Images of the left lobe of the thyroid gland in transverse and longitudinal projections in the Doppler energy mode; and (g and h) Peak systolic blood velocity of the superior thyroid arteries on the right and left

amounts of T3 produced directly by the gland and T3 converted from T4 through deiodination but also the residual amount of this hormone during its accelerated uptake by the body from the serum.

In other words, to maintain proper function, the body likely takes up sufficient FT3 from the serum. Moreover, it is adequate to the extent that FT3 is present in necessary amounts in the serum. Such sufficiency of FT3 is ensured by an increased rate of T4 deiodination. This might be the reason why regardless of the TSH and FT4 levels, classic symptoms of hypothyroidism are sometimes absent in these patients.

An increase in the blood flow rate to a moderate degree and a very high PSV-STA rate in the Doppler mode corresponded with the ultrasound findings obtained in Graves' disease. Evidence shows that a PSV-STA value of >50 cm/s represents a reliable cutoff value for Graves' disease (with a sensitivity and specificity of >80%), whereas a PSV-STA value of >85 cm/s is 100% specific for Graves' disease [8]. In our patient, the PSV-STA value on the right nearly corresponded with this statistically justified 100% specificity for Graves' disease, and the value on the left significantly exceeded this cutoff value.

Despite the signs of Hashimoto's autoimmune thyroiditis in our patient, the direct immune effect on thyroid vascular tone is unknown. The effect of TSH on the vessels is also unknown. However, the autonomic nervous system (ANS) reportedly plays a role in the regulation of blood vessels and thyroid hormonogenesis [9-13]. Therefore, we can assume the leading role of ANS in the excessive stimulation of the thyroid gland and its vascular network. Moreover, it adequately meets the body's needs for hormones in hypothyroidism but inadequately so (excessive) in the case of hyperthyroidism (Graves' disease).

A significant difference between the PSV values in the right and left STA indicates a difference in the magnitude of the excitation of neurons in the right and left centers of the ANS. This finding further supports the involvement of the ANS in the activities of the thyroid gland because hormonal and immune metabolites, including TSH and anti-TPO antibodies, cannot accumulate in one of the thyroid lobes and directly affect the vascular tone.

The assumption of the key role of ANS in excessive thyroid exertion in hypothyroidism to increase the production rate of T4 and T3 may allow us to understand several clinical facts. Among them is not only the increased blood flow in the thyroid lobes but also the transformation from hypothyroidism to hyperthyroidism [14].

Many of the symptoms observed in primary hypothyroidism are not directly related to an excess of TSH and a deficiency of FT4. The fact that our patient had an asymptomatic course of overt hypothyroidism may highlight two factors—an increase in the functional exertion of the thyroid gland for hormone production and an adequate amount of FT3 in the serum because of activation of the deiodination process. However, these signs are often combined with

different symptoms in overt hypothyroidism. Therefore, additional factors affecting the symptoms in hypothyroidism should be studied.

CONCLUSIONS

Based on the sufficient amount of FT3 in the serum in the case of overt hypothyroidism, the symptoms of the disease may not be associated with thyroid hormone metabolism. When diagnosing overt hypothyroidism, FT3 level should be examined together with TSH and FT4 levels. Using Doppler ultrasound, the intensity of blood flow inside each lobe and PSV-STA from both sides should be examined. The diagnosis of Graves' disease based on the PSV-STA value may not be 100% specific.

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