Case Report

A case report of unilateral development of painful thyroiditis used as a hallmark of the nervous nature of its pathogenesis

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Background: Painful thyroiditis (PT) combines several variants of pathology. The most common is subacute thyroiditis (ST). Despite the prevailing view that the factors underlying the development of ST have an infectious origin, its viral and bacterial pathogeneses remain unclear. Moreover, the hypothesis of genetic predisposition to ST is non-absolute. In previous studies, approximately 24–40% patients with ST manifested unilateral thyroid disease; however, the assessment of the pathogenesis of ST did not consider this fact.

Case Description: This case of unilateral PT in a pregnant woman has become an illustrative example for revising the idea of its pathogenesis. Laboratory data did not show obvious signs of inflammation, which is typical for pregnant women and does not exclude ST. At the same time, rare in the literature illustrations of the ultrasound picture of unilateral PT are shown. Pathological parallels with other unilateral thyropathies have been drawn. A possible source of unilateral thyroid changes may be the nerve-conducting mechanism.

Conclusions: The involvement of the nervous system in the inflammatory process and the possibility that unilateral nerve conduction affects only one of the thyroid lobes, as demonstrated in the present case, indicate that the autonomic nervous system (ANS) plays a leading role in PT development.

Keywords: Subacute thyroiditis (ST); painful thyroiditis (PT); unilateral thyroiditis; thyroid ultrasound; case report

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Introduction

Painful thyroiditis (PT) combines several variants of pathology. Subacute thyroiditis (ST) prevails among them. In PT without all laboratory signs of ST, individual signs of inflammation [leukocytosis, increased erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)] are sometimes encountered (1). This circumstance, together with the very small number of "painful hashimoto thyroiditis" (PHT) cases presented in publications (70 published cases in the past 70 years), raises doubts about the existence of an independent of PHT and shows the rationality of a joint study of ST and PT (1,2).

Viral infection is considered the most common cause of ST, despite missing direct evidence. Serological and epidemiological data as well as the study of circulating viruses only suggest but do not confirm the role of infection in the development of ST (3). Moreover, approximately 75% of patients do not present with a history of respiratory infection, suggesting that infectious pathogens are a rare cause of ST (4). Some studies on ST have reported 24–40% of ultrasound-confirmed cases of unilateral inflammation in the thyroid (5-7). Additionally, unilateral pain, as a

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manifestation of ST, was observed in 68% of cases (4). In 80% of cases, unilateral ST was found to be associated with human leukocyte antigen haplotype 18:01 (6). However, this association did not reveal the pathogenesis of ST.

Unilateral PT and its features can be considered important guidelines for understanding the key nature of the disease. Therefore, based on the described case, we suggest considering the facts and arguments in favor of a probable pathogenesis. This case is presented in accordance with the CARE reporting checklist (available at https://acr.amegroups.com/article/view/10.21037/acr-24-97/rc).

Case presentation

A 31-year-old female patient (height, 165 cm; weight, 76 kg) at 20 gestational weeks visited our clinic for a consultation regarding ultrasound signs of ST. Under normal circumstances, the patient had no neck pain or other symptoms. She felt a little soreness only when more intense pressure was applied using an ultrasonic sensor on the right lobe of the thyroid gland.

The anamnesis of the disease revealed no triggering factors [viral diseases, including coronavirus disease 2019 (COVID-19), vaccination, infection of relatives, etc.] or significant changes in well-being. She learned about the disease by chance as a result of pregnancy-related examinations.

Patient's physical examination did not reveal any abnormalities. She did not take any medications. Her arterial blood pressure at rest in the sitting position was 117/78 mmHg, and her heart rate was 63 bpm. Blood serum examination revealed the following: thyroid-stimulating hormone 2.30 mU/L (0.35–4.94 mU/L); free thyroxine 12.50 pmol/L (9.01–19.05 pmol/L); free triiodothyronine 4.13 pmol/L (2.63–5.70 pmol/L); total thyroxine 85.17 pmol/L (71.23–140.10 pmol/L); total triiodothyronine 1.63 nmol/L (0.90–2.20 nmol/L); antibodies against thyroid-stimulating hormone receptors 0.7 IU/L (<1 IU/L); thyroid peroxidase antibodies 1.7 U/mL (<5.6 U/mL) and antithyroglobulin antibodies 3.1 U/mL (<4.1 U/mL); erythrocytes 4.2 million/µL (3.8–5.1 million/µL), hemoglobin 12.7 g/dL (11.7–15.5 g/dL), normal leukocyte count, ESR 17 mL/hour (0–20 mL/hour), CRP 1.3 mg/L (<5 mg/L).

An ultrasound scan of the thyroid gland revealed almost twofold diffuse increase in the volume of the right lobe (6.6 mL) compared with the left lobe (3 mL). In the left lobe, the parenchyma was isoechogenic and mostly homogeneous (*Figure 1*), with normal blood flow. The right lobe had slightly and moderately hypoechogenic parenchyma, which is a sign of swelling of stroma, and a small number of significantly hypoechogenic lobules, which is a sign of destruction and lymphoid replacement (*Figure 1*). Doppler ultrasound revealed normal intensity of blood flow in the right lobe (*Figure 1*). Peak systolic velocities were 19.6 and 27.3 cm/s on the right and left superior thyroid arteries, respectively; in the right and left common carotid arteries, these velocities were 58.6 and of 42.7 cm/s, respectively, provided the arteries were normal and the measurements were performed on the same level.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Highlight box

Key findings

- Unilateral inflammation in the thyroid suggests the neuropathogenesis of painful thyroiditis (PT) and subacute thyroiditis (ST).

What is known and what is new?

- Unilateral ST occurs in 24–40% of cases. The assumption about the infectious nature of ST has contradictions and is therefore not absolute. During pregnancy, ST can occur without noticeable causes or laboratory signs and resolve spontaneously.
- The conclusion of this observation improves the understanding of the pathogenesis of PT and ST.

What is the implication, and what should change now?

- Tactics for PT and ST should include diagnosis and treatment aimed at the neural centers that control the thyroid.

Discussion

The described case of unilateral ST serves as an important guide for a better understanding of the nature of the pathogenesis of diffuse thyroid pathology. After all, well-known classical theories about the mechanisms of thyropathies do not reveal the source of changes in only one lobe of the thyroid gland. However, a complex assessment of this and other facts can improve the understanding of the nature of ST and other thyroid diseases.

In ST during pregnancy, the causes in the anamnesis

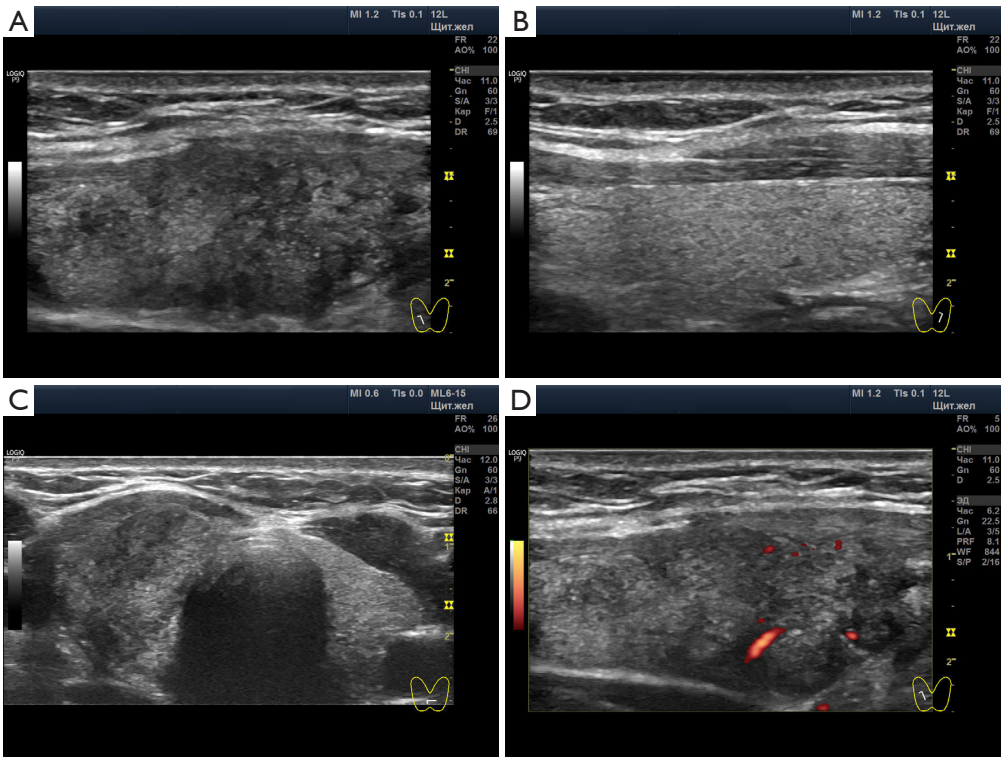

Figure 1 Ultrasound image of the thyroid lobes. (A) Right lobe with hypoechoic areas. (B) Left lobe with isoechoic parenchyma. (C) Transverse view of the gland. (D) Ultrasound Doppler of the right lobe.

may not be determined (8). In particular, the diagnosis of ST in pregnant women may not have a classic laboratory confirmation, and the disease may resolve spontaneously (9). In addition, there are known cases of PT in the postpartum period, in which no signs of inflammation are detected, but a possible nervous etiology (depression and psychosis) is reported (10,11). A similar course of ST, observed in our and other patients, in combination with unilateral changes in the thyroid, suggest a non-infectious pathogenesis of this disease.

Considering the role of the nervous system in the development of inflammation and regulation of immune processes (12,13) as well as the knowledge of direct isolated unilateral nervous regulation of each thyroid lobe (14,15), we can assume that the pathogenesis of ST originates from the nervous system. Specifically, the possibility of unilateral impact from the peripheral nerve centers of the autonomic nervous system (ANS) was considered.

In contrast to the unproven hypotheses of "clonal heterogeneity" or "possible mutations anywhere in the signaling pathway of the thyroid stimulating hormone receptor involving only a part of the normal parenchyma of the thyroid gland" (16), the spread of the pathological process only to a single lobe or its specific segments (lobules, groups of lobules, etc.) can be clearly explained by the separate neurovascular supply to the left and right parts of the gland and segments of its parenchyma (17). This insight also enables us to explain similar manifestations in other thyropathies.

Another similar pathology—the unilateral form of Graves' disease (GD)—helps further refine the involvement of the nervous system in the pathogenesis of PT (16,18). In addition, cases of non-autoimmune and nonhereditary courses of GD (19) indicate the possible primary role of the nervous system and a secondary role of the immune system in the pathogenesis of the disease (20). The stress-induced activation of GD with the involvement of the nervous system supports this finding (20,21).

In the presented case of PT, only the standard diagnostic tests were performed without assessing ANS manifestations. However, the rationale for this paper was a striking example of unilateral thyroid gland involvement and the lack of a comprehensive analysis of the pathogenesis of such cases in the literature. We believe that additional studies on the state of the peripheral ANS in such patients will improve our knowledge of PT and other thyroid pathologies.

Conclusions

The unilateral manifestation of PT, like other thyropathies, should likely be considered with respect to the key involvement of the peripheral ANS in its pathogenesis.

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Footnote

Reporting Checklist: The author has completed the CARE reporting checklist. Available at https://acr.amegroups.com/article/view/10.21037/acr-24-97/rc

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Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://acr.amegroups.com/article/view/10.21037/acr-24-97/coif). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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