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Two Case Studies of Painless Thyroiditis with Special Presentation

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Abstract: This article reports two cases of painless thyroiditis with special manifestations. Patient 1 was a 76-year-old female patient who presented with palpitations and chest tightness and was diagnosed with hyperthyroidism by thyroid ultrasound and electrocardiogram, which is a painless thyroiditis with atrial fibrillation as the first symptom. Patient 2 is a 44-year-old male patient, with only palpitations, diagnosed as T3 thyroiditis by liver function and thyroid function tests, and accompanied by abnormal liver function, belonging to the painless thyroiditis with elevated FT3 only. This article points out that painless thyroiditis has multiple manifestations and is easily misdiagnosed as other diseases. Therefore, patients with symptoms such as palpitations and chest tightness should undergo cytologic or pathologic examination in time to avoid missed diagnosis and misdiagnosis.

Keywords: Painless thyroiditis; Atrial fibrillation; Elevated FT3

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1. Introduction

Painless thyroiditis (PT), also known as silent thyroiditis, subacute lymphocytic thyroiditis, spontaneous remitting thyroiditis, or hyperthyroiditis, can be characterized by a variety of symptoms. Unlike conventional thyroiditis [1], patients with painless thyroiditis often have no fever or significant pain, hence the term “painless.” Atrial fibrillation (AF) is a common arrhythmia that can occur secondary to various conditions such as valvular heart disease, coronary artery disease, and hyperthyroidism. The prevalence of AF is about 10-30% in patients with hyperthyroidism. Elevated thyroid hormones can alter the beta-adrenergic and M2 muscarinic receptors in the heart and enhance sympathetic nerve function, leading to an increased heart rate and shortened atrial refractory period, which promotes atrial fibrillation.

Subclinical hyperthyroidism is also a risk factor for the development of atrial fibrillation. A study by Bel Lassen et al. found that the prevalence of atrial fibrillation was approximately 28% in patients with subclinical hyperthyroidism. Additionally, the risk of developing AF is associated with thyroid-stimulating hormone (TSH) levels, with lower TSH levels correlating with a higher risk of developing AF. However, there are few reports of painless thyroiditis causing AF.

Clinically, thyrotoxicosis is often characterized by a concomitant elevation of free T3 and T4, while TSH levels are below the normal reference range. Studies have shown that in patients with Graves' disease, the elevation of thyroid hormones is mainly due to the higher activity of T3, which contains less iodine, and T4, which contains more iodine. In general, patients with Graves' disease have T3 levels that are four times higher than normal and T4 levels that are two times higher than normal. Amino et al. found in an earlier study that patients with Graves' disease had T3/T4 ratios greater than 20 ng/μg, whereas those with painless goiter had ratios of less than 20. This finding helps differentiate Graves' disease from other forms of destructive thyroiditis, such as postpartum thyroiditis and painless thyroiditis. In addition, the FT3/FT4 ratio in patients with painless thyroiditis is less than 0.4, which also aids in differentiation. However, painless thyroiditis with elevated FT3 alone is clinically very rare.

Painless thyroiditis secondary to transient anemia [2], headache [3], induced acute myocardial infarction [4], and hyperthyroid cyclic paralysis [5] have been reported. Herein, a case of painless thyroiditis with atrial fibrillation as the first symptom and a case of painless thyroiditis with elevated FT3 only are reported in this study.

2. Case information

2.1. Case 1

A 76-year-old female patient was admitted to our hospital due to intermittent palpitations and chest tightness that had lasted for 7 years, with an exacerbation in the last 4 days. The patient had a history of coronary artery disease, hypertension, and diabetes mellitus but denied any history of thyroid disease or atrial fibrillation, and had not used medications such as amiodarone or interferon. Since 2016, she has experienced palpitations and chest tightness after exertion or emotional stress, accompanied by radiating pain in the back of the shoulder and both upper limbs. Each episode lasted about 10 minutes and could be relieved by rest or taking Danshen drip pills. She was diagnosed with "coronary artery disease" at another hospital, and in 2019, her symptoms worsened. Coronary angiography showed severe calcification of the right coronary artery with about 90% stenosis, and two coronary stents were subsequently implanted. During this period, the patient visited the cardiology department multiple times due to precordial discomfort, which improved with treatment, and she was discharged from the hospital.

Four days ago, the patient again experienced symptoms of panic attacks, without obvious chest tightness or breathlessness. There were no symptoms of loss of appetite, easy hunger, shaking hands, or sweating, and her urination and defecation were normal, with no significant change in body weight. She was then admitted to the cardiology department and diagnosed with "coronary atherosclerotic heart disease."

Physical examination upon admission showed: body temperature 36.4℃, pulse 113 beats/min, respiration 19 times/min, blood pressure 123/73 mmHg, clear consciousness, good mental status, no eyelid edema, no conjunctival congestion, symmetrical pupils with responsive light reflex, non-protruding eyeballs, soft neck, non-enlarged thyroid, no tenderness, no vascular murmur, clear breath sounds in both lungs, heart rate 113 beats/min with regular rhythm, no murmur on auscultation, soft abdomen without tenderness or rebound pain, normal muscle tone of the limbs, and no pathological signs. Electrocardiogram showed sinus rhythm with a widened P wave, QS pattern in V1, and widened Q wave in lead III.

The results of routine blood tests, coagulation function, liver and kidney function, blood lipids, cardiac enzymes, BNP, and cardiac ultrasound were normal. Fasting blood glucose was 12.58 mmol/L. Thyroid function tests revealed: TSH < 0.008 μIU/mL (reference range 0.350–4.940 μIU/mL), FT4: 45.99 pmol/L (reference range 9.01–19.05 pmol/L), FT3: 11.01 pmol/L (reference range 2.43–6.01 pmol/L), TRAb < 0.8 IU/L (reference range 0–1.58 IU/L), TgAb: 5.57 IU/mL (reference range 0–4.11 IU/mL), TPOAb: 1.84 IU/mL (reference range

0–5.61 IU/mL), and hematocrit 23 (reference range 0–20). Thyroid ultrasound showed abundant blood flow in the thyroid gland with diffuse lesions and nodules.

After 2 days of hospitalization, the patient's panic symptoms worsened, and another electrocardiogram (**Figure 1**) showed atrial fibrillation with a ventricular rate of 101 beats/min. Based on the patient's symptoms and laboratory test results, the doctor suspected hyperthyroidism and prescribed methimazole 10 mg orally 3 times a day and propranolol hydrochloride 20 mg orally 3 times a day. After one week, to clarify the follow-up treatment plan, a consultation with our department was requested, and it was suggested that the patient be transferred to our department for continued treatment and discontinuation of Cytoxan.

After reviewing the thyroid function, TSH was < 0.008 μIU/mL, FT4: 19.44 pmol/L, and FT3: 4.75 pmol/L. Static thyroid imaging (**Figure 2**) showed unclear thyroid visualization and decreased uptake function, hence thyroiditis was not excluded. The diagnosis was corrected to painless thyroiditis and paroxysmal atrial fibrillation. Treatment with propranolol hydrochloride 10 mg orally 3 times daily was continued. One week later, TSH was 0.022 μIU/mL, FT4: 17.2 pmol/L, and FT3: 1.32 pmol/L, and the electrocardiogram showed sinus rhythm with widening of the P wave. The patient was discharged after her symptoms improved, with recommendations for outpatient follow-up every 2–4 weeks for thyroid function, blood tests, liver function, and electrolytes.

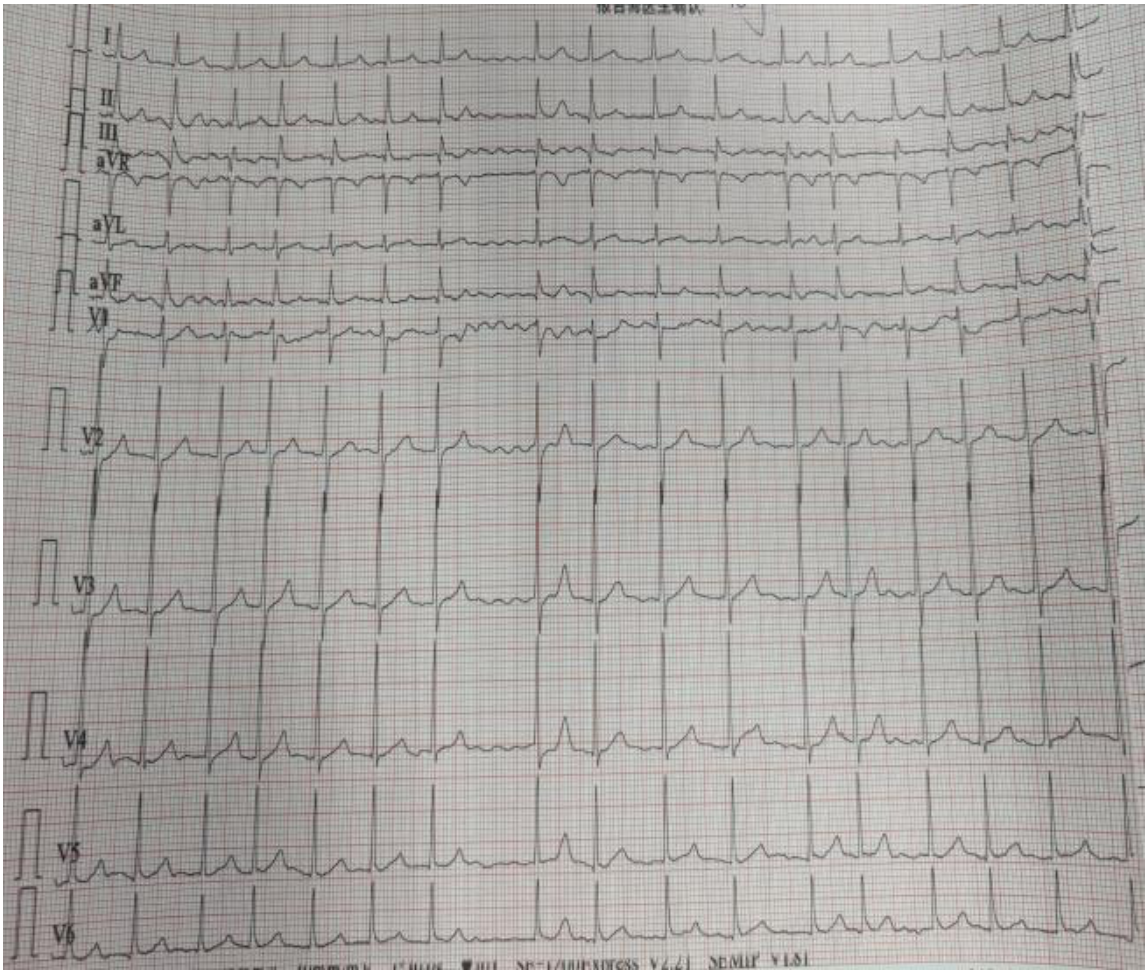

Figure 1. Electrocardiogram showing atrial fibrillation

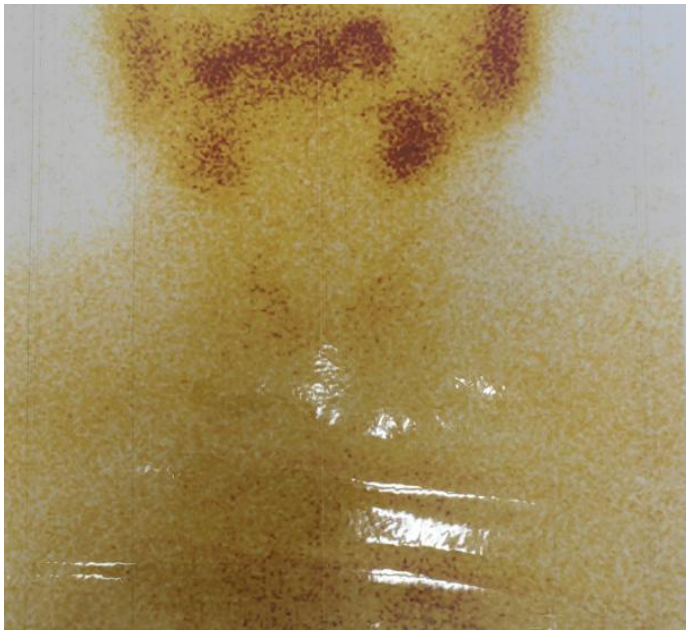

Figure 2. Thyroid static phenomenon $^{99m}TcO_4^-$ decreased uptake

2.2. Case 2

A 44-year-old male patient presented to the hospital's cardiology outpatient clinic with symptoms of palpitations. The patient denied experiencing chest tightness, shortness of breath, excessive sweating, shaking hands, changes in appetite, easy hunger, or fever. His urination and defecation were normal, and there was no significant change in his weight. The patient had no significant past medical history.

Physical examination revealed a temperature of 36.2°C, a pulse of 110 beats/min, respiration of 19 breaths/min, and blood pressure of 120/76 mmHg. He was alert and mentally sound, with no edema in his eyes, no conjunctival congestion, and a normal light reflex. His neck was soft with no palpable thyroid enlargement or tenderness, and no vascular murmur was heard on auscultation. Lung sounds were clear, and his heart rate was 110 beats/min with a regular rhythm. No murmurs were heard on the auscultation of the heart valves. The abdomen was soft with no tenderness or rebound pain, muscle tone of the extremities was normal, and no pathological signs were observed.

An electrocardiogram showed sinus tachycardia. Blood routine, coagulation function, renal function, blood lipids, cardiac enzymes, immunoglobulins, and cardiac ultrasound findings were normal. However, liver function tests showed ALT of 79 U/L (reference value 0–50 U/L), AST of 58 U/L (reference value 0–50 U/L), TBIL of 45.70 μmol/L (reference value 0–26 μmol/L), DBIL of 13.70 μmol/L (reference value 0–8.6 μmol/L), and IBIL of 32 μmol/L (reference value 1.7–17.0 μmol/L).

Thyroid function tests revealed a TSH of 0.033 μIU/mL (reference 0.350–4.940 μIU/mL), FT4 of 12.93 pmol/L (reference 9.01–19.05 pmol/L), FT3 of 15.61 pmol/L (reference 2.43–6.01 pmol/L), and an FT3/FT4 ratio of 1.2. TgAb was < 1.0 U/mL (reference value 0–4.11 IU/mL) and TPOAb was 2.71 IU/mL (reference value 0–5.61 IU/mL).

A review of thyroid function markers 1 day later revealed a TSH of 0.024 μIU/mL, FT4 of 12.53 pmol/L, FT3 of 9.54 pmol/L, an FT3/FT4 ratio of 0.76, a TRAb of 1.17 IU/L (reference value 0–1.58 IU/L), and a sedimentation rate of 5 (reference value 0–20). Further static thyroid imaging showed hypothyroid uptake and poor visualization (as shown in **Figure 3**). The final diagnosis was T3 thyroiditis with abnormal liver function.

For treatment, the patient was given propranolol hydrochloride tablets 10 mg orally 3 times daily and

diammonium glycyrrhizinate enteric-coated capsules 150 mg orally 3 times daily. Ten days later, a follow-up examination showed a TSH of 0.013 μIU/mL, an FT4 of 14.39 pmol/L, an FT3 of > 30.72 pmol/L, an FT3/FT4 ratio of > 2, a TRAb of < 0.8 IU/L, an ALT of 116 U/L, and an AST of 66 U/L. The patient's thyroid function was low, with ALT of 116 U/L, AST of 66 U/L, TBIL of 45.50 μmol/L, DBIL of 12.9 μmol/L, IBIL of 32.6 μmol/L, and normal TgAb, TPOAb, and sedimentation rate.

Seventeen days later, TSH was 0.031 μIU/mL, FT4 was 8.88 pmol/L, FT3 was 3.59 pmol/L, and the FT3/FT4 ratio was 0.4. Liver function was normal. After 1 month of follow-up, tests showed a TSH of 2.056 μIU/mL, FT4 of 8.97 pmol/L, FT3 of 4.02 pmol/L, and an FT3/FT4 ratio of 0.45. A retest 1.5 months later showed a TSH of 1.599 uIU/mL, an FT4 of 9.62 pmol/L, an FT3 of 4.07 pmol/L, and an FT3/FT4 ratio of 0.42. Follow-up over the next year showed that all parameters remained normal.

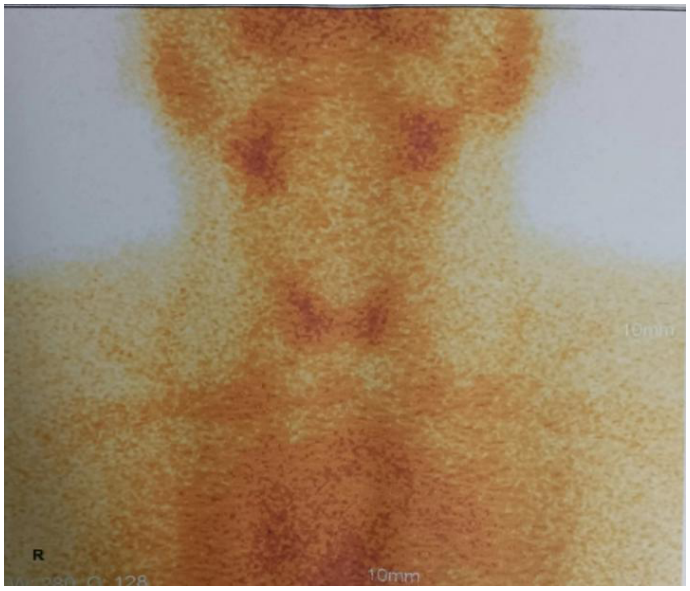

Figure 3. Thyroid static phenomenon $^{99m}TcO_4^-$ absorption decline

Table 1. Comparison of thyroid function, antibodies, and FT3/FT4 values at different times

Timing	10.19	10.20	10.24	10.29	10.30	11.7	11.20	12.5
FT3	15.61	9.54	4.19	> 30.72	> 30.72	3.59	4.02	4.07
FT4	12.93	12.53	9.76	13.11	14.39	8.88	8.97	9.62
TSH	0.033	0.024	0.030	0.025	0.013	0.031	2.056	1.599
TRAb		1.17	3.86	< 0.80	< 0.80	1.35	< 0.80	< 0.80
FT3/FT4	1.2	0.76	0.43	> 2.34	> 2.13	0.40	0.45	0.42
TPOAb	2.71		4.81	1.59	2.55	1.53	1.59	1.36
TGAb	< 1.00		< 1.00	1.49	1.15	< 1.00	1.73	1.33

3. Discussion

Painless thyroiditis is a specific type of thyroiditis that accounts for 1%–23% of thyrotoxicosis and can occur at any age but is more prevalent in women than in men. Approximately 1%–16.7% of pregnant women may develop postpartum thyroiditis. The clinical course of painless thyroiditis usually includes a thyrotoxic phase (lasting 1–3 months) [6], a normothyroxinemic phase, a hypothyroid phase (lasting 1–6 months), and a

recovery phase. In a few patients, hypothyroidism may persist for more than 6 months and may even progress to permanent hypothyroidism. The thyrotoxic phase of painless thyroiditis is characterized by the destruction of the thyroid follicles, resulting in increased release of thyroid hormones. Patients may experience symptoms such as fatigue and weakness, palpitations, excessive sweating, and hand tremors, which are similar to Graves' disease and can be easily misdiagnosed. However, painless thyroiditis is a self-limiting disease and the treatment options are different from those of Graves' disease. While Graves' disease treatments include surgery, radioactive ^{131}I, and antithyroid medications, the treatment of painless thyroiditis is based on glucocorticoids [7-10]. In the thyrotoxic phase, treatment is mainly directed at the symptoms. Beta-blockers may be used to control the heart rate, and a few patients with severe thyrotoxicosis may require glucocorticoid therapy. If painless thyroiditis leads to a thyroid crisis, treatment may be more complicated. In hypothyroidism, mildly elevated TSH may be left untreated. However, if hypothyroidism symptoms are severe or prolonged, treatment with levothyroxine sodium tablets may be considered. Differentiating painless thyroiditis from Graves' disease is important in clinical practice. Static thyroid imaging and thyroid ^{131}I uptake rate are by far the most effective and important methods of differentiating between the two. In addition, thyroid ultrasound and thyroid MRI imaging can also be used for differentiation. In terms of some ancillary tests, TRAb (thyroid receptor antibody) and the ratio of urinary iodine concentration to FT4 or the ratio of FT3 may also be helpful in differentiation. When necessary, a thyroid puncture biopsy may be performed to confirm the diagnosis. It is also important to differentiate painless thyroiditis from subacute thyroiditis because of the similarity of the clinical course and laboratory tests. Subacute thyroiditis is usually accompanied by fever, sore throat, and other prodromal symptoms of respiratory viral infections, whereas painless thyroiditis does not usually present with these symptoms. In addition, blood sedimentation and pathologic tests can be used for differentiation. Blood sedimentation is often elevated in subacute thyroiditis, whereas it is usually normal or mildly elevated in painless thyroiditis. Pathologic examination also usually shows different types of cellular infiltration. Overall, it is important to distinguish painless thyroiditis from other types of thyroid disease to develop the correct treatment plan for the patient.

In summary, for patients presenting with symptoms of thyrotoxicosis, thyroid hormone levels should be tested, along with laboratory tests such as TRAb and blood sedimentation, as well as thyroid ultrasound, thyroid MRI diffusion-weighted imaging, thyroid ^{131}I uptake rate, thyroid static phenomena, and other related tests. Pathologic examination may be considered when indicated. In patients with a short course of disease, no enlargement of the thyroid gland, no tenderness, and no protruding eyes, the possible presence of primary hyperthyroidism (PT) should be considered. Before confirming the diagnosis, it is recommended to give symptomatic treatment, avoid blind use of antithyroid drugs, and strictly prohibit the use of ^{131}I and performing surgical treatment.

Disclosure statement

The authors declare no conflict of interest.

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