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Probable Subacute Thyroiditis Mimicking Levothyroxine Over-Replacement in an Older Woman With Long-Standing Hypothyroidism: A Case Report and Literature Review

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Abstract

Subacute thyroiditis is rarely described in people already taking levothyroxine, in whom its thyrotoxic phase can mimic over-replacement. A woman in her 70s with primary hypothyroidism of about 15 years' duration and undetermined cause was taking levothyroxine 50 µg daily. A week after a febrile sore throat, she developed anterior neck pain, which a general practitioner treated as a viral illness with analgesics and antibiotics. Palpitations and tremor followed four days later. On presentation, her thyroid was markedly tender. Tests showed thyrotoxicosis with a suppressed thyroid-stimulating hormone (TSH), a C-reactive protein (CRP) of 235.2 mg/L, a raised erythrocyte sedimentation rate and a normal leukocyte count. Technetium-99m scintigraphy showed negligible uptake, which argued strongly against Graves' disease and a toxic nodule. The painful gland and intense inflammation made subacute thyroiditis the probable diagnosis, although ultrasound and serum thyroglobulin were unavailable; thyroid antibodies measured six months later were negative. Levothyroxine was withheld, propranolol controlled adrenergic symptoms, and antithyroid drugs were not given. Her neck pain settled within about 10 days; by four weeks, her palpitations had resolved and CRP had normalized. After 66 days without levothyroxine, her TSH was 90.3 µIU/mL, with a low total triiodothyronine and a total thyroxine within the reference range, and levothyroxine was restarted. This rise reflected both the hypothyroid phase and the withdrawal of replacement. In older adults on levothyroxine with a painful thyroid and thyrotoxicosis, subacute thyroiditis should be considered alongside over-replacement; monitoring thyroid function after the thyrotoxic phase may allow prompt resumption of replacement.

Categories: Family/General Practice, Endocrinology/Diabetes/Metabolism
Keywords: de quervain thyroiditis, hypothyroidism, painful thyroid, subacute thyroiditis, thyroid scintigraphy, thyrotoxicosis

Introduction

Subacute thyroiditis, also called de Quervain thyroiditis or subacute granulomatous thyroiditis, is the most common cause of a painful thyroid gland [1,2]. It usually follows a viral upper respiratory infection by two to eight weeks [1] and is inflammatory rather than autoimmune [3]. It is more common in women, and its incidence peaks in the fifth decade of life [4]. Inflamed follicles release their stored hormone, so the patient becomes thyrotoxic even though no new hormone is being made. A transient hypothyroid phase often follows, and 85% to 95% of patients regain normal thyroid function within 12 months [2,3]. Treatment is supportive, and antithyroid drugs have no role [1,2,5].

The cause of thyrotoxicosis determines its treatment [2,5]. Graves' disease and toxic nodular goiter overproduce hormone and show normal or increased uptake on thyroid scintigraphy, an isotope scan that shows how much tracer the gland takes up. Destructive thyroiditis and excess exogenous thyroid hormone both show low uptake [2,5,6]. In a patient taking levothyroxine, low-uptake thyrotoxicosis therefore raises a practical question: is the patient taking too much hormone, or is the gland releasing it? A painful, tender gland with a raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) favors subacute thyroiditis, whereas exogenous hormone suppresses serum thyroglobulin [2,5].

Subacute thyroiditis has been reported only occasionally in people already treated for hypothyroidism. It has been described in patients with long-standing Hashimoto thyroiditis on levothyroxine [7,8], in whom it can cause thyrotoxicosis [8]. Another form of destructive thyroiditis has produced a thyrotoxic phase in a patient on long-term, low-dose levothyroxine [9]. In this setting, thyrotoxicosis is easily attributed to over-replacement, and painful Hashimoto thyroiditis and conversion to Graves' disease must also be considered [10,11].

We describe a woman in her 70s with long-standing primary hypothyroidism of undetermined cause, who

developed probable subacute thyroiditis while taking levothyroxine. The case adds three points to the few published reports. First, she had overt thyrotoxicosis with an intense inflammatory response (CRP 235.2 mg/L), whereas most previously reported patients remained euthyroid (with normal thyroid function) or only mildly thyrotoxic [7,8,12-15]. Second, the diagnosis was reached with inflammatory markers and scintigraphy, without ultrasound or serum thyroglobulin and before thyroid antibodies were measured, a situation common in many settings. Third, her thyroid-stimulating hormone (TSH) rose steeply when levothyroxine was withheld, as in one earlier report [14], which shows how the hypothyroid phase can behave in a patient who already depends on replacement.

Case Presentation

A woman in her 70s first consulted a general practitioner at an outside facility with a two-day history of throat discomfort and pain over the front of the neck. The neck pain had begun about one week after a self-limiting febrile illness with a sore throat. At that visit, she had not yet developed a tremor, a tremulous voice or anxiety. The general practitioner attributed her symptoms to a seasonal viral illness and prescribed analgesics and antibiotics without checking thyroid function. The timeline of events is summarized in Table *1*.

Day	Clinical events	Investigations	Management
About D-12	Self-limiting febrile illness with sore throat	-	-
D-5	Throat discomfort and anterior neck pain began	-	-
D-3	General practitioner at an outside facility diagnosed a seasonal viral illness; no tremor, tremulous voice or anxiety	Thyroid function not checked	Analgesics and antibiotics
D-1	Palpitations and tremor began	-	-
D1	Presented to a tertiary care hospital with neck pain, palpitations and tremor; anxious, with a tremulous voice; afebrile; markedly tender, non-enlarged thyroid	Raised ESR; mild anemia; normal leukocyte count	Empirical ciprofloxacin for 5 days (D1 to D5), paracetamol and a proton pump inhibitor; levothyroxine stopped; propranolol started; thyroid function tests requested
D4	Strong clinical suspicion of subacute thyroiditis	Thyrotoxicosis with suppressed TSH; CRP 235.2 mg/L; raised ESR	Thyroid scintigraphy arranged
D5	Probable subacute thyroiditis diagnosed	Negligible uptake on technetium-99m scan at an affiliated hospital	Levothyroxine kept on hold; antithyroid drugs not given
About D11	Neck pain settled	-	-
D34	Palpitations and tremulous voice resolved	Total T3 and T4 within reference range; TSH 0.25 µIU/mL; CRP normal; ESR still raised	Propranolol continued; levothyroxine kept on hold
D67	No symptoms of hyperthyroidism or hypothyroidism; no levothyroxine taken since D1	TSH 90.3 µIU/mL; low total T3; total T4 within reference range (second laboratory)	Propranolol stopped; levothyroxine 50 µg daily restarted after 66 days off
D188	-	Thyroid peroxidase and thyroglobulin antibodies within reference ranges	-

TABLE 1: Timeline of clinical events

Days are counted from presentation to the tertiary care hospital (D1); D-n is n days before D1. Thyroid function was not tested between D34 and D67.
ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone.

She had primary hypothyroidism of about 15 years' duration. Its cause had not been established, and no

thyroid antibody, thyroid ultrasound or thyroid function results from before this illness were available. She had no history of thyroid surgery, radioiodine treatment, neck radiation or earlier episodes of neck pain. She had been taking levothyroxine 50 µg once daily before this illness. She had type 2 diabetes mellitus of about 20 years' duration, treated with oral agents for the first 15 years and, for the last five years, with twice-daily premixed insulin along with metformin and sitagliptin. She had been treated for hypertension for about 10 years. She was not taking amiodarone or lithium and had not received iodinated contrast in the preceding months.

She presented to our tertiary care hospital three days after the general practitioner visit; this day is designated day 1 (D1). Her main complaints were anterior neck pain, palpitations and tremor; the palpitations and tremor had begun the day before, four days after the onset of neck pain. On examination, she was anxious, with a fine tremor and a tremulous voice. She was afebrile, with a pulse of 110 beats per minute, a blood pressure of 142/94 mmHg and a respiratory rate of 18 breaths per minute, and she weighed 77 kg. The thyroid gland was markedly tender but not enlarged, and there was no bruit over the gland. There was no lid lag or other eye sign, and she reported no weight loss.

The thyroid tenderness raised the possibility of thyroiditis. Because blood results were not yet available, she was started empirically on oral ciprofloxacin to cover a possible bacterial infection of the throat or neck, with paracetamol and a proton pump inhibitor. Blood tests, including thyroid function tests, were requested. Ciprofloxacin was given as a five-day course, from D1 to D5.

Laboratory results are summarized in Table *2* (our hospital laboratory, D1 to D34) and Table *3* (a second laboratory, D67). Blood tests on D1 showed an ESR of 78 mm in the first hour and 114 mm in the second hour, mild anemia (hemoglobin 11.2 g/dL), and a normal total leukocyte count (9,800/µL) without neutrophilia, which made a bacterial infection less likely [2]. When she was reassessed with these results later the same day, levothyroxine was stopped and propranolol was started to control the palpitations and tremor.

Parameter	Unit	Reference range	D1	D4	D34
Hemoglobin	g/dL	12-15	11.2	-	-
Total leukocyte count	cells/µL	4,000-10,000	9800	-	-
Neutrophils	%	40-75	51	-	-
ESR, first hour	mm	5-15	78	78	78
ESR, second hour	mm	10-20	114	135	116
CRP	mg/L	<6.0	-	235.2	2.63
Total T3	ng/mL	0.97-1.69	-	2.27	1.32
Total T4	µg/dL	5.53-11.00	-	13.51	7.78
TSH	µIU/mL	0.46-4.68	-	0.02	0.25

TABLE 2: Laboratory values at our hospital laboratory, D1 to D34

The first-hour ESR was reported as 78 mm on all three occasions; the values were checked against the original reports. Free T3 and free T4 were not measured. ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone

Parameter	Unit	Reference range	D67
Total T3	ng/dL	80-200	61.21
Total T4	µg/dL	4.5-12.5	8.27
TSH	µIU/mL	0.27-4.2	90.3

TABLE 3: Thyroid function tests on D67 at a second laboratory

Measured 66 days after levothyroxine was stopped and before it was restarted. Values are shown in the second laboratory's own units and reference ranges. Free T4 was not measured. T3: triiodothyronine; T4: thyroxine; TSH: thyroid-stimulating hormone

On D4, the ESR remained raised (78 mm in the first hour and 135 mm in the second hour), and the CRP was 235.2 mg/L; because this value was unusually high, it was rechecked, and the result was verified. Thyroid function tests showed thyrotoxicosis, with a raised total triiodothyronine (T3) of 2.27 ng/mL and total thyroxine (T4) of 13.51 µg/dL and a suppressed TSH of 0.02 µIU/mL. The history, examination and blood results raised a strong clinical suspicion of subacute thyroiditis, and thyroid scintigraphy was arranged.

A technetium-99m pertechnetate thyroid scan was performed at an affiliated hospital on D5 to find the cause of the thyrotoxicosis. Images were acquired 30 minutes after intravenous injection of 3 mCi (111 MBq) of the tracer: anterior views without and with markers on the chin and suprasternal notch, and left and right anterior oblique views. There was negligible tracer uptake in the thyroid bed on all views, and the only activity in the neck was physiological uptake in the salivary glands (Figure *1*). Uptake was assessed visually and was not quantified. This pattern indicated severely impaired trapping of tracer by both thyroid lobes. It argued strongly against Graves' disease and an autonomously functioning nodule, both of which take up tracer avidly [2,6].

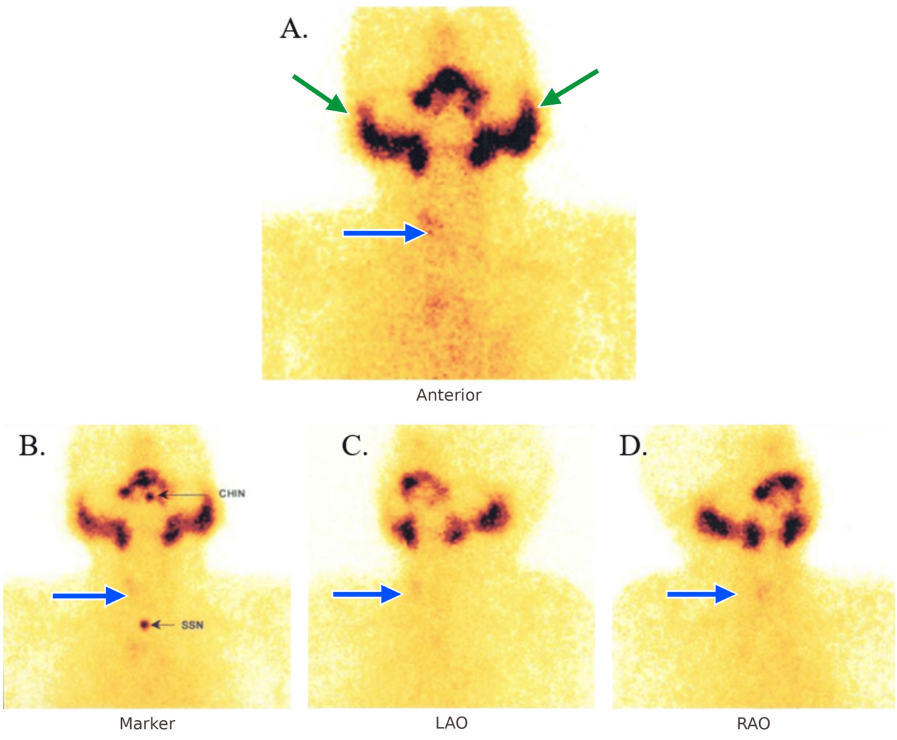


FIGURE 1: Technetium-99m pertechnetate thyroid scintigraphy

(A) Anterior view. (B) Marker view, with markers on the chin and suprasternal notch. (C) Left anterior oblique view. (D) Right anterior oblique view. Blue arrows mark the thyroid bed, which shows negligible tracer uptake on all views. Green arrows (A) mark physiological tracer uptake in the salivary glands. Uptake was assessed visually and was not quantified. SSN: suprasternal notch; LAO: left anterior oblique; RAO: right anterior oblique

On D5, a diagnosis of probable subacute thyroiditis in the thyrotoxic phase was made on the basis of the

painful, tender thyroid, the raised inflammatory markers, the thyrotoxic thyroid function tests and the negligible tracer uptake. No single finding established the diagnosis, and thyroid antibodies, thyroid ultrasound, serum thyroglobulin and cytology were not available at the time. The differential diagnoses considered, and the findings that argued against each, are summarized in Table 4. Excess levothyroxine intake was considered unlikely, because she had been taking the same low dose before this illness, and because excess thyroid hormone intake does not cause thyroid pain, tenderness or an intense inflammatory response [2,5]. Levothyroxine remained on hold. Because the thyrotoxicosis was attributed to the release of stored hormone rather than new hormone synthesis, antithyroid drugs were not given [1,5].

Differential diagnosis	Findings that argued against it in this patient
Excess levothyroxine intake (over-replacement)	Same low dose (50 µg daily, about 0.65 µg/kg/day) as before the illness; painful, tender gland; raised CRP and ESR. Serum thyroglobulin was not measured, and no earlier thyroid function results were available.
Graves' disease	Negligible tracer uptake; no bruit, goiter or eye signs.
Toxic adenoma or toxic multinodular goiter	Negligible tracer uptake; gland not enlarged.
Painless (silent) thyroiditis	Thyroid pain and tenderness; raised CRP and ESR.
Painful Hashimoto thyroiditis	No goiter; symptoms resolved within about four weeks without glucocorticoids. Thyroid antibodies negative on D188. Ultrasound and cytology were not available, so it cannot be excluded.
Conversion of Hashimoto thyroiditis to Graves' disease	Thyrotoxicosis resolved after levothyroxine was stopped; negligible tracer uptake; thyroid antibodies negative on D188.
Acute suppurative thyroiditis	Normal total leukocyte count; uptake absent in both lobes rather than a focal defect.
Drug- or iodine-induced thyrotoxicosis	No amiodarone or lithium and no recent iodinated contrast.

TABLE 4: Differential diagnoses considered

No single finding established the diagnosis. CRP: C-reactive protein; ESR: erythrocyte sedimentation rate

At review on D34, about four weeks after diagnosis, the palpitations and tremulous voice had resolved; the neck pain had settled about 10 days after presentation. The CRP had fallen from 235.2 mg/L to 2.63 mg/L, the total T3 (1.32 ng/mL) and total T4 (7.78 µg/dL) were within the reference range, and the TSH was rising at 0.25 µIU/mL, consistent with a transitional euthyroid phase. The ESR, however, remained raised at 78 mm in the first hour and 116 mm in the second hour. Propranolol was continued, and levothyroxine remained on hold. Thyroid function was not tested again until the next review.

At the next review on D67, 66 days after levothyroxine was stopped, her TSH had risen to 90.3 µIU/mL and her total T3 was low at 61.21 ng/dL, while her total T4 was within the reference range at 8.27 µg/dL (Table 3). These tests were done at a different laboratory, with different units and reference ranges, and free T4 was not measured. She had no symptoms of hyperthyroidism or hypothyroidism at this review, and she had taken no levothyroxine since D1. Propranolol was stopped, and levothyroxine 50 µg once daily was restarted. Her diabetes and antihypertensive treatment were continued, with a plan to monitor thyroid function and adjust the levothyroxine dose during recovery. This was the last recorded clinical review.

Thyroid peroxidase and thyroglobulin antibodies were measured on D188, about six months after presentation, to assess the cause of her hypothyroidism. Both were within the reference ranges: anti-thyroid peroxidase 12.66 IU/mL (reference 0-25) and anti-thyroglobulin 25.63 IU/mL (reference 5-100), measured by chemiluminescence immunoassay.

Discussion

Although this patient was older than most people with subacute thyroiditis, in whom incidence peaks in the fifth decade of life [4], her illness broadly followed the expected course. Her TSH was suppressed on D4, recovering on D34 and raised on D67, consistent with the thyrotoxic, transitional euthyroid and hypothyroid phases [1,3]. Final recovery could not be assessed because follow-up ended on D67.

No single finding established the diagnosis (Table 4). Negligible uptake argued strongly against Graves'

disease and toxic nodular disease, in which uptake is normal or increased [2,6], but it does not separate destructive thyroiditis from excess exogenous hormone. In one study, a technetium uptake cut-off of 1.55% separated Graves' disease from subacute thyroiditis with an accuracy of 92.9% [16]; uptake was not quantified in this patient. Because she was taking levothyroxine when she presented, over-replacement had to be considered. Serum thyroglobulin can help in this setting, because it is raised in thyroiditis but low when thyrotoxicosis is caused by exogenous hormone [5]; it was not measured here. Over-replacement was nonetheless unlikely. She had been taking the same low dose before this illness, and excess hormone intake would not explain her painful, tender gland or her intense inflammatory response [2,5]. No earlier thyroid function results were available, however, to confirm her baseline status.

A raised ESR and CRP in a patient with a painful thyroid support subacute thyroiditis, and the fall in CRP from 235.2 mg/L to 2.63 mg/L by D34 tracked resolving inflammation [2,17]. A CRP of this level is not specific, however, and bacterial infection also had to be considered. The normal leukocyte count and the absence of uptake in both lobes, rather than a focal defect, made acute suppurative thyroiditis unlikely [2]. The ESR fell more slowly and was still raised on D34. ESR rises and falls more slowly than CRP and is also increased by anemia and older age, both present in this patient [18].

The diagnosis was delayed. Her neck pain was first treated as a seasonal viral infection, and she received antibiotics twice before the diagnosis was made: from the general practitioner, and empirically at our hospital before blood results were available. This pattern is common. In a series of 121 patients with subacute thyroiditis, 58.7% received antibiotics before diagnosis, and the median time to diagnosis was longer in those who did (28 vs. 20 days) [19]. When she first saw the general practitioner, she had not yet developed a tremor, a tremulous voice or anxiety, which may have made thyrotoxicosis harder to suspect.

Treatment was supportive. Propranolol controlled her adrenergic symptoms, and antithyroid drugs were avoided because the gland was not making new hormone [1,2,5]. Pain is usually treated with nonsteroidal anti-inflammatory drugs (NSAIDs) or, in more severe cases, glucocorticoids [1,2]. A meta-analysis found that glucocorticoid treatment was associated with a lower incidence of permanent hypothyroidism than NSAID treatment [20]. Despite a CRP of 235.2 mg/L, her pain was managed with paracetamol, and she did not receive NSAIDs or glucocorticoids.

To find comparable cases, we searched PubMed on 7 November 2026 for case reports in English, using ("subacute thyroiditis" OR "de Quervain thyroiditis") AND (levothyroxine OR hypothyroidism OR Hashimoto). Of the 148 records returned, three described subacute thyroiditis in a patient already taking levothyroxine [7,14,15]. Screening the first 50 results of the same search in Google Scholar, and the reference lists of the reports found, added three more [8,12,13]. The six reports are summarized in Table *5*. In five, levothyroxine had been prescribed for Hashimoto thyroiditis or primary hypothyroidism; in the sixth, it had been taken for six years after a hemithyroidectomy [15].

Report	Patient and background	TSH at presentation	ESR	CRP	Key investigation	Treatment and outcome
Chopra et al. [14]	Woman aged 49 at diagnosis of primary hypothyroidism of unclear cause; thyroxine 200 µg daily for about 16 months	Not reported; free thyroxine index slightly raised (3.4; reference 1.6–3.3)	75 mm/h	Not reported	24-hour radioiodine uptake 1%	Stopped thyroxine herself; prednisone; TSH 138 µU/mL three months later, thyroxine restarted; painful goiter recurred; Riedel's struma at partial thyroidectomy a year after onset
Mousa et al. [7]	69-year-old woman; Hashimoto thyroiditis and multinodular goiter; levothyroxine for 7 years	3.94 µIU/mL (euthyroid)	23 mm/h	3.2 mg/L	Hypoechoic, hypovascular area on ultrasound	Methylprednisolone; symptoms resolved by day 10 of treatment
Yalin et al. [12]	42-year-old woman; Hashimoto thyroiditis and multinodular goiter; on levothyroxine	Normal	Mildly raised (up to 24 mm/h)	Mildly raised (30.4 mg/L at first visit)	Enlarging hypovascular areas suspicious for lymphoma; giant cells on fine-needle aspiration	Levothyroxine stopped, then restarted as TSH rose; no thyrotoxicosis over 6 months; declined glucocorticoids
Leong et al. [8]	52-year-old woman; Hashimoto thyroiditis with hypothyroidism for 10 years; levothyroxine 75 µg	0.05 µIU/mL (low)	Not reported	Not reported	Heterogeneous echotexture with increased vascularity on ultrasound	Levothyroxine stopped; euthyroid without treatment after 4 weeks
Saha et al. [15]	36-year-old woman; levothyroxine for 6 years after right hemithyroidectomy for a benign nodule; onset after the second dose of an mRNA COVID-19 vaccine	<0.01 mIU/L (suppressed); free T4 at the upper limit of normal	2 mm/h	Not reported	Thyroid antibodies negative; no imaging reported	Levothyroxine withheld; no glucocorticoids; TSH 14.23 mIU/L at 4 weeks, levothyroxine restarted
Puškarević et al. [13]	69-year-old woman; Hashimoto thyroiditis and multinodular goiter on levothyroxine; after SARS-CoV-2 infection	1.35 µIU/mL (normal, day 14 of illness)	115 mm/h	113.1 mg/L	Enlarged, hypoechoic gland with inflammatory lymph nodes on ultrasound	Ibuprofen and antibiotics; levothyroxine continued; pain settled after 15 days of treatment; CRP 6.5 mg/L at one month; euthyroid throughout
Present case	Woman in her 70s; primary hypothyroidism of undetermined cause for about 15 years; levothyroxine 50 µg	0.02 µIU/mL (suppressed)	78 mm/h	235.2 mg/L	Negligible uptake on technetium-99m scintigraphy	Levothyroxine withheld for 66 days; propranolol; TSH 90.3 µIU/mL on D67; levothyroxine restarted

TABLE 5: Published cases of subacute thyroiditis in patients already taking levothyroxine, compared with the present case

TSH: thyroid-stimulating hormone; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein

Chopra et al. described a woman in whom primary hypothyroidism of unclear cause had been diagnosed at 49 years of age and treated with thyroxine 200 µg daily [14]. About 16 months later, she developed fever, a painful, tender goiter and clinical hyperthyroidism, with a slightly raised free thyroxine index, a 24-hour radioiodine uptake of 1% and an ESR of 75 mm/h. She stopped thyroxine herself and was given prednisone. Three months later her TSH was 138 µU/mL; the painful goiter then recurred, and partial thyroidectomy a year after onset showed Riedel's struma [14]. Mousa et al. described a 69-year-old woman with Hashimoto thyroiditis on levothyroxine for seven years who, like our patient, received analgesics and antibiotics before the diagnosis was made; she remained euthyroid, had little or no rise in ESR and CRP, and responded to methylprednisolone [7]. Yalin et al. reported a 42-year-old woman on levothyroxine whose thyroid function stayed normal and whose ESR and CRP were only mildly raised; enlarging hypovascular areas on ultrasound raised concern for lymphoma until fine-needle aspiration showed giant cells consistent with subacute

thyroiditis [12].

Leong et al. described a 52-year-old woman with Hashimoto thyroiditis and hypothyroidism for 10 years, treated with levothyroxine, who developed mild thyrotoxicosis after a sore throat; levothyroxine was stopped, and she was euthyroid without treatment four weeks later [8]. Saha et al. described a 36-year-old woman who had taken levothyroxine for six years after a right hemithyroidectomy for a benign nodule and developed a tender left lobe, palpitations and heat intolerance after the second dose of an mRNA COVID-19 vaccine [15]. Her TSH was below 0.01 mIU/L, with free T4 at the upper limit of normal and an ESR of 2 mm/h; levothyroxine was withheld without glucocorticoids and restarted when her TSH rose above the reference range, to 14.23 mIU/L at four weeks. Puškarević et al. described a 69-year-old woman with Hashimoto thyroiditis and multinodular goiter on levothyroxine who developed subacute thyroiditis after SARS-CoV-2 infection; despite an ESR of 115 mm/h and a CRP of 113.1 mg/L, she remained euthyroid on levothyroxine, her pain settled after 15 days of treatment, and her CRP had fallen to 6.5 mg/L at one month [13].

Of these patients, only ours and the patient described by Chopra et al. had raised thyroid hormone levels, and in that patient the rise was slight [14]; our patient's CRP was also the highest reported. After thyroxine was stopped, TSH rose steeply in both: to 90.3 μIU/mL on D67 in our patient and to 138 μU/mL three months later in that patient [14]. In the patients described by Yalin et al. and Saha et al., levothyroxine was restarted as TSH rose [12,15], whereas the patient described by Leong et al. was euthyroid without treatment four weeks later [8]. The course after the thyrotoxic phase probably depends on how much functioning thyroid tissue remains. In the published cases, it may also have been modified by pre-existing Hashimoto thyroiditis [12]; in our patient, the cause of hypothyroidism was not established, and thyroid antibodies measured on D188 were negative.

Her TSH of 90.3 μIU/mL on D67 cannot be attributed to subacute thyroiditis alone. Two processes probably contributed. First, the hypothyroid phase of subacute thyroiditis follows depletion of hormone stores in damaged follicles [1,3]. Second, levothyroxine had been withheld for 66 days in a patient whose own gland had needed replacement for about 15 years, so her TSH would probably have risen even without thyroiditis. A third process, further loss of thyroid reserve from autoimmune thyroiditis, is less likely. Autoimmune thyroiditis is the commonest cause of primary hypothyroidism in iodine-sufficient regions [21], and in a series of 226 patients with subacute thyroiditis, coexisting Hashimoto thyroiditis predicted later hypothyroidism [22]. Her thyroid peroxidase and thyroglobulin antibodies, measured on D188, were negative, although a single negative result does not exclude autoimmune thyroiditis. The contribution of each process cannot be separated.

With negative antibodies and no history of thyroid surgery, radioiodine treatment or neck radiation, the cause of her hypothyroidism remains unexplained. An earlier, unrecognized episode of destructive thyroiditis is one possibility: Chopra et al. suggested this for their patient, whose primary hypothyroidism was also of unclear cause with negative thyroid antibodies [14], and some patients remain hypothyroid after subacute thyroiditis [4].

Her low replacement dose suggests that she retained some functioning thyroid tissue. Her dose was about 0.65 μg/kg/day (50 μg at 77 kg), whereas full replacement usually requires about 1.6 μg/kg/day, although older adults often need less [23]. Subacute thyroiditis probably involved this residual tissue: inflammatory destruction of its follicles would have released stored hormone into the circulation and made her thyrotoxic despite long-standing hypothyroidism. A similar sequence has been described with immune checkpoint inhibitor-induced thyroiditis in a man with autoimmune hypothyroidism maintained on a similar dose of 0.6 μg/kg/day. He developed a thyrotoxic phase followed by a severe exacerbation of hypothyroidism and a much higher levothyroxine requirement [9]. In a population-based cohort, 15% of patients with subacute thyroiditis were receiving thyroid hormone replacement at long-term follow-up [4], so her requirement may also rise permanently.

The D67 results were also discordant. A TSH of 90.3 μIU/mL would usually be accompanied by a low T4, yet her total T4 was within the reference range, and she had no symptoms of hypothyroidism. Irregular levothyroxine intake before a blood test is a recognized cause of a raised TSH with a normal T4 [24], but she had taken no levothyroxine since D1. Other explanations are possible. TSH can lag behind changes in circulating thyroid hormone, remaining suppressed after thyrotoxicosis has resolved or rising before hormone levels recover, so results taken while thyroid function is changing can disagree [24]. Total T4 also depends on the concentration of binding proteins, which can change total hormone levels without changing free hormone levels [24]. Finally, the tests were done at a different laboratory, and interference in TSH assays can produce falsely high results [24]. Free T4 was not measured, and the tests were not repeated before levothyroxine was restarted, so these explanations could not be distinguished. The normal total T4 may explain why she had no symptoms at this review, and the clinical presentation of hypothyroidism also varies with age [21].

Thyroid function was not tested between D34, when her TSH was still below the reference range, and D67, although serial testing every two to eight weeks is recommended after the diagnosis [1]. Testing during this interval would probably have detected the rising TSH earlier. Because a hypothyroid phase often follows the

thyrotoxic phase [1,3], this monitoring matters most in patients who already depend on levothyroxine, as their glands have little reserve when replacement is withheld; this suggestion rests on a single case.

Two other conditions deserve mention, because autoimmune thyroiditis is the commonest cause of primary hypothyroidism in iodine-sufficient regions [21]. Painful Hashimoto thyroiditis can mimic subacute thyroiditis, with a tender goiter, a raised ESR and low technetium uptake [10]. It usually occurs in patients with a long-standing goiter, and the pain tends to persist or recur, with a variable response to glucocorticoids, sometimes requiring thyroidectomy [10]. Our patient had no goiter, and her symptoms resolved within about four weeks without glucocorticoids, which favors subacute thyroiditis. Her thyroid peroxidase and thyroglobulin antibodies, measured on D188, were also negative, which argues against an autoimmune thyroiditis; without ultrasound or cytology, however, painful Hashimoto thyroiditis cannot be completely excluded. Conversion of Hashimoto thyroiditis to Graves' disease can also cause thyrotoxicosis in a patient on levothyroxine. It is often first mistaken for over-replacement and is suggested by thyrotoxicosis that persists after levothyroxine is stopped and by increased uptake on scintigraphy [11]. Neither feature was present in our patient.

This report has limitations. The diagnosis is probable rather than definitive, because serum thyroglobulin, thyroid ultrasound and cytology were not available, thyroid antibodies were measured only on D188, and uptake on scintigraphy was not quantified. No thyroid function results from before this illness were available, so her baseline thyroid status on levothyroxine is not documented. Only total, not free, thyroid hormones were measured, and the D67 tests were done at a different laboratory, so the discordant D67 results could not be resolved. Thyroid function was not measured between D34 and D67, and apart from the antibody test on D188, follow-up ended on D67. Her lowest thyroid function, her recovery and her long-term levothyroxine requirement are therefore not known.

Conclusions

Subacute thyroiditis should be considered in any patient with a painful, tender thyroid and thyrotoxicosis, including older adults already receiving levothyroxine for hypothyroidism. In such patients, the thyrotoxic phase can be mistaken for over-replacement and neck pain for a throat infection, and either can delay the diagnosis. In this patient, the painful gland, raised inflammatory markers and negligible uptake on scintigraphy favored subacute thyroiditis, but painful Hashimoto thyroiditis and other alternatives could not be completely excluded. When exogenous thyroid hormone remains a diagnostic concern, serum thyroglobulin may help to distinguish it from destructive thyroiditis. Her TSH rose steeply at about two months, reflecting both the hypothyroid phase and the withdrawal of replacement. In patients who depend on levothyroxine, monitoring thyroid function once the thyrotoxic phase settles may allow replacement to be resumed before such a rise. Longer follow-up would be needed to establish her eventual thyroid status and levothyroxine requirement.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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