

Sustained fever resolved promptly after total thyroidectomy due to huge Hashimoto's fibrous thyroiditis

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Abstract We encountered a 55-year-old female patient with Hashimoto's thyroiditis who showed persistent fever, and could not find any source of fever other than the large nontender goiter. Her fever continued with positive CRP for 6 months. Although we did not assume that the inflammation was related to Hashimoto's thyroiditis, total thyroidectomy was performed for cosmetic reasons; however, fever was resolved immediately after thyroidectomy. Pathological diagnosis was Hashimoto's chronic thyroiditis. Immunohistochemical staining showed that the follicular cells were positive for IL-1alpha, IL-1beta, and TNF-alpha. We believed that fever was induced by inflammatory cytokines produced in thyroid. The case indicated that Hashimoto's thyroiditis with nontender goiter could cause idiopathic fever.

Keywords Hashimoto's thyroiditis · Thyroidectomy · Inflammation · Fever of unknown origin · Nontender goiter

Rare cases of painful Hashimoto's thyroiditis that present with persistent fever and thyroid tenderness have been reported [1–4]. Although most cases of painful Hashimoto's thyroiditis are resolved by the administration of glucocorticoids, total thyroidectomy is required in some cases [1, 2, 5, 6]. Usually, thyroiditis with nontender goiter does not cause a systemic inflammatory reaction. However, we encountered a patient with Hashimoto's thyroiditis who

showed persistent fever, and could not find any source of fever other than the large nontender goiter. The fever was resolved immediately after thyroidectomy. Herein we report this case.

Case report

A 55-year-old woman was admitted to hospital in September 2002, with a 2-week history of fever. She had been diagnosed as having Hashimoto's thyroiditis 20 years earlier, and had remained euthyroid without medication. On physical examination, there were no abnormalities except for large goiter and fever (39.0°C). White cell count was 9,000/mm³. C-reactive protein (CRP) was 21.1 mg per deciliter. There was no sign of nonthyroidal local infection including tuberculosis. Specimens of blood and urine were obtained for culture, but did not yield any bacteria. Although the patient was treated with antibiotics, CRP remained positive. The cause of inflammation was not demonstrated by further close examination. The patient was referred to our hospital in November because only the thyroid was diffusely imaged by gallium scintigraphy.

Thyroid-function tests in our hospital showed subclinical hypothyroidism with slightly elevated serum thyrotropin level, at 6.092 µU/ml (normal range: 0.3–5.0), FT4 at 0.76 ng/dl (0.7–1.6), FT3 at 3.19 pg/ml (1.7–3.7), and a positive test for antimicrosomal antibody, at 1:102,400. The goiter was diffuse and the estimated volume on ultrasonography was 300 cc. The patient reported that there was neither spontaneous pain nor tenderness of goiter. The body temperature was 37.5°C, and CRP was 4.4 mg/dl. She also showed anemia, probably due to chronic inflammation. We assumed the slight possibility that inflammation was related to Hashimoto's thyroiditis at that point.

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Thereafter, her fever continued with positive CRP, at 3.89–18.37 mg/dl.

The patient visited our hospital again and desired thyroidectomy for cosmetic reasons in February 2003. A total thyroidectomy was performed on March 17. Table 1 shows laboratory data before thyroidectomy. Postoperatively, CRP decreased dramatically, and was negative on postoperative day 18 (Fig. 1). Anemia and hypoalbuminemia

Table 1 Laboratory data before thyroidectomy

<i>Blood cell count</i>		
WBC	6,000/ μ l	(3,500–9,000)
Monocyte	4%	(4–7)
Neutrocyte	79%	(45–70)
Eosinocyte	1%	(0.2–5)
Lymphocyte	14%	(30–45)
RBC	275×10^4 / μ l	(380×10^4 – 500×10^4)
Hb	7.1 g/dl	(12–16)
Ht	22.80%	(36–48)
MCV	82.9 fl	(83–100)
MCH	25.8 pg	(28–35)
MCHC	31.1 g/dl	(32–36)
PLT	43.0×10^4 / μ l	(12×10^4 – 500×10^4)
<i>Thyroid function</i>		
FT4	0.62 ng/dl	(0.7–1.6)
TSH	6.101 μ IU/ml	(0.3–5.0)
MCPA	1:102,400	(<100)
TGPA	1:1,638,400	(<100)
<i>Blood chemistry</i>		
TP	8.8 g/dl	(6.5–8.3)
Alb	2.7 g/dl	(3.8–5.2)
T-Bil	0.3 mg/dl	(0.2–1.0)
AST	11 U/l	(5–40)
ALT	12 U/l	(5–35)
γ -GTP	50 U/l	(0–40)
ALP	368 U/l	(105–340)
LDH	126 U/l	(105–215)
ZTT	52.7 K-U	(4–12)
BUN	8 mg/dl	(8–20)
Cre	0.6 mg/dl	(0.5–1.3)
FBG	117 mg/dl	(70–110)
CRP	9.7 mg/dl	(0–0.5)
<i>Serological data</i>		
IgG	3,940 mg/dl	(870–1,700)
IgA	243 mg/dl	(110–410)
IgM	111 mg/dl	(46–260)
IL-6	77.0 pg/ml	(<4.0)
IL2R	1,430 U/ml	(220–530)

Normal values in parentheses. FBG, fasting blood glucose; CRP, C-reactive protein; IL, interleukin; MCPA, microsome particle agglutination; TGPA, thyroglobulin particle agglutination

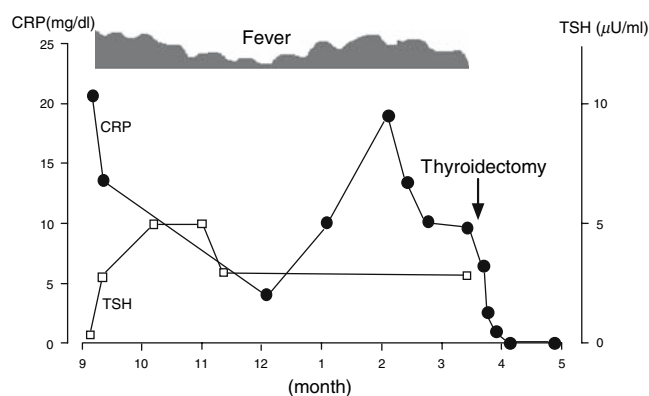


Fig. 1 Fever resolved by thyroidectomy in a 55-year-old woman with Hashimoto's thyroiditis and nontender goiter. Closed circle: serum C-reactive protein (CRP) levels Open square: serum thyrotropin (TSH) levels

was resolved 3 months after thyroidectomy. We believed that these abnormalities were due to persistent inflammation. ZTT was normalized 2 years after thyroidectomy.

The isolated thyroid weight was 370.6 g, and the pathological diagnosis was Hashimoto's chronic thyroiditis. Histopathological features were mild fibrous change, lymphocytic and plasmacytic infiltration, and oxyphil changes in follicular cells (Fig. 2). There was no evidence of infectious disease including tuberculosis and acute suppurative thyroiditis. Immunohistochemical staining was performed (Fig. 3); Oxyphilic follicular cells were positive for IL-1alpha, IL-1beta, and TNF-alpha, and negative for IL-6. A small number of IL-6-positive lymphocytes were focally observed.

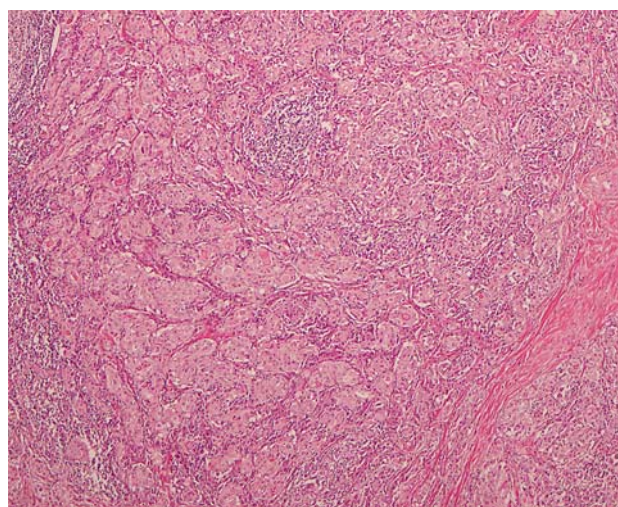


Fig. 2 Mild fibrous change, lymphocytic and plasmacytic infiltration, and oxyphil changes in follicular cells, and degenerated thyroid follicular structure. (Hematoxylin-eosin, $\times 40$)

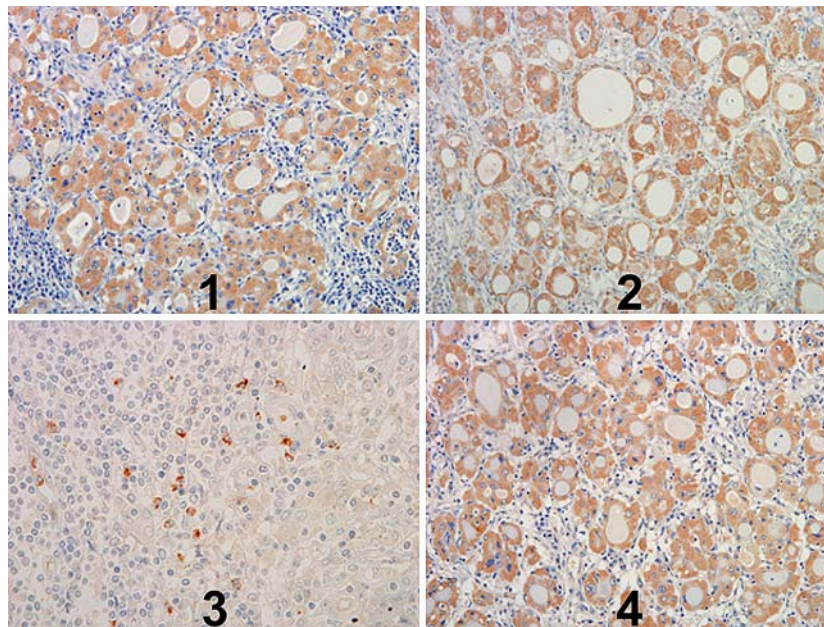


Fig. 3 Oxyphilic follicular cells were positive for IL-1alpha, IL-1beta, and TNF-alpha, and negative for IL-6. A small number of IL-6-positive lymphocytes were focally observed. Immunohistochemical staining was performed using the following primary antibodies: (1) IL-1alpha (Alpha 29, monoclonal, 1:200, Immunotech, Marseille, France), (2) IL-1beta (H-153, monoclonal, 1:500, Santa Cruz Biotech, Santa Cruz, CA, USA), (3) IL-6 (1:6000, Gilbertsville, PA, USA), and

(4) TNF-alpha (2C8, monoclonal, 1:2000, Biogenesis, Kingston, NH, USA). For this staining, thick sections (4 micron) were cut from formalin-fixed and paraffin-embedded tissue blocks. Pretreatment for IL-1beta and IL-6 was done by an autoclave (121°C, 15 min). Localization of bound antibodies was performed with a DAKO (Carpinteria, CA, USA) labeled streptavidin-biotin kit (K0675)

The patient recovered well, and has shown no fever or anemia for 3 years following the operation.

Discussion

Bando et al. reported the first case of acute exacerbation of Hashimoto's thyroiditis with a nontender thyroid [7]. Fever and inflammatory reaction were relieved by oral naproxen, and did not recur on withdrawal in their case. However, there was no conclusive evidence that the inflammation was due to thyroiditis in their case. Although thyroidectomy and resolution of inflammation may not be coincidental in our case as well, it is quite likely that the inflammation was caused by Hashimoto's thyroiditis because it was resolved right after thyroidectomy. According to this fact, inflammatory cytokines seemed to be produced only in thyroid. The results that the patient's follicular cells were positive for IL-1alpha, IL-1beta, and TNF-alpha which are well known as endogenous pyrogens by immunohistochemical staining support our notion [8].

Patients with painful Hashimoto's thyroiditis that required total thyroidectomy to relieve thyroid pain have been reported [1, 2, 5, 6]. Although corticosteroids are useful to relieve their symptoms, pain and fever relapse

following withdrawal in these cases. We did not administrate corticosteroids because there was a slight possibility of thyroid lymphoma. Since histopathologic features are altered by corticosteroids, it is difficult to make a correct diagnosis. Histopathologic features were similar to those of painful Hashimoto's thyroiditis in previous reports [2, 3, 6, 9].

The most important point the present case indicated is that Hashimoto's thyroiditis with nontender goiter can cause idiopathic fever. We believe that Hashimoto's thyroiditis should be noted as a cause of fever of unknown origin.

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