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An autopsy case of thyroid storm associated with chronic lymphocytic thyroiditis

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Abstract

A Japanese woman in her 30s was found dead on a mattress. She had had fever, cough, and dyspnea for about 2 weeks. Gross examination at autopsy revealed slight enlargement of the thyroid gland and histopathological examination resulted in a diagnosis of chronic lymphocytic thyroiditis. The concentration of triiodothyronine in the cadaveric blood was extraordinarily high, whereas that of thyroid stimulating hormone was below the detection limit. Autoimmune antibodies against thyroid tissue were positive. The cause of death was assumed to be congestive heart failure caused by thyroid storm associated with chronic lymphocytic thyroiditis. Systemic histopathological examination of tissues and postmortem biochemistry can enable a diagnosis in medicolegal autopsies.

Key words: Thyroid toxicosis, Hashimoto thyroiditis, postmortem biochemistry, medicolegal autopsy.

[1]

[1] **Abbreviations**: CRP, C-reactive protein; T3, triiodothyronine; T4, thyroxine; TSH, thyroid stimulating hormone.

1. Introduction

The thyroid hormones—triiodothyronine (T3) and thyroxine (T4)—influence the cardiovascular status via genomic and non-genomic actions on cardiomyocytes and effects on the peripheral circulation [1–3]. These hormones regulate several cardiac genes, including those for components of the contractile apparatus, calcium reuptake regulators in the sarcoplasmic reticulum, and beta-adrenergic receptors. Additionally, thyroid hormones affect the ion channels in cardiomyocyte cell membranes and decrease systemic vascular resistance. Thus, the combination of hypervolemia, reduced myocardial contractile reserve, and tachyarrhythmia associated with hyperthyroidism can result in high-output cardiac failure.

Chronic lymphocytic thyroiditis, also known as Hashimoto thyroiditis, is the commonest cause of hypothyroidism; however, it rarely presents as transient hyperthyroidism, which is caused by destruction of the thyroid follicles, resulting in massive release of thyroid hormones [4].

We here report an autopsy case of hyperthyroidism associated with chronic lymphocytic thyroiditis that was not diagnosed antemortem.

2. Case presentation

2.1. Case history

A Japanese woman in her 30s was found dead on a mattress. She had had fever, cough, and dyspnea, for about 2 weeks for which she had taken over-the-counter cold medicines without being assessed by a medical practitioner. She had also complained of intolerance to heat. Neither illicit drugs nor weight-reducing medications were found at the scene of death. The deceased had no history of serious illness.

2.2. Autopsy findings

To identify the cause of death, medicolegal autopsy was performed 22 h postmortem. The deceased was 156 cm in height and 47 kg in weight; body mass index was 19.3 kg m^{-2}. She did not have hyperpigmentation of the skin. The heart, which weighed 355 g, had neither coronary atherosclerosis nor hypertrophy. The left ventricle showed mild dilatation. There was a small fibrotic lesion with scattered reddish spots in the posterior wall of the left ventricle (Fig. 1A). The left and right lungs weighed 350 and 571 g, respectively, and were edematous and congested. The lower lobes of both lungs showed centrilobular pale pink lesions with white purulent matter. The left and right pleural cavities contained 570 and 800 mL, respectively, of light reddish effusion. The thyroid gland had a large pyramidal lobe and weighed 26.6 g (the mean weight of the thyroid of age-matched Japanese women is 15.34 g and the standard deviation 4.91) (Fig. 1B) [5]. The pituitary gland was congested and showed no neoplastic changes.

Histological examination of the thyroid gland revealed moderate fibrosis and infiltration by

lymphocytes and plasma cells forming lymphoid follicles with germinal center (Fig. 2A). The epithelial cells showed eosinophilic change with several Hürthle cells and anisokaryosis. These findings are consistent with chronic lymphocytic thyroiditis. The heart showed focal fibrosis, interstitial edema, and microvessel dilatation with petechial hemorrhages with no evidence of inflammatory reaction and other pathological changes (Fig. 2B). Immunohistochemical analysis of the pituitary gland showed negative staining for thyroid stimulating hormone (TSH) (Fig. 2C) and positive staining for adrenocorticotropic hormone (Fig. 2D), prolactin, and growth hormone. Hepatic sinusoidal dilatation was detected, predominantly in the centrilobular area (Fig. 2E). Edematous fluid was shown in the alveoli and hemosiderin-laden macrophages were identified in the lungs by Berlin blue staining (Fig. 2F). Infiltrates of neutrophils and macrophages into the intra- and peri-bronchiolar spaces in the lower lobes of both lungs indicated mild bronchopneumonia.

The free T3 concentration was markedly higher than normal in postmortem femoral blood, whereas the TSH concentration was low (Table). C-reactive protein (CRP) and N-terminal prohormone brain natriuretic peptide concentrations in femoral blood were 0.13 mg dL^{-1} and 1730 pg mL^{-1}, respectively. Autoimmune antibodies against thyroid tissue were detected. Toxicological screening was negative.

3. Discussion

The postulated cause of the present individual's death was congestive heart failure in a setting of thyroid storm caused by destruction of thyroid follicles related to autoimmune thyroiditis that was not diagnosed antemortem. Concomitant bronchopneumonia was relatively mild, and the postmortem concentration of the inflammatory marker CRP was relatively low.

Sudden death is sometimes attributable to known thyroid disorders [6]; additionally, several deaths caused by undiagnosed thyroid disease have been reported [7–11]. Even in individuals with known thyroid disorders, most sudden deaths are related to hyperthyroidism caused by Graves disease and toxic multinodular goiter [6]. To the best of our knowledge, death caused by hyperthyroidism based on undiagnosed chronic thyroiditis has never been reported.

Hyperthyroidism can induce congestive heart failure, which is mediated by a combination of hypervolemia, reduced myocardial contractile reserve, and tachyarrhythmia related to genomic and non-genomic actions of thyroid hormones [1–3, 12–14]. Chronic lymphocytic thyroiditis, which is the commonest cause of acquired hypothyroidism, rarely presents as transient hyperthyroidism, which is caused by massive release of stored thyroid hormones as a result of inflammation-mediated destruction of the thyroid follicles [4].

Thyroid storm, a life-threatening fulminant form of hyperthyroidism, has a high mortality rate of above 10% [12, 13]. Diagnostic criteria for thyroid storm include clinical features and high concentrations of thyroid hormones [15, 16]. Although the presence of these criteria cannot be

reliably established postmortem, our case's features of probable antemortem fever and postmortem evidence of congestive heart failure are consistent with thyroid storm. Infection, surgery, and other events can reportedly precipitate thyroid storm; however, an absence of identifiable risk factors is not unusual. In the present case, concomitant bronchopneumonia may have contributed to precipitating thyroid storm.

Histological examination of the myocardium revealed focal myocardial fibrosis without overt coronary atherosclerosis, which is in accordance with previous case reports. Several cases of hyperthyroidism with histologically confirmed focal myocardial necrosis [17, 18] and of clinically diagnosed acute myocardial infarction with normal coronary angiographic findings [19, 20] have been reported.

Although the causes of focal myocardial necrosis in an individual with hyperthyroidism are unclear, the following three mechanisms have been proposed. The first is an imbalance between oxygen supply and demand in the cardiomyocytes. By exerting cardiac chronotropic and inotropic effects, thyroid hormones induce a hyperdynamic circulation, which results in increased oxygen demand [1]. The second mechanism is coronary spasms, which can reportedly be triggered by thyroid hormones [21]. The third is thromboembolism of the coronary arteries. The incidence of atrial fibrillation is higher in patients with thyrotoxicosis than in the general population [3], and atrial fibrillation is a major risk factor for arterial thromboembolism. Hyperthyroidism also shifts the hemostatic system towards a more coagulative and less fibrinolytic state [22].

In the present case, focal fibrosis was limited to the posterior wall, suggesting local rather than diffuse ischemia associated with a systemic increase in oxygen demand. Whether the present individual had had coronary spasms or atrial fibrillation could not be ascertained postmortem. No coronary thrombi were identified macroscopically or microscopically, and no other organs showed infarction. For these reasons, we were unable to determine the mechanism underlying the patchy myocardial fibrosis in the absence of coronary atherosclerotic lesions.

Because the gross appearance is close to normal in some individuals with fatal thyroid disease [6], it is difficult to assess the contribution of thyroid disease to causing death purely on the basis of macroscopic autopsy findings. Because symptoms and clinical signs of endocrine disorders are due to an excess or decrease in bioactive hormones, evaluation of hormone profiles is necessary to establish a postmortem diagnosis of an endocrine disorder.

The postmortem diagnosis of thyroid dysfunction is challenging because no postmortem reference values have been defined. Postmortem concentrations of free T3 and free T4 have been variously reported as both higher and lower than antemortem values [23–25].

The diagnostic value of serum TSH concentration is also controversial. While Edston et al. reported

generally low TSH concentrations in postmortem blood [25], Coe reported that TSH concentrations are stable within the first 24 h postmortem [23]. In the present case, postmortem examination was performed within 24 h of death and the TSH concentration in blood collected during the postmortem was below the detection limit, which is much lower than that reported for individuals with pathologically normal thyroid glands [25]. The very low TSH may reflect negative feedback caused by hyperthyroidism. The negative staining for TSH in the pituitary gland is consistent with this possibility [26].

The present individual had had cold-like symptoms for 2 weeks; this may correspond to the duration of her hyperthyroid state. Nabhan et al. [4] reported that the duration of hyperthyroidism with spontaneous resolution in patients with autoimmune thyroiditis ranged from 1 to 5 months, which is comparable to 2 weeks duration in our case. In living individuals, administration of levothyroxine causes increases in blood T4 concentrations and suppression of TSH within 74 h [27], suggesting that a 2-week duration of hyperthyroidism would be long enough to result in abnormalities in laboratory thyroid-related tests.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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Table

Results of postmortem testing of thyroid function and autoimmune antibodies to thyroid tissue.

		clinical reference
Thyroid function		
free T4	2.63 ng dL^{-1}	(0.9 – 1.7 ng dL^{-1})
free T3	> 32.5 pg⁄ mL^{-1}	(2.3 – 4.3 pg mL^{-1})
TSH	< 0.005 µIU mL^{-1}	(0.50 – 5.0 µIU mL^{-1})
Autoimmune antibodies		
TgAb	45 IU mL^{-1}	(< 28 IU mL^{-1})
TPOAb	339 IU mL^{-1}	(< 16 IU⁄ mL^{-1})
TRAb	29.6%	(< 10%)

Hormones and autoimmune antibodies were quantified in the femoral blood. T3, triiodothyronine; T4, thyroxine; TgAb, anti-thyroglobulin antibody; TPOAb, anti-thyroid peroxidase antibody; TRAb,

TSH receptor antibody; TSH, thyroid stimulating hormone.

Figure Legends

Fig. 1. Macroscopic appearances of the myocardium and thyroid gland.

A) Photograph of a cross section of the left ventricle revealing mild dilatation and fibrosis with scattered hemorrhage (the area indicated by the black arrows). B) Photograph of the thyroid gland showing a large pyramidal lobe.

Fig. 2. Histological examinations.

A) Photomicrograph of section of the thyroid gland revealing moderate fibrosis and lymphocyte and plasma cell infiltration forming lymphoid follicles with germinal center. Epithelial cells show eosinophilic change with several Hürthle cells and anisokaryosis. These findings are consistent with chronic lymphocytic thyroiditis (hematoxylin and eosin staining, bar = 50 μm). B) Photomicrograph of a section of the posterior wall of the left ventricle showing fibrosis and microvessel dilatation with hemorrhages (hematoxylin and eosin staining, bar = 100 μm). Photomicrograph of an immunohistochemically stained section of the pituitary gland negative for thyroid stimulating hormone (TSH) (C) but positive for adrenocorticotropic hormone (ACTH) (D) (bars = 20 μm). E) Photomicrograph of a section of the liver revealing sinusoidal dilatation predominantly in the centrilobular areas, suggesting impairment of the hepatic venous outflow (hematoxylin and eosin staining, bar = 100 μm). F) Photomicrograph of a section of the lung showing congestion with edematous fluid (hematoxylin and eosin staining, bar = 50 μm). Berlin blue staining revealed hemosiderin-laden macrophages (inset, bar = 20 μm).