

Hepatic Failure Resulting From Thyroid Storm With Normal Serum Thyroxine and Triiodothyronine Concentrations

Chin-Sung Kuo^{1,2}, Wen-Ya Ma³, Yi-Chun Lin^{1,2}, Hong-Da Lin^{1,2*}

¹Division of Endocrinology and Metabolism, Department of Medicine, Taipei Veterans General Hospital, ²National Yang-Ming University School of Medicine, and ³Cardinal Tien Hospital, Taipei, Taiwan, R.O.C.

A 63-year-old male presented with productive cough, fever, palpitation, shortness of breath, and mental confusion. Fulminant hepatic failure occurred with high aminotransferase and severe jaundice. Thyroid function tests showed thyroid-stimulating hormone level of 0.7 $\mu\text{U}/\text{mL}$ (normal range, $<6.2 \mu\text{U}/\text{mL}$), with normal serum thyroxine and triiodothyronine levels. He died on post-admission day 5. Autopsy revealed diffuse hyperplasia of the thyroid gland, centrilobular necrosis of the liver, and congestion of the gastrointestinal tract, spleen, and adrenal glands. These pathological findings were compatible with decompensated hyperthyroidism. Thyroid storm may present with normal serum triiodothyronine, thyroxine, and hepatic failure. Such presentation is rare. [*J Chin Med Assoc* 2010;73(1):44–46]

Key Words: hepatic failure, hyperthyroidism, thyroid crisis

Introduction

Thyroid storm, or crisis, is a life-threatening exacerbation of hyperthyroidism in which there is evidence of decompensation in 1 or more organ systems.^{1,2} The clinical presentations include fever, tachycardia with arrhythmia, jaundice, congestive heart failure, and consciousness disturbance. Invariably, a precipitating factor can be identified that contributes to the progression of thyrotoxicosis to thyroid storm.² Infection is a common and important precipitating factor. Thyroid function tests in thyroid storm almost always reveal elevated serum triiodothyronine (T3) and thyroxine (T4) but suppressed thyroid-stimulating hormone (TSH). Normal serum T4 level (T3 thyrotoxic storm)¹ or normal serum T3 concentration (T4 thyrotoxic storm)^{3–6} are occasionally reported. To our knowledge, thyroid storm associated with both normal serum T3 and T4 levels is extremely rare. Here, a rare case of bronchopneumonia-precipitated thyroid storm presenting with

hepatic failure and normal serum T4 and T3 levels is reported.

Case Report

A 63-year-old man suffered from heart palpitation and chronic cough for 3 years. Thyroid function tests revealed a T3 level of 498 ng/dL (normal range, 85–165 ng/dL) and a T4 level of 16.6 $\mu\text{g}/\text{dL}$ (normal range, 6–12 $\mu\text{g}/\text{dL}$) 3 years before this admission. However, he did not seek any medical help before this admission. Productive cough, palpitation and shortness of breath worsened about 1 week before this admission. He was in a mentally confused state and was first sent to another hospital. On examination, he had a temperature of 38.2°C, respiratory rate of 22 breaths/min, blood pressure of 150/60 mmHg, and irregular heart rate of 120 beats/min with grade 5/6 systolic murmur over apex, with the liver palpable 3 cm below the right costal margin. Blood analysis



*Correspondence to: Dr Hong-Da Lin, Division of Endocrinology and Metabolism, Department of Medicine, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, R.O.C. E-mail: hdlin@vghtpe.gov.tw • Received: April 15, 2009 • Accepted: September 25, 2009

revealed white blood cell count of 18,100 with neutrophils predominating (87%). Chest X-ray showed pneumonic patch over the right lower lung field. Echocardiography revealed suspicious vegetations over both mitral valve leaflets.

The patient was admitted to the intensive care unit with a diagnosis of bacterial endocarditis. Blood biochemical analysis revealed serum albumin of 3.3 g/dL (normal range, 3.7–5.3 g/dL), cholesterol of 75 mg/dL (normal range, 125–245 mg/dL), total bilirubin of 5.2 mg/dL (normal range, 0.2–1.6 mg/dL), alkaline phosphatase of 190 mU/mL (normal range, 10–80 mU/mL), alanine aminotransferase of 1,157 mU/mL (normal range, <40 mU/mL), aspartate aminotransferase of 3,312 mU/mL (normal range, <45 mU/mL), creatinine of 1.3 mg/dL (normal range, 0.6–1.4 mg/dL), and negative hepatitis B surface antigen. The patient was treated with antibiotics. Thyroid function tests showed T4 of 11.1 µg/dL, T3 of 142 ng/dL and TSH of 0.7 µU/mL (normal range, <6.2 µU/mL).

The patient was transferred to our hospital 2 days later in a comatose state. Neck stiffness was suspected on the first day of admission, but lumbar puncture showed negative findings. Initial laboratory studies at our hospital were T4 of 5.3 µg/dL, T3 of 80 ng/dL, total bilirubin of 13.1 mg/dL, alkaline phosphatase of 250 mU/mL (normal range, 10–100 mU/mL), and lactate dehydrogenase of 547 mU/mL (normal range, 131–250 mU/mL). In addition to antibiotics, because the patient had a history of untreated hyperthyroidism for 3 years, he was treated with large doses of propylthiouracil, propranolol and Lugol's solution by nasogastric tube, and also with intravenous hydrocortisone. These regimens were discontinued the next day because of normal T3 and T4 levels. He was treated as a fulminant hepatitis with hepatic coma case. Unfortunately, he died on post-admission day 5.

The postmortem autopsy revealed diffuse hyperplasia of the thyroid gland (weight, 50 g; Figure 1), centrilobular necrosis of the liver (Figure 2), and congestion of the gastrointestinal tract, spleen, and adrenal gland. These pathological findings were compatible with a decompensated state of hyperthyroidism, i.e. thyroid storm, rather than fulminant hepatitis. In addition, bronchopneumonia, focal myocardial necrosis, slightly focal fibrosis, and calcification of both mitral valve leaflets without vegetations were found.

Discussion

The diagnosis of thyroid storm is currently based on the clinical evaluation. Burch and Wartofsky reviewed

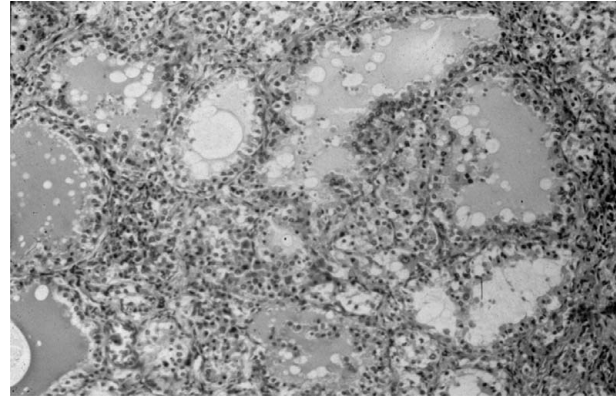


Figure 1. Thyroid gland of autopsied patient shows diffuse hyperplasia (hematoxylin & eosin, 100×).

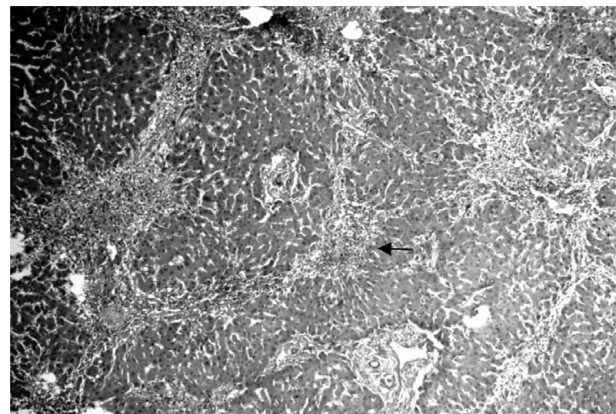


Figure 2. Liver of autopsied patient shows centrilobular hemorrhagic necrosis (hematoxylin & eosin, 40×).

the published diagnostic criteria and established a diagnostic point scale for the purpose of enabling a semiquantitative distinction among uncomplicated thyrotoxicosis, impending, and established thyroid storm.¹ These diagnostic criteria might be masked by nonthyroidal illness, especially in elderly patients. It is important to keep the possibility of thyroid storm in mind for any patient with long-term untreated hyperthyroidism who has developed tachycardia, a decompensated central nervous system, gastrointestinal-hepatic and/or cardiovascular dysfunction despite their serum T3 and T4 being within normal limits. It was sufficient to make the diagnosis of established thyroid storm in this case with a score of 110 according to the criteria. However, normal serum TSH, T3, and T4 levels were noted. This patient's serum TSH concentration was 0.7 µU/mL (normal range, 0.5–5.0 µU/mL), as determined by first-generation TSH radioimmunoassay, which is not sensitive enough to distinguish between hyperthyroidism and a euthyroid state.⁷

In nonthyroidal illness syndrome, the induction of type 3 deiodinase and a reduction of type 1 deiodinase

may contribute to the low T3 levels.⁸ If it progresses, the hypothalamic-pituitary axis is further suppressed, with a consequent reduction in serum T4 levels.⁹ In our case, the mechanism of normal serum T3 and T4 may be similar to the alterations of thyroid economy with nonthyroidal illness syndrome.^{8,10,11} Accordingly, it is reasonable to hypothesize that thyroid storm with normal serum T3 and T4 concentrations may be associated with a poor prognosis.

The hepatic injury associated with hyperthyroidism can vary from mild liver function test abnormalities to severe central hepatic ischemia.^{12,13} The frequency of jaundice varies from 5.3% of uncomplicated hyperthyroid patients to 79% if congestive heart failure is present.^{14,15} Inoue et al reported the first case of thyroid storm complicated by hepatic failure with centrilobular necrosis in 1988.¹³ Several mechanisms have been suggested to explain why thyroid crisis causes hepatic injuries, including malnutrition, the direct effects of thyroid hormones, association with heart failure, and relative local ischemia.^{16,17} Chung et al reported that plasma isocitrate dehydrogenase level or isocitrate dehydrogenase/alanine aminotransferase ratio is useful for distinguishing centrilobular necrosis from periportal necrosis and for monitoring the degree of hepatic necrosis in patients with hyperthyroidism.¹⁸

Thyroid storm can present with normal serum T3 and T4 levels and hepatic failure. Such presentation is rare. However, early recognition and proper management, including prompt antithyroid therapy, adrenergic depletion, and treatment of systemic decompensation might result in a better prognosis.

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