

CASE REPORTS

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Thyroid Storm Due to Functioning Metastatic Thyroid Carcinoma in a Burn Patient

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Thyroid storm as a result of functioning metastatic thyroid carcinoma is exceedingly rare.¹ We describe a patient with functioning distant metastases from adenocarcinoma of the thyroid in whom thyroid storm developed in the course of care for extensive burns.

Case Report

A 54-yr-old man was hospitalized for treatment of a severe burn injury. He gave a history of hormone-producing follicular adenocarcinoma with widespread metastases and resultant thyrotoxicosis. He had undergone total thyroidectomy 14 months before the onset of the burn injury. Although no functional tissue of the thyroid gland was left after the surgery, normal T₃ and thyroid-stimulating hormone (TSH) levels with slightly decreased T₄ level were found. Detailed endocrinologic examination revealed that distant metastases in the left scapula, left iliac bone, and sacral bone were endocrinologically functioning and producing major amounts of T₄ and T₃. Another metastasis in the anterior chest wall proved to be nonfunctioning. He subsequently received ¹³¹I-therapy twice for bone metastases. After the radioiodine therapy, he became slightly hypothyroid and required hormone replacement, using 50 µg of levothyroxine per day. After discharge he remained euthyroid, and periodic hormone determination revealed no major change in the T₄, T₃, and TSH levels.

One year after the discharge, he lit fire to his gasoline-soaked clothes in an attempt to commit suicide. On admission, he was alert but had signs of hypovolemic shock. His second-degree deep dermal and third-degree burns involved 60% of the total body surface area. Fluid resuscitation was performed using hypertonic sodium solution and protein-containing colloid solution.² Low-dose dopamine was used to maintain renal and splanchnic blood flow.

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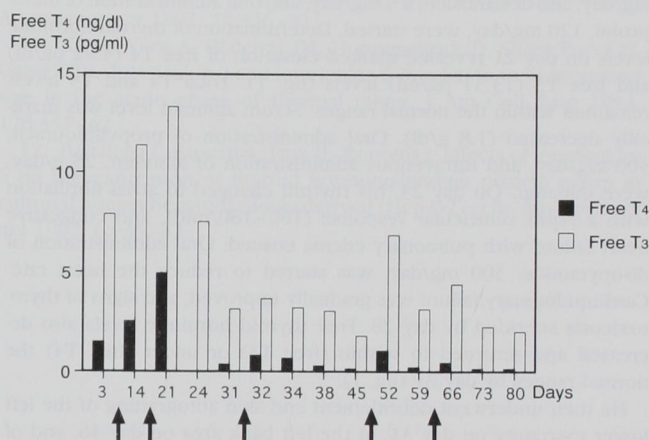


Fig. 1. Changes of free T₄ and T₃ levels after the severe burn injury. The x axis indicates days after the onset of the burn injury. Major increases in free thyroid hormone levels were observed after each surgical procedure of débridement and skin autografting (indicated by arrows).

Thyroid function studies were performed on day 3. Total T₄ level was 5.8 µg/dl (normal, 5.0–14.0); free T₄, 1.46 ng/dl (normal, 0.99–1.54); total T₃, 2.13 ng/ml (normal, 0.8–2.0); and free T₃, 7.90 pg/ml (normal, 2.51–4.01), with an undetectable TSH level. Blood pressure was 100–120/50–60 mmHg; heart rate, 90–100 beats/min; respiratory rate, 16–20 breaths/min; and temperature, 36.2–36.6°C. Because of the elevated T₃ and free T₃ levels, levothyroxine administration was discontinued.

On day 10, débridement and skin autografting of the anterior chest wall were performed. General anesthesia was induced with thiamylal, 5 mg/kg, droperidol, 0.1 mg/kg, and fentanyl, 4 µg/kg, and endotracheal intubation was facilitated using vecuronium, 0.15 mg/kg. Anesthesia was maintained with 60% N₂O and 0.5–1.0% sevoflurane. Duration of anesthesia was 180 min, and blood loss was 602 g. The postoperative course was uneventful, and he remained hemodynamically stable. On day 14, thyroid hormone levels were determined again. Although the levothyroxine administration had been discontinued since day 1, free T₃ and free T₄ levels were even more elevated (fig. 1). Total T₄ and T₃ levels were within the normal ranges, and no serious signs of thyrotoxicosis were observed.

On day 17, débridement and skin autografting of the both thighs were performed. General anesthesia was induced and maintained using the same technique. Duration of anesthesia was 180 min, and

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blood loss was 772 g. Anesthesia and surgery were uneventful, except for sinus tachycardia around 120/min. He was transferred to the intensive care unit. In the following 12-h period, no remarkable changes of his vital signs were observed except for the persistent tachycardia around 110–140/min. On day 18, hypertension (150–180/50–62 mmHg) and hyperthermia (38–39°C) developed. Antibiotic therapy using amikacin and imipenem was not effective to alleviate the fever. On day 19, confusion, disorientation, and delirium were observed. On day 20, progressive worsening of hypermetabolic state, characterized by marked tachycardia, 140–160/min; hypertension, 194–238/50–68 mmHg; hyperthermia, 39.6°C; and tachypnea, 32/min was noticed. Intravenous administration of hydrocortisone, 100 mg/day, and deslanoside, 0.4 mg/day, and oral administration of metoprolol, 120 mg/day, were started. Determination of thyroid hormone levels on day 21 revealed marked elevation of free T₄ (4.92 ng/dl) and free T₃ (13.34 pg/ml) levels (fig. 1). Total T₄ and T₃ levels remained within the normal ranges. Serum albumin level was markedly decreased (1.8 g/dl). Oral administration of propylthiouracil, 300 mg/day, and intravenous administration of albumin, 25 g/day, were initiated. On day 23, his rhythm changed to atrial fibrillation with a rapid ventricular response (160–180/min), and congestive heart failure with pulmonary edema ensued. Oral administration of disopyramide, 300 mg/day, was started to reduce the heart rate. Cardiopulmonary failure was gradually improved, and signs of thyrotoxicosis subsided by day 28. Free thyroid hormone levels also decreased and returned to within (free T₃) or under (free T₄) the normal ranges by day 31 (fig. 1).

He then underwent débridement and skin autografting of the left lower extremity on day 31, in the left back area on day 46, and of the neck on day 59, respectively. Postoperative course was uneventful each time. Although no signs of exacerbation of thyrotoxicosis were observed during this period, determination of thyroid hormone levels revealed small but significant increase of free thyroid hormone levels after each surgical procedure (fig. 1). Total T₄ and T₃ levels remained within or below the normal ranges during this period. The series of skin autografting was successful, and the wound infection subsided. Reduction of medication to propylthiouracil, 60 mg/day, and metoprolol, 60 mg/day, became possible with progression of wound healing.

On day 76, muscle weakness of extremities was noticed. Then, quadriplegia developed within a few days despite various conservative therapies. Detailed examination revealed that destruction of the second, sixth, and eighth vertebrae by metastases had caused rapidly progressive quadriplegia and phrenic nerve palsy. Respiratory failure caused by respiratory muscle paralysis progressed rapidly, and the patient died on day 86.

Discussion

Thyrotoxicosis resulting from functioning metastatic thyroid carcinoma is uncommon.^{1,3,4} It is suggested that the mass of functioning metastatic tissue is crucial to the onset of thyrotoxicosis; because of low inherent hormone-producing capacity, functioning metastatic thyroid carcinoma produces thyrotoxicosis when the mass of tissue is sufficiently great to provide an excess of thyroid hormones.^{1,4} Unlike these reported cases,

sudden onset of thyrotoxicosis in our patient was characterized by the critical failure of vital organs, known as *thyroid storm*. Thyroid storm caused by functioning metastatic thyroid carcinoma is extremely uncommon, and its pathogenesis perioperatively remains unclear.⁵

In general, thyroid storm develops in those with untreated or undertreated thyrotoxicosis.⁶ Our patient was receiving periodic thyroid function testing during the 1-yr period before suffering the burn injury. He was shown to remain euthyroid with levothyroxine replacement, which indicates that the mass of functioning metastatic tissue was not big enough to produce an excess of thyroid hormones at the onset of the burn injury. It is well-known that conditions such as surgery and extensive burns suppress host tumor immunity, resulting in accelerated growth of carcinoma tissue in cancer patients.^{7,8} In our patient, newly developed metastases in the cervical vertebrae were found. However, repeated determination of thyroid hormone levels revealed that total T₄ level remained within or below the normal range after receiving the burn injury. Total T₃ level, which was slightly increased on day 3, returned within the normal range promptly and remained within or below the normal range thereafter. It is therefore unlikely that an excess of thyroid hormone production induced by growth of the functioning metastatic tissue is the responsible mechanism of development of thyroid storm in this patient.

Thyroid storm usually is associated with some precipitating events.⁵ Situations known to trigger thyroid storm include surgery, infections, and trauma. Although the exact mechanism of triggering thyroid storm has not been completely elucidated, elevation in free thyroid hormone levels is suggested as a cause.⁹ In the present patient, repeated determination of thyroid hormone levels revealed major increases of free thyroid hormone levels after each surgical procedure. Serum albumin level was markedly decreased at the onset of the thyroid storm. Hypoalbuminemia is common in a patient of severe burn injury with repeated surgical treatments. Surgery and severe burn injury are known to induce major elevation of plasma interleukin-6 level.^{10,11} Interleukin-6 is reported to inhibit production of transthyretin and thyroxine-binding globulin by hepatocytes.¹² It is suggested that transient deficiency of thyroid hormone-binding proteins, such as transthyretin, thyroxine-binding globulin, and albumin, and resultant elevation of free T₃ and T₄ levels are responsible for the thyroid storm in this patient.⁹

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