

# Low Serum Cortisol After Surgery for Cushing's Syndrome Causes Hyperthyroidism Due to Inappropriate Secretion of TSH

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Tamada D, Onodera T, Kitamura T, Yamamoto Y, Hayashi Y, Murata Y, Otsuki M, Shimomura I. Hyperthyroidism due to thyroid stimulating hormone secretion after surgery for Cushing's syndrome: a novel cause of the syndrome of inappropriate secretion of thyroid stimulating hormone. *J Clin Endocrinol Metab.* May 13, 2013 [Epub ahead of print].

## SUMMARY ●●●●●●●●●●●●●●●●

### Background

The syndrome of inappropriate secretion of TSH in the presence of high levels of thyroid hormones (SITSH) is rare and usually due to a TSH-secreting pituitary tumor or resistance to thyroid hormone. In the present report, the authors describe several cases of patients in whom SITSH developed after treatment of Cushing's syndrome when on low glucocorticoid replacement, a new finding.

### Case Reports

**Case 1** was a 45-year-old woman who had typical features of Cushing's syndrome that progressed during a 4-year period. She had high serum cortisol and urinary free cortisol and undetectable plasma ACTH. CT of the abdomen showed a 3-cm adrenal tumor that was removed laparoscopically. She was treated with 30 mg of hydrocortisone, and on postoperative day 18, the dose was reduced to 15 mg. After this, she experienced palpitation, fatigue, and weight loss. On day 40, she had an elevated free  $T_4$  of 2.1 ng/dl, with TSH of 2.5, indicating SITSH. Further evaluation showed no pituitary tumor or findings of autoimmune thyroid disease. When the dose of hydrocortisone was increased to 30 mg/day, her symptoms and thyroid hormone levels improved promptly. When the

dose of hydrocortisone was reduced progressively to 10 mg/day, her serum TSH increased and free  $T_3$  increased in association with her symptoms of hyperthyroidism. Again, 30 mg of hydrocortisone normalized thyroid function.

**Case 2** was a 37-year-old man with ACTH-dependent Cushing's disease caused by a 6-mm pituitary adenoma. After successful removal of the adenoma, SITSH developed, with elevated free  $T_3$  when his replacement hydrocortisone dose was reduced to 20 mg/day. He was restarted on 30 mg followed by dose reduction of 10 mg every 4 days. On 10 mg of hydrocortisone per day, TSH increased and free  $T_3$  rose above normal. He was discharged on 20 mg/day and remained euthyroid.

Seven additional patients with Cushing's syndrome had evaluation of thyroid function after surgery, and 4 of them had SITSH. All of those with SITSH had serum cortisol that was suppressed to  $<1.0$  mcg/dl 5 days after surgery.

### Conclusions

Insufficient replacement of hydrocortisone after surgery for Cushing's syndrome causes hyperthyroidism due to inappropriate secretion of TSH.

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## ANALYSIS AND COMMENTARY ● ● ● ● ●

The authors have made a unique observation, probably catalyzed by the symptoms of hyperthyroidism in case 1. The degree of hyperthyroidism, based on free T<sub>4</sub> and T<sub>3</sub> levels, is very mild, but TSH is clearly inappropriately normal in this situation. This paper should stimulate evaluation of patients for this post-Cushing's SITSH.


What is the pathogenesis of this condition? Cortisol is known to attenuate TSH secretion (1). Elevated

serum TSH has been reported in Addison's disease; it has been attributed to autoimmune thyroid disease and has not been associated with increased levels of thyroid hormones. Cortisol increases type 2 deiodinase (D2), which could result in increased T<sub>3</sub> in the hypothalamus and pituitary, in turn suppressing serum TSH (2). A lack of cortisol could attenuate D2, thereby increasing the secretion of TSH. This mechanism could explain the syndrome of SITSH when glucocorticoid deficiency is present, especially after the persistent stimulation of D2 is withdrawn.

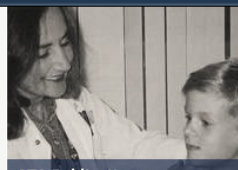

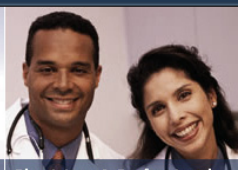
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