

Letter to the Editor

A significant adverse correlation between serum cortisol and TSH in a case of cyclic Cushing's disease based on a continuous three-year observation

To the Editor;

The suppressive effects of exogenous glucocorticoid on the hypothalamo-pituitary-thyroid axis is a well-known fact [1–3]. There have also been many studies of healthy volunteers [1], patients with Cushing's syndrome [4] and patients with congenital adrenal hyperplasia [5], regarding the role of endogenous glucocorticoid in the regulation of TSH. However, there have been no reports on the relationship of serum cortisol and TSH in cyclic Cushing's syndrome.

A 71-year-old woman with clinical signs of Cushing's disease was observed continuously for three years during which serum cortisol levels fluctuated

from 10 to 57 µg/dl and serum TSH levels ranged 0.05 to 3.15 µIU/ml. As can be seen in the main Fig. 1, cortisol levels peaked twice during the first two years. Beginning in May 1997 the patient began receiving 120–180 mg/day of trilostane, and seemed to respond. However, in July 1998, her serum cortisol levels began to rise to about 20 µg/dl (this period is not shown in the main Fig. 1). The patient demonstrated two important features of cyclic Cushing's disease: absence of ACTH response to CRH administration and non-suppressibility in response to high dose dexamethasone other than the cyclicity of ACTH and cortisol. Repeated tests over an interval of one year gave similar results. Moreover, these features were present even during the normocortisolemic state. Dynamic MRI on admission (January, 1966) revealed a microadenoma in the left part of the pituitary.

In this case the correlation between serum cortisol and TSH was examined in 20 pairs (inserted Fig. 1). Hormone values which may have been influenced by loading tests, including dexamethasone suppression tests, were eliminated. There was a significant adverse correlation between serum cortisol and TSH ($r = 0.86$,

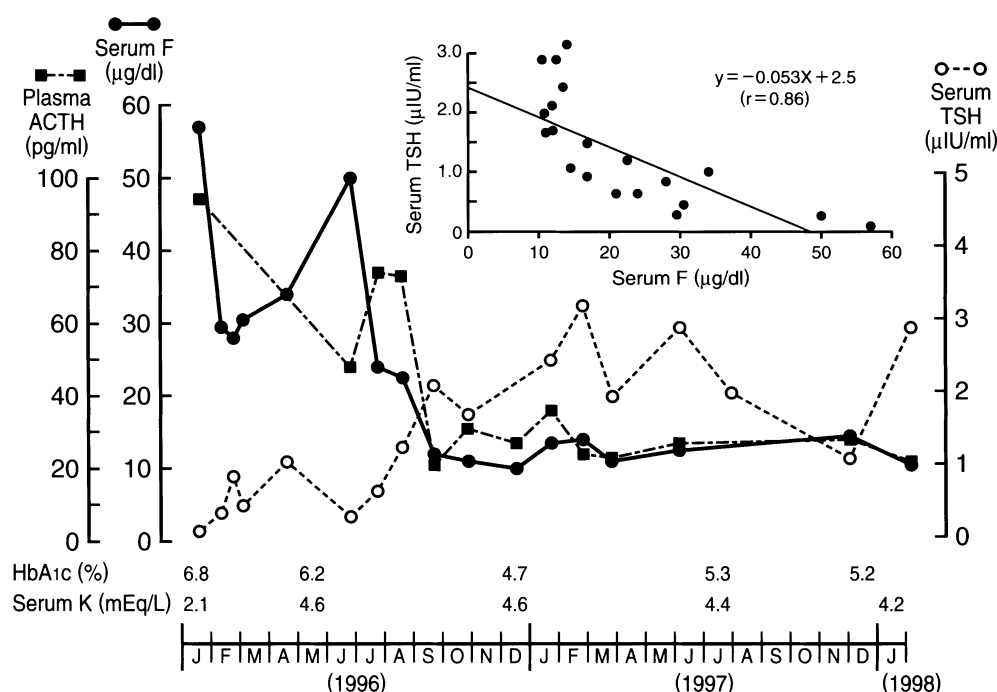


Fig. 1. In the main Fig. 1, profiles of plasma ACTH, serum cortisol (F) and TSH for 2 years are depicted and serial changes in glycohemoglobin (HbA1c) and serum potassium (K) are also shown. Correlations between serum cortisol and TSH for a 3 year observation period are shown in the inserted Fig. 1. The methods of TSH and cortisol measurement were two site immunoassay (AIA-1200XL, TOSOH) and turbidimetric immunoassay (COBAS MIRA S, Roche), respectively. The TSH assay was not a high sensitivity one.

$p = 0.0003$), but not between serum cortisol and prolactin ($p = 0.12$). Serum free thyroxine values changed according to the TSH values, but did not reach the hypothyroid range. The range of fluctuation of serum cortisol in previous reports on the suppressive effect of endogenous cortisol were 10 to 20 $\mu\text{g/dl}$ in Cushing's disease [4] and 5 to 15 $\mu\text{g/dl}$ in congenital adrenal hyperplasia [5]. To our knowledge there have been no reports regarding the suppressive effects of endogenous cortisol on TSH secretion in a case with a great range of serum cortisol fluctuation such as this one.

This report confirmed the reciprocal relationship between TSH and endogenous cortisol in a case involving a wider range of serum cortisol levels. These observations are also compatible with a previous paper [1] stating that prolactin was not influenced by glucocorticoid.

Acknowledgement

We thank Dr. K. Iwasato for his helpful advice in the statistical analysis.

References

1. Re RN, Kourides IA, Ridgway EC, Weintraub BD, Maloof F (1976) The effect of glucocorticoid administration on human pituitary secretion of thyrotropin and prolactin. *J Clin Endocrinol Metab* 43: 338–346.
2. Samuels MH, McDaniel PA (1977) Thyrotropin levels during hydrocortisone infusions that mimic fasting-induced cortisol elevations: A clinical research center study. *J Clin Endocrinol Metab* 82: 3700–3704.
3. Brabant G, Brabant A, Ranft U, Ocran K, Köhrle J, Hesch RD, von zur Mühlen A (1987) Circadian and pulsatile thyrotropin secretion in euthyroid man under the influence of thyroid hormone and glucocorticoid administration. *J Clin Endocrinol Metab* 65: 83–88.
4. Adriaanse R, Brabant G, Endert E, Wiersinga WM (1994) Pulsatile thyrotropin secretion in patients with Cushing's syndrome. *Metabolism* 43: 782–786.
5. Ghizzoni L, Mastorakos G, Street ME, Vottero A, Mazzardo G, Vanelli M, Chrouzos GP, Bernasconi S (1997) Spontaneous thyrotropin and cortisol secretion interactions in patients with nonclassical 21-hydroxylase deficiency and control children. *J Clin Endocrinol Metab* 82: 3677–3683.

KOHEI Yamaguchi and YASUHIRO Hashiguchi
 Department of Endocrinology and Metabolism, Oita Prefectural
 Hospital, 470 Bunyo, Oita 870-8511, Japan