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A Case of Idiopathic Thyrotropin (TSH) Deficiency

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The first case of idiopathic thyrotropin (TSH) deficiency in an old woman with thyroid functioning adenoma was reported. She got subtotal thyroidectomy before about four years of her admission to our hospital because of fatigability, puffy face and leg edema. At that time, she had low TSH and free T_4 levels despite replacement therapy with desiccated thyroid. No response of only serum TSH after adminstration of combined stimulant containing TRH and repeated TRH suggested the failure of TSH secretion. CT MRI did not show any abnormality. These results indicated that her hypothyroidism was due to acquired idiopathic TSH deficiency.

Key Words: *Pituitary hypothyroidism, TRH, TSH deficiency*

INTRODUCTION

Isolated deficiency of a single anterior pituitary hormone is by now accepted as a clinical entity, even if uncommon, although this entity may be heterogenous. Idiopathic isolated adrenal corticotropic hormone (ACTH) or TSH deficiency is generally discovered in subjects over 40 years of age (1). In such patients, it is difficult to deduce if the defect is a developmental or genetic one. Reported here is a case regarded as being compatible to an acquired defect of TSH secretion in the pituitary itself without an ascertainable cause.

CASE REPORT

A woman, 76 years old, was admitted to our hospital for fatigability, puffy face and leg edema in August, 1992. In 1985, she had suffered from a right thyroid tumor. The data of thyroid function tests are shown in Table 1. The ^{99m}Tc and ^{123}I thyroid scintigraphy indicated large functioning thyroid nodule in right thyroid lobe [^{123}I uptake: 37.6% (3h), 40.6% (6h) (normal range 6h. 8-25%)] with suppresstion of left lobe. In the following year, she got an operation of the thyroid gland for functioning follicular adenoma of the right lobe and nodular hyperplasia (adenomatous goiter) of the left one. The right lobe of the thyroid had been totally resected and only half of the left lobe remamed. Before and after the operation, free T_4 and TSH levels were below normal range and desiccated thyroid was administered. The thyroid evaluation, performed after three months following the operation, was hypothyroid state as follows; T_3 (66ng/dl), T_4 (5.3 μg/dl), F-T_4 (0.29 μg/dl) and TSH (32.3 μU/ml) (Table 1.). The dosage of desiccated thyroid was increased to 60mg and serum TSH level became low level. In May, 1991, thyroid function test showed normal serum total thyroid hormone, suppressed TSH and low free T_4 levels. Thereafter her compliance of taking drugs was insufficient.

On admission, (in August, 1992), she appeared clinically to be myxoedematous because of puffy face and non-pitting leg edema. On physical examination, the body temperature was 36.5℃, pulse rate 72 beats per minute and regular, and blood pressure 132/70mmHg. The hair and skin were normal. Thyroid gland which remained was not palpable.

Urinalysis, hemogram, levels of electrolytes, blood urea nitrogen, blood glucose, uric acid, cholesterol and liver function were within normal limits. The roentogram of the chest revealed an enlarged

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Table 1. Changes of Thyroid Function

Date	TSH μU/ml	FT_4 ng/dl	T_4 μg/dl	T_3 ng/dl	Therapy (Desiccated Thyroid) (Daily doses)
24/12/1985	1.8	1.73	14.0	264	
11/01/1986	<1.0	1.43	9.4	139	
20/11/1988	<0.1	0.57			
08/12/1988	(Operation)				
14/12/1988	<0.1	0.58	4.5	23	25mg
05/03/1990	32.3	0.29	5.3	66	↓
09/03/1990	36.5	0.47	6.4	82	↓
23/03/1990	0.1	0.71	4.1	68	↓
17/05/1991	<0.1	0. 5	8.6	98	60mg
29/08/1992	<0.1	0.15	1.6	15	↓
Normal range	0.1-4.0	0.8-2.0	5.5-12.0	90-160	

TSH: thyrotropin, FT_4:free thyroxine, T_4:thyroxine, T_3: triiodothyronine
From 1985 to 1986, the TSH value was measured by radioImmunoassay(RIA) and, after 1988, by immunoradiometric assay (IRMA).

Table 2. Changes in Serum TSH Levels after TRH Administration and Pituitary to Stimulation Test

Date	Hormone	Before	Time(min) after stimulation			
			30	60	90	120
30/08/1992	TSH(uU/ml)	0.09	0.34	0.39		
31/08/1992	TSH	0.09	0.57	0.72		
01/09/1992	TSH	0.22	0.58	0.79		
02/09/1992	TSH	0.30	0.71	1.23	1.44	1.45
	GH (ng/ml)	21.8	15.1	57.1	41.2	27.7
	LH (mIU/ml)	59.0	70.2	123.2	133.4	142.1
	FSH (mIU/ml)	148.0	151.0	194.0	209.0	213.0
	PRL (ng/ml)	18.5	47.9	59.3	59.2	59.0
	Cortisol(ug/dl)	16.1	11.7	19.8	21.7	24.8

GH: Growth hormone, LH: luteinizing hormone, FSH: follicle stimulating hormone, PRL:prolactin
TRH (2mg) was administrated by drip infusion and repeated for 4 days in early morning. On final day, mixed pituitary stimulation test (regular insulin 0.1U/kg, LH-RH 0.1mg) was performed simultaneously.

heart. Electrocardiogram showed left ventricular hypertrophy. To evaluate the pituitary-thyroid function, the administration of desiccated thyroid was discontinued for one week after this admission. TSH was still suppressed despite low level of T_4 (1.6 μg/dl), T_3 (15ng/dl), free T_4 (0.15ng/dl) and free T_3 (below 0.4). Serum TBG level was 20.5 μg/ml and anti-thyroglobulin, microsome antibodies, TSH receptor antibody and anti-TSH antibody were negative. As shown in Table 2, a significant increase in serum TSH levels did not occur after drip infusion (2mg) of TRH for 30 minutes. After repeated injection of TRH (2mg/day) for 4 consecutive days, serum TSH levels were still suppressed (maximum level: 1.45 μU/ml in 120 minutes of final injection day). With the final TRH injection, combined pituitary stimulation test by intravenous injection of 0.1units/kg reglar insulin, 0.1mg LH-RH was performed. Growth hormone (GH), LH, FSH, prolactin (PRL) and cortisol kept almost normal responses (Table 2). The pituitary MRI and CT did not show any abnormality. These results were consistent with secondary hypothyroidism derived from the isolated deficiency of TSH.

DISCUSSION

Isolated TSH deficiency was first reported in 1953 by Shuman[2]. Since then, more than 30 patients with isolated TSH deficiency have been reported. These patients were diagnosed by exogenous TRH administration test and the direct determination of TSH in serum[3-11]. Recently, the advance of endocrinology and radiology is explaining the pathogenesis of isolated TSH deficiency, which is classified as disorders of pituitary lesion associated with central hypothyroidism. The pituitary causes can be broadly divided into mass lesions, infiltrative diseases, pituitary atrophy due to necrosis or autoimmune destruction and idiopathic TSH deficiency. The diagnostic criteria of idiopathic TSH deficiency are to satisfy 1) low serum levels of thyroid hormones, 2) low or undetectable TSH levels, 3) no TSH response to exogenous TRH, 4) no evidence of other pituitary hormone deficiencies, 5) no abnormalities on radiographic studies[14]. Laboratory data of our patient are generally compatible with idiopathic TSH deficiency.

Our case first occurred undetectable TSH and low FT_4 before the operation of functioning adenoma, and abruptly became hypothyroidism with transient rise of TSH. When the dose of desiccated thyroid was increased, serum T_4 and T_3 normalized, in spite of low free T_4 and suppressed TSH level. Thereafter, our patient had mild clinical signs for about 2 years. It is assumed that isolated TSH deficiency in adult populations shows commonly absent or mild symptoms of hypothyoidism. Finally, she had various symptoms of hypothyroidism such as fatigability, puffy face, leg edema and cardiomegaly because of insufficiently taking drugs.

This case showed resistance to prolonged TSH stimulation by continuous and massive TRH administration. The TSH values were measured many times by means of immunoradiometric assay (IRMA) and the results were almost the same. Furthermore, anti-TSH antibody was negative. The characteristic finding of hypothalamic hypothyroidism is that a significant secretion of TSH occurs following repeated injection of TRH[12, 13]. In hypothalamic hypothyroidism, normal responsiveness of TSH to TRH usually persists despite of many years continuing pituitary hypofunction[13, 14]. High basal level of growth hormone in our case may be due to her poor nutrition. The responsiveness of pituitary hormones, except of rTSH, were intact and the brain MRI showed no abnormality. Though the etiology of isolated TSH deficiency was speculated as genetic origin[15], it is not true in our case as she had no family history and had once experienced the TSH elevation in 1990. Thus, we diagnosed our patient as acquired and idiopathic isolated TSH deficiency based on these findings.

None of the reported cases had a past history of thyroid functioning adenoma. The relationship between thyroid functioning adenoma and pituitary hypothyroidism is unknown and the cause of the disease remains obscure, though arteriosclerotic cerebrovascular disease[16] and autoimmune damage to the anterior pituitary[17] may be suggested as possible causes.

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