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HASHIMOTO THYROIDITIS AND OBSTRUCTIVE SLEEP APNEA SYNDROME: IS THERE ANY RELATION BETWEEN THEM?

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Abstract: Hashimoto thyroiditis (HT), which is an autoimmune disease of tyhroid gland, has been declared to present with concomitant several systemic diseases. In this study, the coexistence of the Hashimoto disease with the sleep apnea syndrome has been examined.

Seven female patients (33-66 year of age) with Hashimoto thyroiditis were evaluated for sleep apnea syndrome. The diagnosis of Hashimoto disease was based on the high titers of anti-thyroid antibodies and histological findings .None of the patients had any complaints of sleep disturbances. Seven healthy subjects with similar age and sex characteristics were taken as the control group. All the patients and the control subjects were undertaken a full polysomnography (PSG).

Five patients with HT showed the characteristics of obstructive sleep apnea syndrome (one severe, one moderate and three mild OSAS), whereas no sleep breathing disturbance was found in the control group. These findings suggest that sleep related breathing problems may develop in the patients with autoimmune thyroiditis even if they are euthyroid.

Key words: Sleep apnea, Hashimoto thyroiditis, polysomnography, autoimmune disease.

INTRODUCTION

Hashimoto thyroiditis (HT) is one of the autoimmune diseases of the thyroid gland. It is characterized by the elevated levels of serum thyroid autoantibodies (antithyroglobulin and antithyroid peroxidase). The disease has been suggested to be the clinical expression of cell mediated immunity leading to the destruction of thyroid cells. Hashimoto thyroiditis is mostly seen among middle aged women with diffuse goiter and the prevalence is nearly 2 %. Patients with HT are generally euthyroid, but hypothyroidism may also develop [10]. Recently, Hashimoto thyroiditis has been considered as a systemic disorder [6, 9, 14].

Obstructive sleep apnea syndrome (OSAS) is a common disorder characterized by apnea, hypopnea, oxygen desaturation and arousal attacks with intermittent narrowing of the upper airway during sleep. It can be seen with a variety of diseases and may occur due to central or peripheral reasons [12]. Patients with OSAS often present with symptoms of daytime somnolence, apathy, depressed mood, impaired concentration and fatigue. These signs can also be seen in individuals with hypothyroidism and sometimes cause to a misdiagnosis. Moreover, hypothyroid patients are at risk for secondary sleep-disordered breathing [8]. Although hypothyroidism has been approached as a risk factor for OSAS in a number of studies, there is no data about sleep related breathing pattern of euthyroid patients with autoimmune thyroiditis. In this study we evaluated whether any sleep related disturbance exists in patients with Hashimoto thyroiditis without thyroid dysfunction.

MATERIAL AND METHOD

Seven patients with the diagnosis of HT were included in the study. Four of them had mild to moderate degrees of goiters while remaining three patients showed no thyroid enlargement, and radionuclide scanning of thyroid glands supported these findings. Histopathology and increased autoantibody titers proved the clinical diagnosis. Out of seven patients, newly diagnosed five were euthyroid. The remaining two patients had no hypothyroidic period during their 10 year follow-up period. As a control group, age and sex matched, seven healthy subjects were included in the study. Thyroid function tests of the control patients were in the normal range. The ear-nose and throat examinations of the patients and the control subjects revealed no anatomic defect to cause an upper airway obstruction.

All individuals participated in a detailed overnight study by Medilog MPA 15 channel polysomnography (Oxford Medical Limited,Oxon, England). Polysomnographic evaluation included single channel electroencephalogram (EEG), two channel electrooculograms (EOG), submental electromyogram (EMG) and electrocardiogram (ECG). Breathing was monitored with chest and abdominal belt. Airflow was monitored by oro-nasal thermistor. Finger pulse oximeter was used for oxygen saturation and pulse monitoring. Motion sensors were placed on each leg to record leg movements. Respiratory parameters were determined automatically by medilog replay software. Airflow cessation at least 10 seconds duration were considered as apnea and a decrease of 3% or more capillary oxygen saturation was accepted as desaturation. An episode of reduced airflow by at least 50% during sleep lasting 10 seconds or longer with a desaturation or arousal has been accepted as a hypopnea. Sleep staging and respiratory events were interpreted manually. The diagnosis of OSA was based on a Respi-

ratory Disturbance Index (RDI) defined as the average number of obstructive events with significant desaturations per hour of sleep of >5 events /h. Average number of significant oxygen desaturation per hour of sleep was defined as Oxygen Desaturation Index (ODI).

Results

The characteristics of the patients and control subjects are shown in Table 1 and 3. Among patients with HT, five showed the characteristics of OSAS (one severe, one moderate and three mild OSAS) (Table 2). Respiratory disturbances index were in the normal range in the remaining two patients. Only one patient which showed moderate OSAS had snoring as a symptom of OSAS. The other four patients described no symptoms related to OSAS. Polysomnography results of the normal patients were all in normal limits.

Table 2. Polysomnography results of the patients.

No	Apnea	Hypopnea	RDI	ODI	Min Desaturation
1	4	5	9	14	75
2	10	12	22	18	92
3	7	14	21	24	79
4	0	3	3	7	90
5	2	6	8	2	92
6	0	9	9	12	90
7	0	1	1	6	94

RDI:Respiratory disturbance index
ODI: Oxygen Desaturation Index

Discussion

Our findings suggest that obstructive sleep apnea syndrome can exist in the patients with autoimmune thyroid disorder even if they are euthyroid. So far, it has been shown by various studies that obstructive sleep apnea and hypothyroidism are causally linked. The mechanisms proposed to explain this coexistence were mucoprotein deposition in the upper airway, decreased neural output to the upper airway musculature, obesity and abnormalities in ventilatory control [8]. Recently, a review pointed out that the sleep apnea syndromes may be caused by a variety of endocrine diseases including diabetes mellitus, acromegaly, Cushing disease and hyperandrogenism [3]. Different mechanisms are implied in sleep-disordered breathing in different endocrine diseases. However, there is no data about the presence of breathing disturbances during sleep in the patients with thyroid disorders such as autoimmune or other type of thyroiditis.

Autoimmune thyroid disease is proposed to be considered as a systemic disease affecting multisystems such as musculoskletal, cardiovascular and neuromus-

Table 1. The characteristics and laboratory results of the patients.

No	Age	Sex	BMI	T3	T4	FT3	FT4	TSH	Anti TPO	Anti TG
1	46	F	35	2.8	1.7			4.8		518
2	34	F	24	2.1	21	5.2	12.1	0.053	2174	4000
3	66	F	34	1.2	16.1	4.4	17.3	0.907	118	>4000
4	55	F	28	1.1	4.7			4	4923	3267
5	44	F	25	4.1	12	1.7	10.8	2.570	2681	2459
6	37	F	29	1	6.7	4.2	15.2	4.8	452	478
7	33	F	28	1.4	6.7	4.9	15.6	1.6	441	25

BIM: Body/mass index Anti-TPO: Anti-tyhroid peroxidase Anti-TGO:Anti-thyroglobulin

Table 3. The features and the polysomnography results of the normal group.

No	Age	Sex	BMI	Apnea	Hypopnea	RDI	ODI	Min.Desaturation
1	44	F	27	0	1	1	1	94
2	46	F	24	1	1	2	3	92
3	30	F	30	1	0	1	2	94
4	44	F	26	0	0	0	0	94
5	62	F	20	2	2	4	3	92
6	44	F	22	1	0	1	1	94
7	47	F	24	0	0	0	0	96

RDI: Respiratory disturbance index
ODI: Oxyhen desaturation index

cular systems [4]. The diseaese was shown to cause myopathy and was proven by electromyography [2, 5]. Multifocal motor neuropathy, which is associated with multifocal conduction blocks and represents a recently identified autoimmune disorder of the peripheral nerve myelin, have been also reported to occur in Hashimoto thyroiditis as well as in other thyroid diseases (hypothyroidism, hyperthyroidism and neoplasms) [13].

There are two main principals in the pathophysiology of the sleep apnea syndrome; (1) obstruction of upper airways due to various reasons (anatomic pathology of the upper airways, tonsillary and adenoid hypertrophies, obesity, hypothyroidism, disturbances of the neuromuscular junction, acromegaly etc.) and (2) decreased ventilatory response. Upper airway obstruction during sleep can only be prevented by genioglossus muscle. Therefore, OSAS can easily develop in the patients with a problem in the neuromuscular junction. If a decrease occurs in the ventilatory response, upper airway can not compensate even a minimal collapse.

Taken together these data, obstructive sleep apnea syndrome in our five patients with Hashimoto may be due to an upper airway obstruction related to neuromuscular pathology or decreased ventilatory response, caused by autoimmune thyroiditis [13]. None of the seven patients with thyroiditis had as large goiter as to be a reason of obstruction of the upper airway. Another autoimmune disease, myasthenia gravis has been reported to cause central and peripheral type of sleep apnea even though the disease is under control [1]. Respiratory problems due to fatigue of diaphragm and other respiratory muscles have been implicated as the cause of sleep disorders in myasthenia [11]. Similar mechanisms may play a role for the development of obstructive sleep apnea syndromes in our patients.

Another recent review pointed out that intense local and systemic inflammation were present in the patients with OSAS. It was proposed by the authors that increased pro-inflammatory cytokines, such as tumor necrosis factor (TNF-α) and IL-6 in OSAS might promote pharyngeal inspiratory muscle dysfunction thereby worsening apneic episodes during sleep [7]. From this point of view, Hashimoto thyroiditis which is an autoimmune inflammatory disease of thyroid gland probably systemic in nature, seems likely to cause to sleep-disordered breathing.

In conclusion, our findings suggest that Hashimoto thyroiditis may cause to some degree of sleep breathing disturbances as well as in hypothyroidism. However, whether a subclinic hypothyroidism exists in these patients still remains a matter of suspect. Obviously, larger studies are required to clarify this association.

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