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Arteriosclerotic Changes as Background Factors in Patients with Peripheral Vestibular Disorders

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Abstract: Symptoms such as vertigo and unsteady gait occur in various diseases and are among the relatively common chief complaints. Even at present, the mechanisms underlying these disorders are unclear. We considered the possibility of peripheral vestibular disorders correlating with lifestyle-related illnesses. Under these circumstances, we assessed correlations of lifestyle-related illness as background factors for peripheral vestibular disorders and associated arteriosclerotic changes. Using carotid ultrasonography, we assessed maximum intima-media thickness (max IMT) and maximum common carotid artery IMT and evaluated biochemical examinations in 85 patients with peripheral vertigo. The patients were divided into two groups: those with benign paroxysmal positional vertigo (BPPV) and those with peripheral vestibular disorders. The frequency of abnormal IMT was significantly higher in those in the BPPV group. Calculating for average age, max IMT was significantly higher in the BPPV group. The correlation coefficient between age and max IMT was 0.343 ($p < .001$). All other correlation coefficients also reached statistical significance. Our results indicate that cervical ultrasonography is useful for noninvasive examination of arteriosclerotic changes in patients with peripheral vestibular disorders. Our results also indicated that peripheral vestibular disorder patients show progression of arteriosclerotic changes.

Key Words: benign paroxysmal positional vertigo (BPPV); intima-media thickness; peripheral vestibular disorder; vertigo

Symptoms such as vertigo and unsteady gait occur in various diseases and are among the relatively common chief complaints. In our otorhinolaryngology department, patients with the chief complaints of vertigo and unsteady gait considered to be attributable mainly to peripheral vestibular disorders are routinely examined and treated. Typical examples of peripheral vestibular disorders are benign paroxysmal positional vertigo (BPPV), Ménière's disease, and vestibular neuronitis. Even at present, the mechanisms underlying these disorders are unclear. Therefore, quite a number of patients have experienced distress in treatment. However, Sunami et al. [1] reported the presence of a significant correlation between recurrence of BPPV and histories of lifestyle-related illnesses, including hypertension and hyperlipemia. Wada et al. [2] also reported a significant correlation between a prolonged period until resolution of BPPV and histories of lifestyle-related illnesses, including hypertension and hyperlipemia. We considered the possibility of BPPV's correlating with lifestyle-related illnesses. Under these circumstances, we assessed correlations of lifestyle-related illnesses as background factors for BPPV and associated arteriosclerotic changes. We also assessed the usefulness of evaluating these correlations. We examined patients with peripheral vestibular disorders for the presence or absence of hypertension, diabetes mellitus, and lipid abnormalities and determined carotid artery intima-media thickness (IMT) by carotid (arterial) ultrasonography. IMT can be determined simply and noninvasively by ultrasonography and is regarded as a nonspecific indicator of systemic arteriosclerosis promoted by various factors, including hypertension, diabetes mellitus, lipid abnormalities, and aging. Previous studies have shown cross-sectional associations between

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IMT and cardiovascular risk factors and the prevalence of cardiovascular disease [3–5]. However, there have been no reports on IMT in patients with peripheral vestibular disorders or the reliability of IMT in these patients. We divided patients with vertigo and unsteady gait into two groups—those with BPPV and those with peripheral vestibular disorders—and discussed IMT and morbidity from underlying diseases.

METHODS

The subjects of this study were 85 patients who had vertigo and unsteady gait as chief complaints and were examined at Kitasato University Hospital between April 2007 and January 2008. BPPV was diagnosed by the following: a history of episodes of positional vertigo and a characteristic torsional paroxysmal positional nystagmus that was observed visually in performing the Dix-Hallpike test.

Peripheral vestibular disorders were diagnosed by the following: (1) a clinical history of clearly defined rotational vertigo or presence of spontaneous nystagmus, (2) normal results in the eye tracking test, (3) absence of a structural abnormal lesion on magnetic resonance imaging, and (4) absence of any central nervous symptom. The exclusion criterion was clinical diagnosis of BPPV. Written informed consent for participating in the study was obtained from all patients.

The mean age was 62 ± 10.5 years in the 32 men and 53 women. The BPPV group was composed of 31 patients; the posterior canal type was found in 28 patients, and the horizontal canal type was seen in 3 patients. The peripheral vestibular disorder group was composed of the other 54 patients. Within 1 month after the initial examination, ultrasonography and magnetic resonance imaging were conducted.

At the initial examination, we determined serum total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglyceride, blood glucose, and glycosylated hemoglobin (HbA1c) levels. When fasting blood glucose was ≥126 mg/dl, nonfasting blood glucose was ≥200 mg/dl, or HbA1c was ≥6.5%, the patient was given the diagnosis of diabetes mellitus. When total cholesterol was ≥220 mg/dl, LDL cholesterol was ≤140 mg/dl, or HDL cholesterol was ≤40 mg/dl, the patient was given the diagnosis of hypercholesterolemia. When systolic blood pressure was ≥140 mm Hg or diastolic blood pressure was ≥90 mm Hg, the patient was given the diagnosis of hypertension.

Cervical ultrasonography was conducted with an SSD-5500 (Aloka Co., Ltd., Tokyo, Japan) with a B-mode linear probe (15 MHz) in all patients. The test was conducted with patients in a supine position. The maximum IMT (max IMT) was defined as the maximum thickness of the blood vessel wall in the area of the common carotid artery (CCA) and the internal carotid artery. The maximum CCA IMT (max CCA IMT) was defined as the maximum thickness of the blood vessel wall in the area of the CCA. When IMT was ≥1.1 mm, the patient was given the diagnosis of abnormal blood vessel wall thickening.

All B-mode ultrasonographic images of the carotid artery also were obtained with an Aloka SSD-5500 system with a 15-MHz probe (Aloka). Patients were examined in the supine position. The protocol involved obtaining a single longitudinal lateral view of the distal 10 mm of the right and left CCAs and three longitudinal views (anterior-oblique, lateral, and posterior-oblique) of each internal carotid artery. The *internal carotid artery* was defined as including the carotid bulb. When an inner carotid region exhibited a thickening, we measured the inner carotid artery. *Max IMT* was defined as the single thickest wall of the far right and left walls of the CCA and internal carotid artery. *Maximum CCA IMT* (max CCA IMT) was defined as the thickest wall of the far right and left walls of the CCA. In addition, we prescribed a thickness of more than 1.1 mm as an abnormal thickening.

The data were analyzed by paired or unpaired *t*-tests and chi-squared tests. Correlation between two indices was analyzed using Spearman's correlation coefficient. We posited that p values of $<.05$ could be taken to be significant.

RESULTS

We compared clinical data obtained from subjects in the BPPV group and those in the peripheral vestibular disorder group (Table 1). The frequency of abnormal IMT was significantly higher in those in the BPPV group. Calculating for average age, max IMT was significantly higher in those in the BPPV group. Table 2 shows correlations among max IMT, max CCA IMT, age, and triglyceride, total cholesterol, LDL cholesterol, HDL cholesterol, and HbA1c levels.

DISCUSSION

Carotid ultrasonography, a noninvasive examination for arteriosclerotic changes, is useful for determining max IMT and max CCA IMT. According to the determination guidelines established by the Japanese Society for Ultrasonography, normal values of both max IMT and max CCA IMT are <1.1 mm. The max IMT was 1.58 mm in subjects in the BPPV group and 1.20 mm in those in the peripheral vestibular disorder group. The proportion of patients with max IMT ≥1.1 mm (i.e., thickening) was 71% in subjects in the BPPV group and 43% in those in the peripheral vestibular disorder group. Both

Table 1. Comparison of Clinical Data from Subjects in the BPPV and Peripheral Vestibular Disorder Groups

Parameter	BPPV ($n = 31$)	Peripheral Vertigo ($n = 54$)	Statistical Significance (p Value)
Male gender, *n* (%)	9 (29)	23 (43)	NS
Age (years)	65.9 ± 10.1	60.3 ± 10.4	.01
Hypertension, *n* (%)	14 (45)	27 (50)	NS
Diabetes mellitus, *n* (%)	7 (23)	17 (31)	NS
Hypercholesterolemia, *n* (%)	19 (61)	36 (67)	NS
Serum total cholesterol (mg/dl)	225.8 ± 59.0	226.8 ± 38.8	NS
Serum HDL cholesterol (mg/dl)	67.6 ± 14.4	62.5 ± 15.2	NS
Serum LDL cholesterol (mg/dl)	138.8 ± 40.9	143.3 ± 34.7	NS
Serum triglycerides (mg/dl)	177.6 ± 113.3	143.9 ± 82.9	NS
Serum HbAlc (%)	5.62 ± 0.64	5.57 ± 0.89	NS
Max IMT (mm)	1.58 ± 0.84	1.20 ± 0.64	<.01
Max CCA IMT (mm)	1.21 ± 0.83	1.03 ± 0.48	NS
Abnormal thickening (max IMT ≥1.1 mm), *n* (%)	22 (71)	23 (43)	<.05

BPPV = benign paroxysmal positional vertigo; CCA = common carotid artery; HbAlc = glycosylated hemoglobin; HDL = high-density lipoprotein; IMT = intima-media thickness; LDL = low-density lipoprotein; NS = not significant.

groups (i.e., peripheral vestibular disorder patients as a whole) can be said to have shown progression of arteriosclerotic changes when evaluated using max IMT as the indicator, because normal max IMT is <1.1 mm.

We added to data in the peripheral vestibular disorders group an increase of IMT that occurred with differences in the patients' average age, excepting the influence of the increase of IMT that occurs naturally with aging in all individuals. Among Japanese people, IMT increases by 0.008–0.01 mm for each year of age [6]. Because average ages differed by 5.6 years between the two groups, we added to data in the peripheral vestibular disorders group 0.056 mm as the increase of IMT that occurred with the average age difference. Then, max IMT and max CCA IMT data for the BPPV group and for the peripheral vestibular disorders group in which we had added the age-associated IMT increase were compared (Table 3). The proportion of patients with max IMT remained significantly higher in the BPPV group, regardless of the influence of age-related IMT increase.

Table 2. Correlations among Max IMT, Max CCA IMT, Age, and Triglyceride, Total Cholesterol, LDL Cholesterol, HDL Cholesterol, and HbA1c Levels

Parameter	Correlation Coefficient	p Value
Total chol, LDL chol	0.951	<.001
Max IMT, max CCA IMT	0.801	<.001
Age, max IMT	0.343	<.001
Age, HbAlc	0.290	<.01
HbAlc, TG	0.287	<.05
LDL chol, TG	0.284	<.05
HbAlc, total chol	0.267	<.05
Total chol, TG	0.258	<.01
HbAlc, LDL chol	0.248	<.05

CCA = common carotid artery; chol = cholesterol; HbAlc = glycosylated hemoglobin; HDL = high-density lipoprotein; IMT = intima-media thickness; LDL = low-density lipoprotein; max = maximum; TG = triglyceride.

Mutoh et al. [6] reported that the risk of cardiovascular disorders is significantly elevated in those with progressive arteriosclerosis (i.e., a max IMT of at least 1.1 mm) as compared to normal subjects with a max IMT <1.1 mm. Watanabe et al. [7] reported that monocytic active oxygen production is significantly increased in those with a max IMT ≥1.1 mm, as compared to subjects with a max IMT <1.1 mm. Oxidative stress, such as active oxygen species, is known to play an important role in the morbid condition of cardiovascular disorders. This finding is expected to lead to elucidation of the mechanisms underlying cardiovascular disorders in patients with progressive arteriosclerosis with a max IMT ≥1.1 mm. Kitahara et al. [4] reported the multivariate relative risk of stroke for the highest versus lowest quintiles of the maximum CCA IMT (≥1.07 mm versus <0.77 mm) to be 3.0 (95% confidence interval [CI], 1.1–8.3). The Cardiovascular Health Study Collaborative Research Group reported the multivariate risk of stroke for the highest versus lowest quintiles of the maximum CCA IMT (≥1.18 mm versus <0.87 mm) to be 2.13 (95% CI, 1.38–3.28), and the multivariate risk of myocardial infarction for the highest versus lowest quintiles of the maximum CCA IMT (≥1.18 mm versus <0.87 mm) to be 2.46 (95% CI, 1.51–4.01) [3].

We investigated relationships among max IMT, max CCA IMT, age, and triglyceride, total cholesterol, LDL cholesterol, HDL cholesterol, and HbA1c levels. Correlations were revealed and were considered to exert synergistic effects that promoted arteriosclerotic changes.

Lindsay and Hemenway [8] advocate circulatory disorder as an etiology of BPPV due to the degeneration brought about by the occlusion of the anterior vestibular artery. We report the presence of a factor that promotes

Table 3. Comparison of Max IMT and Max CCA IMT Data from Subjects in the BPPV and Peripheral Vestibular Disorders Groups after Revision of Latter Group's Data to Account for Age-Related Increases in IMT among Japanese Persons

Parameter	BPPV ($n = 31$)	Peripheral Vestibular Disorders, Data Revised for Average Age Differences ($n = 54$)	Statistical Significance (p Value)
Max IMT (mm)	1.58 ± 0.84	1.25 ± 0.67	<.05
Max CCA IMT (mm)	1.21 ± 0.83	1.09 ± 0.50	NS

BPPV = benign paroxysmal positional vertigo; CCA = common carotid artery; IMT = intima-media thickness; NS = not significant.

arteriosclerosis and arteriosclerotic changes in patients with BPPV and peripheral vestibular disorders. If an inner-ear disorder is generated by microcirculatory damage, sensory epithelial dysfunction will occur, detachment of the otolith from the otolith membrane will increase, and dysfunctional absorption of the otolith in vestibular dark cells may occur. Furthermore, a floating otolith can cause the onset of BPPV.

Our results indicate that cervical ultrasonography is useful for noninvasive examination of arteriosclerotic changes in patients with peripheral vestibular disorders. Our results also indicate that peripheral vestibular disorder patients demonstrate progression of arteriosclerotic changes.

These observations indicate that precise evaluation and treatment of arteriosclerotic changes, which are present as background factors in peripheral vestibular disorder patients, can reduce the risk of cerebral infarction, cerebral hemorrhage, myocardial infarction, and angina pectoris.

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