The Frequency and Risk Factors for Ischemic Stroke in Myotonic Dystrophy Type 1 Patients

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Introduction: Patients with myotonic dystrophy type 1 have several cardiac abnormalities, especially myocardial conduction disorders. Few studies have investigated cerebral infarction. We investigated the frequency of both symptomatic and asymptomatic ischemic strokes in patients with myotonic dystrophy type 1. *Methods:* Patients who were diagnosed with myotonic dystrophy type 1 using genetic testing or clinical examinations at Asahikawa Medical Center were included. We retrospectively reviewed their medical history, neuroradiological imaging, electrocardiograms, and treatment. Their CHADS2 and CHA2DS2-VASc scores were calculated. *Result:* A total of 108 patients were diagnosed with myotonic dystrophy type 1. Magnetic resonance imaging was performed in 72 and 1 patient whose results were not available was excluded. Among these, 2 patients had atrial flutter and 3 had atrial fibrillation. Regarding the CHADS2 score, 11 patients scored more than 2. Regarding the CHA2DS2-VASc score, 22 patients scored more than 2. Ischemic strokes were found in 9 patients with 1 having an atrial flutter and 4 having atrial fibrillation. All patients with stroke had CHADS2 and CHA2DS2-VASc scores higher than 2. There were significant differences between the 2 groups in atrial fibrillation ($P < .001$), CHADS2 score ($P < .001$), and CHA2DS2-VASc score ($P < .001$). *Conclusions:* Ischemic stroke in patients with myotonic dystrophy type 1 is associated with atrial fibrillation. The CHADS2 score seems to be useful for the management of patients with myotonic dystrophy type 1. Repeated electrocardiograms are necessary for managing these patients. **Key Words:** Myotonic dystrophy type 1—ischemic stroke—risk factor—atrial fibrillation—atrial flutter.
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Introduction

Myotonic dystrophy type 1 (DM1) is an autosomal dominant inherited disorder related to the expansion of a trinucleotide CTG repeat in the 3′-untranslated region of the dystrophia myotonica protein kinase gene, located on chromosome 19.[1,2] Although this expanded region is a noncoding sequence, several symptoms may yet arise from abnormal RNA.[3,4] Clinical features of DM1 include muscle atrophy and weakness, grip and percussion myotonia, hatchet face, and involvement of the central nervous, ocular, and endocrine systems. Patients with DM1 may have several cardiac abnormalities, especially myocardial conduction disorders.[5] Some conduction disorders, such as atrial fibrillation, may cause cerebral infarction. Patients with DM1 frequently have metabolic abnormalities such as diabetes mellitus and hyperlipidemia,[6,7] which are known risk factors for stroke. However, few studies have reported on cerebral infarction in patients with DM1,[8] and none included computed tomography or magnetic resonance imaging (MRI). We investigated the incidence of both symptomatic and asymptomatic ischemic strokes in patients with DM1.

Methods

Patients who were diagnosed with DM1 through genetic testing or clinical examination at Asahikawa Medical Center were included. We retrospectively investigated their medical records for their medical history, sex, age, follow-up duration, CTG repeats, neuroradiological imaging, electrocardiogram, and treatment. A certificated stroke specialist categorized the ischemic strokes according to the Trial of ORG 10172 in Acute Stroke Treatment guidelines.[9] We divided patients into 2 groups based on whether or not they had an ischemic stroke on MRI. In addition, the CHADS2[10] and CHA2DS2-VASc[11] scores were calculated to evaluate ischemic stroke risk. The CHADS2 score was calculated by assigning 1 point for congestive heart failure, hypertension, age>=75, and diabetes mellitus. A further 2 points was added for the criterion of previous stroke or TIA. The expanded CHA2DS2-VASc score scheme is based on a point system in which 2 points each are assigned for age>=75 and for history of stroke, TIA, or thromboembolism and 1 point is assigned for congestive heart failure, hypertension, diabetes mellitus, age 65~75 years, vascular disease (coronary artery disease, peripheral artery disease, aortic atherosclerosis), and female sex category. We analyzed risk factors with a chi-square test and Mann–Whitney U test using IBM SPSS version 20 software (IBM Corp., Armonk, NY).

Standard Protocols and Patient Consent

Ethical approval was obtained from the National Hospital Organization Asahikawa Medical Center Ethic Committee.

Results

A total of 108 patients were diagnosed with DM1 of which 105 patients were followed up (50 male; mean age 56.8; standard deviation 10.2) (Table 1). MRIs were performed in 72 patients. Symptomatic ischemic stroke was found in 4 patients (1 cardiac embolism, 1 lacunar infarction, and 2 of unknown origin) of which 1 had undergone an MRI but the results were unavailable; hence, this patient was subsequently excluded from our analysis. Another 6 patients had an asymptomatic ischemic stroke (5 cardiac embolisms, 1 lacunar infarction). A 24-hour Holter monitoring electrocardiogram was performed in 44 patients. Because 3 of 5 patients were found to have atrial fibrillation or flutter on a 12-lead electrocardiogram, only 2 patients underwent a 24-hour Holter monitor electrocardiogram.

Several risk factors were present in all patients with MRI (n = 71); 20 had hyperlipidemia, 18 had diabetes mellitus, 2 had atrial flutter, 3 had atrial fibrillation, 38 had an atrioventricular block (first degree in 32, third degree

Table 1. *Patient characteristics*

	MRI positive (n = 9)	Symptomatic	Asymptomatic	MRI negative (n = 62)	P value (MRI positive versus MRI negative)
Male : female	3:6	1:2	2:4	26:36	.62
Age	55.2	49.8	58.3	55.1	.38
Symptomatic	3/9	3/3	0/6	0	N/A
Cardiac embolism	6	1	5	-	N/A
Arteriosclerosis	0	0	0	-	N/A
Lacunar	2	1	1	-	N/A
Unknown	1	1	0	-	N/A
Hypertension	0/7	0/2	0/5	1/60	.73
Hyperlipidemia	2/7	1/2	1/5	15/60	.83
Diabetes mellitus	1/7	1/2	0/5	12/60	.72
Atrial flutter or fibrillation	4/7	2/2	2/5	1/58	<.001
Atrial flutter	1/7	0/2	1/5	1/58	.07
Atrial fibrillation	3/7	2/2	1/5	0/58	<.001
AV block	3/8	1/2	2/5	25/59	.91
LBBB	1/7	0/2	1/5	6/58	.75
RBBB	0/7	0/2	0/5	6/58	.37
Antiplatelet	1/7	0/2	1/5	3/62	.44
Anticoagulant	0/7	0/2	0/5	1/60	.73
Antiarrhythmic	4/8	1/2	3/5	2/59	<.001
PMI	0/7	0/2	0/5	2/59	.62

Abbreviations: AV, atrioventricular; LBBB, left bundle branch block; MRI, magnetic resonance imaging; PMI, pacemaker implantation; RBBB, right bundle branch block.