Clinical manifestations of cerebellar infarction according to specific lobular involvement

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Clinical manifestations of cerebellar infarction according to specific lobular involvement

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The Master's Thesis
submitted to the Department of Medicine
the Graduate School of Yonsei University
in partial fulfillment of the requirements for the degree
of Master of Medical Science

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December 2010

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The Graduate School
Yonsei University

December 2010

ACKNOWLEDGEMENTS

It is an honor for me to thank my supervisor, Professor Ji Hoe Heo, whose encouragement, guidance, and support from the initial to the final level enabled me to write this thesis. Also, I am very thankful to Professor Seung Min Kim and Professor Taek-Sang Nam for their valuable feedback and comments.

Next, I would like to thank those who made this thesis possible with their kind concern and help, Dr. Young Dae Kim, Dr. Hyo Suk Nam, and Hye Sun Lee.

Lastly, I offer my regards and blessings to all of those who supported me, including my family, and my wife.

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ABSTRACT

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Lesions in the cerebellum produce various symptoms related to balance and motor coordination. However, the relationship between the exact topographical localization of a lesion and the resulting symptoms is not well understood in humans. In this study, we analyzed 66 consecutive patients with isolated cerebellar infarctions demonstrated on diffusion-weighted magnetic resonance imaging. We identified the involved lobules in these patients using a cross-referencing tool of the picture archiving and communication system, and we investigated the relationships between the sites of the lesions and specific symptoms using χ^2 tests and logistic regression analysis. The most common symptoms in patients with isolated cerebellar infarctions were vertigo (87%) and lateropulsion (82%). Isolated vertigo or lateropulsion without any other symptoms were present in 38% of patients. On the other hand, limb ataxia was a presenting symptom in only 40% of the patients. Lateropulsion, vertigo, and nystagmus were more common in patients with a lesion in the caudal vermis. Logistic regression analysis showed that lesions in the posterior paravermis or

nodulus were independently associated with lateropulsion. Lesions in the nodulus were associated with contralateral pulsion, and involvement of the culmen was associated with ipsilateral pulsion and isolated lateropulsion without vertigo. Nystagmus was associated with lesions in the pyramis lobule, while lesions of the anterior paravermis were associated with dysarthria and limb ataxia. Our results showed that the cerebellar lobules are responsible for producing specific symptoms in cerebellar stroke patients.

Key words : cerebrovascular disease · MRI · cerebellum · lateropulsion

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I. INTRODUCTION

The cerebellum may be considered as a coordination center for the maintenance of equilibrium and movement through complex regulatory and feedback mechanisms. The cerebellum consists of anterior, posterior, and flocculonodular lobes, which are further divided into several small lobules. Lesions in the cerebellum cause a variety of signs and symptoms. However, the exact topographical localization of cerebellar lesions responsible for these symptoms in humans is not well understood. Although the cerebellum is grouped functionally into the spinocerebellum, vestibulocerebellum, and pontocerebellum, based on the origins of afferent fibers, these classifications do not precisely correspond to topographical localization. Consequently, rather broad areas in the cerebellum have been correlated with specific symptoms; for example, hemispheric lesions produce limb ataxia, and midline lesions produce

lateropulsion. Most studies investigating the function of the cerebellum in humans have been based on correlating clinical symptoms with the involved arterial territories in stroke patients[1-5]. Such studies have shown that dysarthria is most commonly associated with lesions in the territory of the superior cerebellar artery, whereas vertigo and lateropulsion are more often seen in lesions involving the territory of the posterior inferior cerebellar artery[1, 3, 6].

In the present study, we enrolled patients with isolated cerebellar infarctions demonstrated on diffusion-weighted magnetic resonance imaging (DWI). We identified the involved lobules in these patients using a picture archiving and communication system (PACS) and investigated the locations of lesions in the cerebellar lobules that are responsible for specific symptoms. In particular, we focused on the topographic localization of lesions associated with lateropulsion because the laterality of lateropulsion in relation to anatomical location has not been clearly elucidated[7].

II. MATERIALS AND METHODS

1. Patients

We enrolled consecutive patients with an isolated infarction in the cerebellum, as demonstrated on DWI identified from the Yonsei Stroke Registry (YSR)[8] between January 1999 and July 2008. The YSR is a prospective hospital-based registry for patients with cerebral infarction or transient ischemic attack (TIA)

who were admitted to the neurology department within seven days after symptom onset. The YSR includes data from brain and vascular imaging studies, cardiac evaluations, laboratory tests, past medical history, treatment, and outcomes. During the study period 4,176 patients were registered in the YSR, and, after excluding 355 patients with TIA, 3,821 patients were considered for the study. Among these, 164 consecutive patients (4.29%) were identified as having infarctions in the cerebellum. We excluded patients with any of the following: (1) concomitant infarction outside of the cerebellum (50 patients); (2) unavailable DWI images (26 patients); (3) failure to examine the presence of lateropulsion due to impairment of consciousness or lack of patient cooperation (9 patients); (4) inability to assess the presence of lateropulsion due to previous stroke with residual weakness or gait ataxia (6 patients); (5) previous cerebellar infarction confirmed by MRI (2 patients); and (6) no lesions visualised on DWI (5 patients). The final analysis included 66 patients, of whom 64 underwent angiographic studies (digital subtraction analysis in 13, magnetic resonance angiography (MRA) in 33, and both digital subtraction angiography and MRA in 18). Five patients with previous infarctions outside the cerebellum were included because they did not have neurologic deficits including problems in gait and body balance before index cerebellar infarctions. This study was approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System.

2. Clinical findings and laterality of lateropulsion and nystagmus

Clinical features were investigated retrospectively based on medical records and the YSR. Each symptom or sign was determined only when the presence or absence was clearly documented in the medical records. We collected the clinical data which was obtained between the time of admission and the time of MRI acquisition. The directions of lateropulsion and nystagmus were evaluated in patients with unilateral cerebellar lesions. Lateropulsion contralateral and ipsilateral to the cerebellar lesion was referred to as contralateral pulsion and ipsilateral pulsion, respectively. Similarly, the direction of nystagmus was termed contralateral nystagmus or ipsilateral nystagmus according to the side of the cerebellar lesion. Other clinical signs and symptoms, such as limb ataxia, nystagmus, vertigo, headache and dysarthria, were also assessed. Limb ataxia was defined as abnormal findings on finger-to-nose, heel-to-shin, or rapid alternating tests. Vertigo was defined as an illusion of moving sensation of the environment. Severity of lateropulsion was graded as mild (postural imbalance during tandem gait), moderate (postural imbalance on standing and tandem gait), and severe (inability to stand or sit without support).

3. Location of the lesions in the cerebellum

In all patients, magnetic resonance image (MRI) including DWI and MRA were performed shortly after the onset of symptoms (median interval 1.2 days, range: 3 to 154 hours). The presence of acute ischemic lesions was determined

by stroke specialists at the time of stroke conference. All the diffusion abnormalities were confirmed on apparent diffusion coefficient maps. The exact lobular localization of the lesion was determined by consensus between two investigators (B.S.Y., J.H.H.). We determined the locations of the infarctions based on axial DWI according to previously published templates for axial[9] and sagittal[10] sections and a three-dimensional MRI atlas of the human cerebellum[11]. For accurate centrocaudal localization of lesions, cross-referencing tools of our PACS, which permit simultaneous visualization of the three cardinal planes, were used on sagittal and/or coronal images (Fig. 1). Major fissures, including the preculminate, primary, horizontal, prepyramidal and secondary fissures, were identifiable on mid-sagittal images, and we localized the vermis lobules according to these fissures (Fig. 2). Localization of hemispheric structures was determined according to the axial DWI and coronal images because the differentiation between major fissures and other smaller fissures was uncertain on sagittal images. Accordingly, hemispheric structures were broadly classified into the anterior lobe and posterior lobe by the primary fissure and then subdivided into the paravermis, located adjacent to the vermis, and the hemisphere. The range of the paravermis was designated up to a fifth point close to the vermis between the vermis and lateral border of the hemisphere.

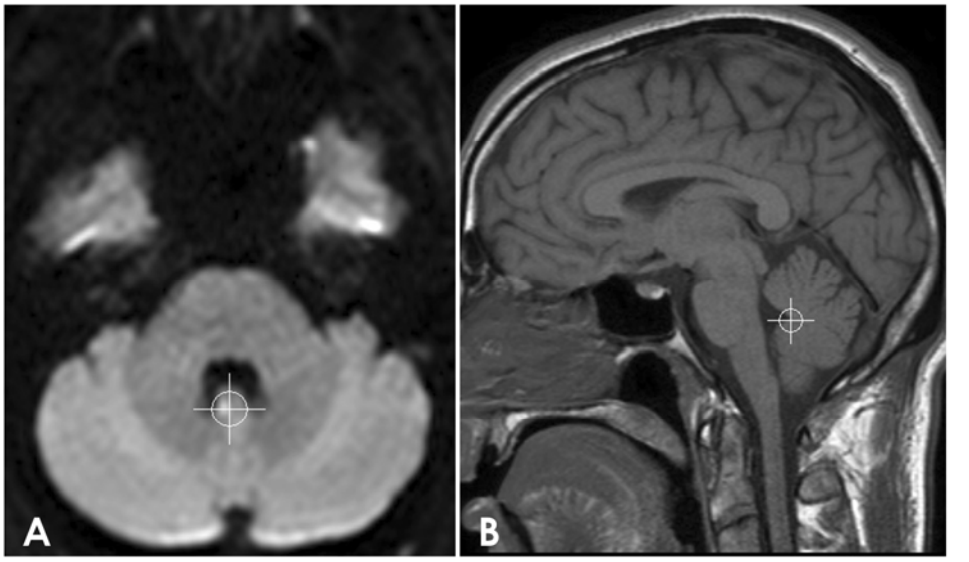

Fig. 1. The cross-referencing tool of a picture archiving and communication system used for localization of an infarction. Pointing to the lesion on diffusion-weighted axial MRI image (A) shows the site of the lesion on the T1-weighted sagittal MRI image (B), which enables accurate localization of the lesion.

The cerebellum was, thus, divided into 13 lobular portions: anterior and posterior hemisphere, anterior and posterior paravermis, rostral vermis (including lobules for the lingula-centralis and culmen), and caudal vermis (including lobules for the declive, folium-tuber, pyramis, uvula, tonsil, nodulus, and flocculus) (Fig. 2).

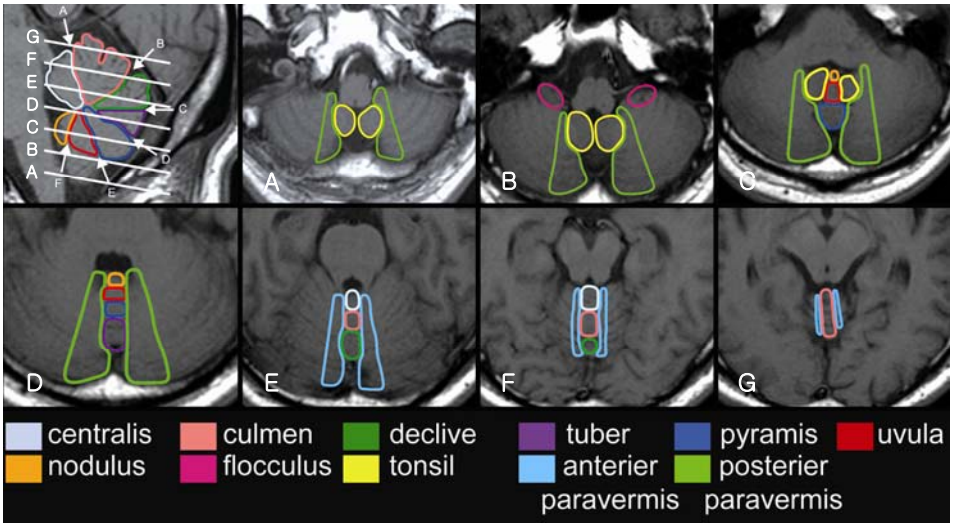

Fig. 2. Axial and sagittal templates for localization of cerebellar lobules. Axial localization of the vermal lobule depended on the major fissures (a: preculminate; b: primary; c: horizontal; d: Prepyramidal; e: secondary; and f: posterolateral) identified on the sagittal template. Imaginary lines for each axial template are drawn on the sagittal template (A to G).

4. Risk factors and mechanisms of infarctions

Hypertension was diagnosed when a patient had recorded high blood pressure (systolic ≥140 mm Hg or diastolic ≥90 mm Hg) or when the patient had been treated with antihypertensive medication. Diabetes mellitus was diagnosed when a patient had a high fasting plasma glucose value (≥7 mmol/L) or had been treated with oral hypoglycaemic agents and/or insulin. Hypercholesterolemia was defined as a high lipid profile (fasting serum total

cholesterol level ≥6.2 mmol/L or low-density lipoprotein cholesterol >4.1 mmol/L) or a history of treatment with lipid-lowering drugs after diagnosis of hypercholesterolemia. Patients were considered to be smokers if they had smoked any cigarette within the three months prior to admission. A history of previous stroke included old cerebral infarction or TIA, and a history of ischemic heart disease included myocardial infarction, unstable angina, percutaneous coronary artery angioplasty/stent, and/or bypass graft surgery.

The vascular territories were determined according to predetermined templates[9] into superior cerebellar artery (SCA), posterior inferior cerebellar artery (PICA), and anterior inferior cerebellar artery (AICA) territories. The etiologic mechanism of strokes was classified according to the Trial of ORG 10172 in Acute Stroke Treatment classification[12], which included large artery atherosclerosis, cardioembolism, lacune, stroke of other determined etiology, and stroke of undetermined etiology (due to two or more identified causes, negative evaluation, or incomplete evaluation).

5. Statistical analysis

Spearman's correlation analysis was used to find pairs of closely related cerebellar lobular involvement. Strength of correlation was estimated using Spearman's rank correlation coefficients (R) and considered significant when $R > 0.5$. The χ^2 test and logistic regression analysis were used to detect

associations between clinical features and lesion locations. Logistic regression analyses were used when the number of cases with a specific symptom was greater than 15 and when two or more lobules showed significant association with a specific symptom in the χ^2 test. For logistic regression analysis, if there was significant correlation ($R > 0.5$) between lobules, only one was entered into the model to avoid multicollinearity. All statistical tests were performed using SPSS for Windows (SPSS version 12.0, SPSS Inc., Chicago, IL, USA), except for the exact logistic regression analysis for lateropulsion, which was performed using Statistical Analysis System software (SAS version 9.1, SAS Inc., Cary, NC, USA) due to the extreme distribution of the cases. Statistical significance was set at $p < 0.05$.

III. RESULTS

1. Demographic features and risk factors

Isolated cerebellar infarctions were found in 2.98% (114/3821) of the patients considered for the study. The final 66 patients who were enrolled in this study included 50 men and 16 women with a median age of 62 years (range 20–83). Hypertension was the most common risk factor, followed by smoking and diabetes mellitus (Table 1). Potential cardiac sources of embolism were present in 22 patients, and other rare causes were present in 6 patients (Table 1).

Table 1. Demographic features and risk factors of the study sample

	N	%
Sex		
Male	50	75.8
Female	16	24.2
Median age (years)	62 (range, 20–83)	
Vascular risk factors		
Hypertension	44	66.7
Diabetes	13	19.7
Hyperlipidemia	7	10.6
Previous stroke	5	7.6
Smoking history		
Current smoker	17	25.8
Mean Pack Years	14.3 (range, 0-60)	
TOAST classification*		
Large artery atherosclerosis	22	33.3
Cardioembolism	18	27.3
Stroke of uncertain etiology due to two or more causes identified	3	4.5
Negative evaluation	17	25.8
Stroke of other determined etiology	6	9.1
Potential cardiac sources of embolism	21**	31.8

Atrial fibrillation	7	10.6
Patent foramen ovale	11	16.7
Mechanical valve	2	3.0
Mitral regurgitation	2	3.0
Mitral stenosis without atrial fibrillation	1	1.5
Intracardiac thrombi	1	1.5
Other etiologies	6	9.1
Vertebral artery dissection	4	6.1
Radiation therapy to neck	1	1.5
Status migrainosus	1	1.5

* *TOAST* Trial of Org 10172 in Acute Stroke Treatment

** One patient with patent foramen ovale and one with intracardiac thrombi had concomitant atrial fibrillation. One patient with mitral regurgitation had concurrent patent foramen ovale.

2. Clinical findings

Vertigo and lateropulsion were the most frequent manifestations, occurring in 87.3% and 81.8% of patients, respectively. Twenty-five patients (38%) showed isolated vertigo and/or lateropulsion without any other symptoms (vertigo only in 6 patients, lateropulsion only in 5, and vertigo with lateropulsion in 14). Limb ataxia was present in 39.4% of patients (Table 2). The direction of lateropulsion

could be assessed in 40 patients with unilateral cerebellar lesions. Of these, 31 patients (77.5%) demonstrated lateropulsion, and 13 patients (32.5%) fell to the contralateral side of the lesion or bilaterally. Nystagmus was present in 24 patients. Among the 40 patients with unilateral lesions, ipsilateral nystagmus was more common than contralateral nystagmus (Table 2). We graded the severity of lateropulsion. Among 54 patients with lateropulsion, it was mild in 22 (40.7%), moderate in 15 (27.8%), and severe in 17 (31.5%) patients.

Table 2. Clinical findings of the patients in the study sample

Symptoms and signs	**Number***	**Frequency**
Lateropulsion	66	54 (81.8)***
Contralateral**	40	6 (15.0)
Ipsilateral**	40	18 (45.0)
Bilateral**	40	7 (17.5)
Nystagmus	65	24 (36.9)
Contralateral**	40	3 (7.5)
Ipsilateral**	40	9 (22.5)
Bilateral**	40	3 (7.5)
Vertigo	63	55 (87.3)
Limb ataxia	66	26 (39.4)

Headache	60	18 (30.0)
Dysarthria	62	8 (12.9)

* Number with clear description in medical records concerning the presence or absence of each symptom/sign.

** Laterality of the pulsion and/or nystagmus was assessed in 40 patients with unilateral lesions.

*** Numbers in parentheses are percentages.

3. Distribution of the cerebellar infarctions

The most frequently involved site was the posterior paravermis (n=54, 81.8%), followed by the posterior hemisphere (n=48, 72.7%), tonsil (n=40, 60.6%), uvula (n=27, 40.9%), nodulus (n=27, 40.9%), and pyramis (n=20, 30.3%). Lesions were more frequently observed in the caudal vermis (n=47, 71.2%) than in the rostral vermis (n=11, 16.7%), and in the posterior paravermis and/or hemisphere (n=58, 87.9%) than the anterior paravermis and/or hemisphere (n=13, 19.7%).

Nine of 66 patients (13.6%) had lesions confined to a single cerebellar lobule: 1 patient had a lesion in the lingula-centralis; 3 in the posterior paravermis; 3 in the posterior hemisphere; 1 in the anterior paravermis; and 1 in the anterior hemisphere. However, the majority of patients had lesions involving multiple

cerebellar lobules. All 27 patients with lesions in the nodulus had concomitant lesions in other cerebellar lobules. Many lobules were found to be concurrently involved (correlation coefficient > 0.7 between the pyramis and the folium-tuber and the anterior paravermis and the anterior hemisphere), and these were adjacently located (Table 3).

4. Correlations between clinical symptoms and MRI lesions

Clinical symptoms and signs correlated with 13 lesion locations by χ^2 testing (Table 4). Patients with lesions in the caudal vermis (folium-tuber, uvula, tonsil, and nodulus) and posterior paravermis were more likely to have lateropulsion than those without lesions in these locations, and all patients with lesions in the folium-tuber or nodulus showed lateropulsion. Nystagmus was more frequent in patients with lesions in the caudal vermis (folium-tuber, pyramis, uvula, tonsil, and nodulus) and posterior paravermis than in those without such lesions. Patients with lesions in the anterior paravermis and anterior hemisphere were more likely to have dysarthria and limb ataxia. Dysarthria and limb ataxia were also more common in the patients with lingual-centralis and culmen, respectively. Vertigo was frequently observed in patients with lesions involving the posterior paravermis. In the investigation of the severity of lateropulsion, patients with lesions in the uvula (40.7% vs. 15.4%, p = 0.026), nodulus (44.4% vs. 12.8%, p = 0.009), and tonsil (37.5% vs. 7.7%, p = 0.009) lobules showed

Table 3. Cerebellar lobules with concurrent tendency

	Lingula-centralis	Culmen	Declive	Folium-tuber	Pyramis	Uvula	Tonsil	Nodulus	Flocculus	Posterior paravermis	Posterior hemisphere	Anterior paravermis	Anterior hemisphere
Lingual-centralis													
Culmen	0.678**												
Declive	0.348**	0.458**											
Folium	-0.203	-0.249*	0.261*										
Pyramis	-0.227	-0.279*	0.117	0.743**									
Uvula	-0.187	-0.094	0.167	0.426**	0.591**								
Tonsil	-0.427**	-0.351**	-0.022	0.333**	0.397**	0.545**							
Nodulus	-0.187	-0.180	0.167	0.567**	0.658**	0.561**	0.482**						
Flocculus	-0.099	-0.121	-0.135	0.224	0.310*	0.228	0.231	0.228					
Posterior paravermis	-0.220	-0.129	0.120	0.278*	0.225	0.232	0.424**	0.232	-0.013				
Posterior hemisphere	-0.121	-0.026	0.024	0.205	0.182	0.025	0.272*	0.025	0.047	0.417**			
Anterior paravermis	0.603**	0.677**	0.389**	-0.188	-0.225	-0.153	-0.424**	-0.153	-0.135	-0.185	-0.241		
Anterior hemisphere	0.638**	0.718**	0.316**	-0.263*	-0.295*	-0.207	-0.471**	-0.207	-0.128	-0.211	-0.183	0.843**	

A number in each cell is a Spearman's rank correlation coefficient.

* Correlation with $p < 0.05$, ** Correlation with $p < 0.01$

more frequent severe lateropulsion than those without.

Three of the 10 patients (30.0%) with a culmen lobular lesion showed lateropulsion without vertigo, whereas only 4 of the 55 patients (7.3%) without this lesion showed lateropulsion without vertigo ($p = 0.067$). Logistic regression analyses showed that lesions of the posterior paravermis or nodulus were independently associated with lateropulsion, although the statistical significance was not reached for the posterior paravermis ($p = 0.059$). Lesions of the pyramis were associated with nystagmus and those of the folium-tuber were associated with headache (Table 5).

5. Direction of lateropulsion and nystagmus

The direction of lateropulsion was further analysed in 40 patients with unilateral lesions (Table 5). Six of the 12 patients (50%) with unilateral lesions in the nodulus showed contralateral pulsion, compared with none of the 28 patients without nodulus lesions ($p < 0.001$). The remaining patients with unilateral nodulus lesions showed ipsilateral pulsion (3 patients) or bilateral pulsion (3 patients). Patients with a lesion involving the culmen were more likely to show ipsilateral pulsion than those without such lesions ($p = 0.073$). Ipsilateral nystagmus was associated with lesions in the pyramis, uvula, and tonsil (Table 4).

Table 4. Differences in symptoms/signs according to locations of cerebellar lesions

			Lateropulsion	Contralateral pulsion	Ipsilateral pulsion	Nystagmus	Vertigo	Headache	Dysarthria	Ataxia	Lateropulsion without vertigo	Ipsilateral nystagmus
Rostral vermis	Lingual-centralis	+	6 (7, 85.7%)	0 (4, 0%)	2 (4, 50.0%)	2 (7, 28.6%)	6 (7, 85.7%)	2 (7, 28.6%)	3 (7, 42.9%)	5 (7, 71.4%)	1 (7, 14.3%)	1 (4, 25.0%)
		–	48 (59, 81.4%)	6 (36, 16.7%)	16 (36, 44.4%)	22 (58, 37.9%)	49 (56, 87.5%)	16 (53, 30.2%)	5 (55, 9.1%)	21 (59, 35.6%)	6 (58, 10.3%)	8 (36, 22.2%)
		P	1.0	1.0	1.0	1.0	1.0	1.0	0.040	0.102	0.568	1.0
	Culmen	+	10 (10, 100%)	0 (6, 0%)	5 (6, 83.3%)	4 (10, 40.0%)	7 (9, 77.8%)	1 (9, 11.1%)	3 (10, 30.0%)	7 (10, 70.0%)	3 (10, 30.0%)	2 (6, 33.3%)
		–	44 (56, 78.6%)	6 (34, 17.6%)	13 (34, 38.2%)	20 (55, 36.4%)	49 (55, 89.1%)	17 (51, 33.3%)	5 (52, 9.6%)	19 (56, 33.9%)	4 (55, 7.3%)	7 (34, 20.6%)
		P	0.187	0.565	0.073	1.0	0.135	0.255	0.111	0.041	0.067	0.602
Caudal vermis	Declive	+	12 (12, 100%)	1 (6, 16.7%)	4 (6, 66.7%)	6 (12, 50.0%)	10 (12, 83.3%)	5 (11, 45.5%)	1 (9, 11.1%)	7 (12, 58.3%)	2 (12, 16.7%)	1 (6, 16.7%)
		–	42 (54, 77.8%)	5 (34, 14.7%)	14 (34, 41.2%)	18 (53, 34.0%)	45 (51, 88.2%)	13 (49, 26.5%)	7 (53, 13.2%)	19 (54, 35.2%)	5 (53, 9.3%)	8 (34, 23.5%)
		P	0.104	1.0	0.381	0.335	0.641	0.279	1.0	0.193	0.604	1.0
	Folium-tuber	+	17 (17, 100%)	3 (9, 33.3%)	4 (9, 44.4%)	11 (17, 64.7%)	15 (16, 93.8%)	9 (15, 60.0%)	0 (14, 0%)	8 (17, 47.1%)	1 (16, 6.3%)	4 (9, 44.4%)
		–	37 (49, 75.5%)	3 (31, 9.7%)	14 (31, 45.2%)	13 (48, 27.1%)	40 (47, 85.1%)	9 (45, 20.0%)	8 (48, 16.7%)	18 (49, 36.7%)	6 (49, 12.2%)	5 (31, 16.1%)
		P	0.027	0.115	1.0	0.009	0.667	0.007	0.181	0.567	0.671	0.168
	Pyramis	+	19 (20, 95.0%)	3 (9, 33.3%)	3 (9, 33.3%)	14 (20, 70.0%)	18 (19, 94.7%)	9 (18, 50.0%)	0 (16, 0%)	10 (20, 50.0%)	1 (19, 5.3%)	5 (9, 55.6%)
		–	35 (46, 76.1%)	3 (31, 9.7%)	15 (31, 48.4%)	10 (45, 22.2%)	37 (44, 84.1%)	9 (42, 21.4%)	8 (46, 17.4%)	16 (46, 34.8%)	6 (46, 13.0%)	4 (31, 12.9%)
		P	0.088	0.115	0.476	0.001	0.417	0.035	0.099	0.282	0.663	0.016
	Uvula	+	26 (27, 96.3%)	4 (13, 30.8%)	4 (13, 30.8%)	16 (27, 59.3%)	25 (27, 92.6%)	11 (26, 42.3%)	2 (24, 8.3%)	14 (27, 51.9%)	2 (27, 7.4%)	6 (13, 46.2%)
		–	28 (39, 71.8%)	2 (27, 7.4%)	14 (27, 51.9%)	8 (38, 21.1%)	30 (36, 83.3%)	7 (34, 20.6%)	6 (38, 15.8%)	12 (39, 30.8%)	5 (38, 13.2%)	3 (27, 11.1%)
		p	0.020	0.075	0.312	0.004	0.448	0.091	0.468	0.124	0.690	0.038

			Lateropulsion	Contralateral pulsion	Ipsilateral pulsion	Nystagmus	Vertigo	Headache	Dysarthria	Ataxia	Lateropulsion without vertigo	Ipsilateral nystagmus
	Tonsil	+	36 (40, 90.0%)	5 (21, 23.8%)	9 (21, 42.9%)	19 (39, 48.7%)	37 (40, 92.5%)	14 (39, 35.9%)	1 (37, 2.7%)	17 (40, 42.5%)	3 (40, 7.3%)	8 (21, 38.1%)
		–	18 (26, 69.2%)	1 (19, 5.3%)	9 (19, 47.4%)	5 (26, 19.2%)	18 (23, 78.3%)	4 (21, 19.0%)	7 (25, 28.0%)	9 (26, 34.6%)	4 (25, 16.0%)	1 (19, 5.3%)
		P	0.050	0.186	1.0	0.020	0.129	0.241	0.006	0.610	0.415	0.021
	Nodulus	+	27 (27, 100%)	6 (12, 50.0%)	3 (12, 25.0%)	15 (27, 55.6%)	26 (27, 96.3%)	8 (26, 30.8%)	0 (23, 0%)	13 (27, 48.1%)	1 (27, 3.7%)	5 (12, 41.7%)
		–	27 (39, 69.2%)	0 (28, 0%)	15 (28, 53.6%)	9 (38, 23.7%)	29 (36, 80.6%)	10 (34, 29.4%)	8 (39, 20.5%)	13 (39, 33.3%)	6 (38, 15.8%)	4 (28, 14.3%)
		P	0.001	< 0.001	0.165	0.011	0.123	1.0	0.021	0.306	0.224	0.097
	Flocculus	+	5 (5, 100%)	2 (3, 66.7%)	1 (3, 33.3%)	3 (5, 60.0%)	5 (5, 100.0%)	2 (5, 40.0%)	0 (5, 0%)	1 (5, 20.0%)	0 (5, 0%)	2 (3, 66.7%)
		–	49 (61, 80.3%)	4 (37, 10.8%)	17 (37, 45.9%)	21 (60, 35.0%)	50 (58, 86.2%)	16 (55, 29.1%)	8 (57, 14.0%)	25 (61, 41.0%)	7 (60, 11.7%)	7 (37, 18.9%)
		P	0.575	0.054	1.0	0.350	1.0	0.631	1.0	0.641	1.0	0.121
Extra -vermis	Posterior paravermis	+	48 (54, 88.9%)	6 (30, 20.0%)	15 (30, 50.0%)	23 (53, 43.4%)	48 (52, 92.3%)	16 (50, 32.0%)	4 (50, 8.0%)	22 (54, 40.7%)	4 (53, 7.5%)	8 (30, 26.7%)
		–	6 (12, 50.0%)	0 (10, 0%)	3 (10, 30.0%)	1 (12, 8.3%)	7 (11, 63.6%)	2 (10, 20.0%)	4 (12, 33.3%)	4 (12, 33.3%)	3 (12, 25.0%)	1 (10, 10.0%)
		P	0.005	0.307	0.464	0.043	0.026	0.708	0.039	0.751	0.111	0.404
	Posterior hemisphere	+	41 (48, 85.4%)	3 (26, 11.5%)	12 (26, 46.2%)	19 (47, 40.4%)	41 (46, 89.1%)	17 (46, 37.0%)	4 (45, 8.9%)	19 (48, 39.6%)	5 (47, 10.6%)	6 (26, 23.1%)
		–	13 (18, 72.2%)	3 (14, 21.4%)	6 (14, 42.9%)	5 (18, 27.8%)	14 (17, 82.4%)	1 (14, 7.1%)	4 (17, 23.5%)	7 (18, 38.9%)	2 (18, 11.1%)	3 (14, 21.4%)
		P	0.284	0.646	1.0	0.401	0.671	0.045	0.198	1.0	1.0	1.0
	Anterior paravermis	+	10 (12, 83.3%)	1 (8, 12.5%)	4 (8, 50.0%)	4 (12, 33.3%)	9 (10, 90.0%)	1 (10, 10.0%)	6 (11, 54.5%)	10 (12, 83.3%)	2 (12, 16.7%)	1 (8, 12.5%)
		–	44 (54, 81.5%)	5 (32, 15.6%)	14 (32, 43.8%)	20 (53, 37.7%)	46 (53, 86.8%)	17 (50, 34.0%)	2 (51, 3.9%)	16 (54, 29.6%)	5 (53, 9.4%)	8 (32, 25.0%)
		P	1.0	1.0	1.0	1.0	1.0	0.256	< 0.001	0.001	0.604	0.655

		Lateropulsion	Contralateral pulsion	Ipsilateral pulsion	Nystagmus	Vertigo	Headache	Dysarthria	Ataxia	Lateropulsion without vertigo	Ipsilateral nystagmus
Anterior hemisphere	+	10 (11, 90.9%)	0 (7, 0%)	5 (7, 71.4%)	3 (11, 27.3%)	8 (10, 80.0%)	1 (11, 9.1%)	5 (11, 45.5%)	8 (11, 72.7%)	3 (11, 27.3%)	1 (7, 14.3%)
	−	44 (55, 80.0%)	6 (33, 18.2%)	13 (33, 39.4%)	21 (54, 38.9%)	47 (53, 88.7%)	17 (49, 34.7%)	3 (51, 5.9%)	18 (55, 32.7%)	4 (54, 7.4%)	8 (33, 24.2%)
	P	0.673	0.567	0.211	0.733	0.602	0.148	0.003	0.019	0.088	1.0

Table 5. Involvement of cerebellar lobules as predictors of specific signs (results of logistic regression analysis)

Signs (Total No.)	Cerebellar lobule (n)	Patients with symptom, No. (%)	*P* value	OR (95% CI)
Lateropulsion (66)	Nodulus		0.008	3.43 (1.31, 999.99)*
	+ (27)	27 (100)		
	- (39)	27 (69.2)		
	Posterior paravermis		0.059	1.79 (0.97, 6.02)
	+ (54)	48 (88.9)		
	- (12)	6 (50.0)		
Nystagmus (65)	Pyramis		0.006	6.42 (1.67, 21.34)
	+ (20)	14 (70.0)		
	- (45)	10 (22.2)		
Headache (60)	Folium-tuber		0.017	4.83 (1.32, 17.73)
	+ (15)	9 (60.0)		
	- (45)	9 (20.0)		
Ataxia (66)	Anterior paravermis		0.021	15.02 (1.49, 151.00)
	+ (12)	10 (83.3%)		
	- (54)	16 (29.6%)		

OR, odds ratio; +, present; −, absent

6. Etiologic mechanisms and involved arterial territories

Large artery atherosclerosis (n=22) was the most common mechanism of isolated cerebellar infarction, followed by cardioembolism (n=18). Other etiologies were found in 6 patients, and 4 had vertebral artery dissection (Table 1). Of the total 66 patients, 56 demonstrated lesions that involved a single cerebellar artery territory, while 10 had lesions that involved multiple territories. PICA involvement was most common (52 patients). SCA involvement was observed in 19 patients, whereas only 6 patients had lesions in the AICA territory.

IV. DISCUSSION

In this study, the most common symptoms in patients with isolated cerebellar infarctions were vertigo and lateropulsion, which were both observed in approximately 85% of the patients. Moreover, approximately 38% of the patients had isolated vertigo and/or lateropulsion without any other cerebellar signs. While physicians may expect the presence of cerebellar-type limb ataxia as a representative sign of cerebellar infarctions, it was only observed in approximately 40% of our patients. These findings suggest that great attention should be paid to patients with vertigo or lateropulsion and stroke risk factors, even if they do not have any other cerebellar symptoms or signs, as it was suggested in a previous study[6].

Lateropulsion is an irresistible sensation of falling to one side and is a

well-known clinical feature of posterior circulation stroke. Lateropulsion has been reported in infarctions of the lateral and medial medulla oblongata, pons, midbrain, thalamus, and various locations in the cerebellum. The direction of the lateropulsion is ipsilateral to lesions in the vestibular nerve, vestibular nucleus, lateral medulla oblongata, and inferior cerebellar peduncle[13-17]; however, it may be contralateral to lesions involving the nucleus prepositus hypoglossi, medial medulla oblongata, pontine tegmentum, and rostral paramedian midbrain[18-21]. The present study demonstrated that lesions involving the nodulus were associated with contralateral pulsion, as described in a few previous case reports[7, 22]. Furthermore, this study clearly showed that nodulus involvement is critically responsible for the direction of lateropulsion, because contralateral pulsion was only observed in cases with nodulus involvement, even when adjacent structures of the vermis or paravermis were involved concomitantly.

In contrast, lesions involving the culmen lobule were independently associated with ipsilateral lateropulsion. Isolated lateropulsion without vertigo was also associated with lesions of the culmen. Additionally, isolated lateropulsion has been reported in a patient with a lesion in the rostral vermis[23]. The culmen lobule, which is a structure of the rostral vermis, is one of the arrival sites of the spinocerebellar tract[24, 25]. The dorsal spinocerebellar tract conveys unconscious proprioceptive information from the leg and the lower

trunk. In humans, lesions of the dorsal spinocerebellar tract produce ipsilateral falling without vertigo or nystagmus[16]. These findings suggest that ipsilateral pulsion in lesions involving the culmen, which often occurs without vertigo, may be related to damage of a pathway involving the spinocerebellar tract.

Body balance is maintained primarily by vestibular function and unconscious proprioceptive function. Lesions involving the folium-tuber, uvula and nodulus, which are structures of the caudal vermis, produced lateropulsion and nystagmus. These findings suggest that vestibular dysfunction may be responsible for the development of lateropulsion in patients with a lesion involving the caudal vermis. The Purkinje cells in the vermis have an inhibitory influence on the ipsilateral fastigial nucleus,[26, 27] and the caudal fastigial nucleus has an excitatory connection with the contralateral vestibular nucleus[28]. Lesions in the vestibular nucleus result in ipsilateral falling[29]. Therefore, dysfunction of the ipsilateral vermal Purkinje's cells may disinhibit the ipsilateral caudal fastigial nuclei and consequently activate the contralateral vestibular nucleus, resulting in ipsilateral lateropulsion.

In contrast to other areas of the vermis, a lesion involving the nodulus resulted in contralateral pulsion. The nodulus projects to areas in the inferior vestibular nucleus[30] that receive afferents from the contralateral fastigial nucleus[31]. Timed stimulation of the nodulus inhibits the ipsilateral vestibular

nucleus, which is activated by contralateral caudal fastigial stimulation[32]. Thus, a lesion in the nodulus may disinhibit the ipsilateral inferior vestibular nucleus, resulting in contralateral pulsion.

We also analysed the laterality of nystagmus according to the side of the lesion. Ipsilateral nystagmus was found more frequently with lesions in lobules of the caudal vermis, including the pyramis, uvula and tonsil. It is plausible that dysfunction of the vestibuloocular reflex caused by disruption of the cerebellovestibular connection is responsible for this ipsilesional nystagmus[24]. Our findings are consistent with previous studies showing that, in addition to lesions in the flocculonodular lobe, lesions in the caudal vermis might also cause spontaneous and positional nystagmus or other ocular motor deficits[33, 34].

In the present study, headache was more frequent in lesions involving the folium-tuber, pyramis, or posterior hemisphere, which are parts of the PICA territory. Previous studies have shown that headache is common in infarctions involving the PICA territory[2]. More frequent occurrence of dysarthria in lesions involving the lingual-centralis, anterior paravermis, and anterior hemisphere is comparable with previous findings that showed frequent dysarthria in SCA territorial infarctions, because these areas are supplied by the SCA[2, 35, 36]. The more frequent occurrence of limb ataxia in lesions of the culmen, anterior paravermis, and anterior hemisphere may be related to the cerebellar

homunculus because the main activation areas for movement of the hands and feet are known to be located in the ipsilateral anterior lobe[37, 38].

Certain methodological issues should be addressed regarding data analysis in this study. First, it is not always easy to determine involvement of specific lobules based on visually guided assessment of axial CT or MRI images. Therefore, we assessed lesion locations using cross-referencing tools on a PACS system, which provide more precise determination than visually guided judgement of the lesion location. Second, we used statistical analyses, including χ^2 tests and logistic regression analysis, to determine clinico-lesion correlation. The exact functions of specific lobules of the human cerebellum are not well understood because of the relative lack of clinico-lesion correlation studies based on specific cerebellar lobules. In most cases, cerebellar diseases affect more than one lobule because small lobules are located adjacently in the cerebellum[24]. This may be especially true for cerebellar infarctions because three cerebellar arteries supply many different lobules. In our study, most cases had lesions involving more than one lobule. We, therefore, used the χ^2 test and logistic regression analysis because their usefulness for this application has been demonstrated in other studies[39].

A limitation of this study is the fact it was a retrospective study. Also, investigation and exact analyses of eye movements could not be performed.

Although all of the patients had acute cerebellar infarctions, some clinical features might have improved by the time of examination; therefore, the frequencies of certain symptoms might be underestimated. Certain clinical features might not be picked-up on DWI in cases that the interval between onset of symptoms and MRI acquisition was very short. Five patients with previous extra-cerebellar strokes were included in this study. Although they had no remaining neurologic deficits, there might be some confounding effects caused by cerebellar compensation after the previous strokes. We took relatively consistent evaluation processes and achieved consensus between neurologic examinations. However, there might be some selection bias in neurologic examination findings because multiple neurologists with variable expertise performed neurologic examination during the study period. Also, some patients with mild symptoms (such as isolated vertigo) might not visit or be referred to our hospital because the study hospital is a large university hospital.

V. CONCLUSION

With MRI and clinical data obtained from patients with isolated cerebellar infarctions, we determined lobular localization of cerebellar lesions using a PACS system and statistical analyses. Our results showed that vertigo and lateropulsion are the most common symptoms of isolated cerebellar infarctions. Our findings also suggest that contralateral pulsion was associated with lesions involving the nodulus, while ipsilateral pulsion was associated with lesions

involving the culmen. Nystagmus was associated with lesions in the pyramis lobule, while dysarthria and limb ataxia were associated with lesions of the anterior paravermis.

Our results showed that the cerebellar lobules are responsible for producing specific symptoms in cerebellar stroke patients.

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ABSTRACT(IN KOREAN)

소뇌경색에서 침범된 소엽에 따른 임상증상의 발현

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예병석

소뇌의 병변은 자세 안정 및 운동 조절에 관련된 다양한 증상을 유발한다. 하지만 소뇌의 국소해부학적 병소의 위치와 그로 인한 증상과의 연관성은 아직 명확히 밝혀지지 않았다. 이 연구에서 우리는 뇌 자기공명영상에서 소뇌에 국한된 병변을 가진 것이 확인된 66명의 소뇌 경색 환자를 분석하였다. Cross-referencing tool of the picture archiving and communication system로써 확인된 소뇌 경색의 소엽(lobule)의 위치와 임상증상과의 연관성을 카이 제곱 및 로지스틱 회귀분석으로 확인하였다. 소뇌에 국한된 뇌경색에서 가장 흔한 증상은 현훈(87%)과 가쪽 쏠림(82%)이었고, 다른 소뇌 증상이 동반되지 않고 현훈이나 가쪽 쏠림 증상만 있었던 경우도 전체의 38%에서 확인되었다. 반면, 팔과 다리의 운동실조 증상은 전체의 40%에서만 관찰되었다. 가쪽 쏠림, 현훈, 안진은 뒤 소뇌벌레(caudal vermis)에 병변이 있는 환자에서 흔했고, 로지스틱 회귀분석 결과 뒤 방충부(posterior paravermis)나 결절(nodulus)이 가쪽 쏠림과 독립적으로 연관되어 있었다. 결절(nodulus)의 병변은 병변 반대측으로의 쏠림과 관련이 있었고, 소뇌 정상(culmen)의 병변은 병변 방향으로의 쏠림 및 현훈이 없는 가쪽 쏠림과 연관되어 있었다. 안진은 소뇌 피라미드(pyramis)의 병변과 연관이 있었던 반면, 앞 방충부(anterior paravermis)의 병변은 구음 장애와 운동 실조와

연관이 있었다. 우리는 연구의 결과로 소뇌의 특정 소엽이 특정 소뇌 증상과 관련되어 있음을 확인하였다.

핵심되는 말 : 뇌혈관 질환, 자기공명영상, 소뇌, 가쪽 쏠림

PUBLICATION LIST

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