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The Relationship Between Vertebral Artery Hypoplasia and Posterior Circulation Stroke

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ABSTRACT

Introduction: Vertebral artery hypoplasia (VAH) is a common variation; however, its role in posterior circulation stroke (PCS) has not been fully elucidated. Thus, this study aimed to evaluate the relationship between VAH and PCS with clinical and laboratory parameters.

Methods: Between January 2016 and June 2020, 178 patients with PCS who were hospitalized in the neurology department were included. The demographic characteristics, vascular risk factors, stroke patterns, and the National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) scores of patients were recorded. Patients with VA diameter of ≤2.0 mm or 1:1.7 ratio difference in computed tomography angiography were included in the VAH group.

Results: This study included 115 females and 63 males. The mean age of patients was 65.8±12 years. VAH was determined in 74 (41.6%) patients, whereas none in 104 patients (58.4%). No significant difference was determined in terms of gender and age in patients with and without VAH (p=0.310 and p=0.676, respectively). No statistically significant difference was found between the two groups in terms of vascular risk factors (p>0.05). Lacunar stroke pattern was less frequently found in patients with VAH (p=0.045). Other stroke patterns were similar in both groups (p>0.05). The NIHSS (p=0.01) and mRS (p=0.018) scores were significantly higher in patients with VAH than those without.

Conclusion: The presence of VAH in PCS may adversely affect the clinical severity.

Keywords: Vertebral artery hypoplasia, posterior circulation stroke, clinical severity, stroke pattern

Introduction

Posterior circulation stroke (PCS) occurs within the vascular region of the vertebrobasilar arterial system. Anatomical variations are very common in the posterior circulation vessels, and the vertebral arteries, particularly, are highly variable in diameter, length, and course (1,2). Vertebral artery hypoplasia (VAH) is a common embryonic variation of the posterior circulation (mostly seen in the right) with reported frequencies between 1.9% and 26.5%. Despite its high prevalence, relatively little information is known about the clinical significance of VAH (3).

VAH has become the focus of interest in many studies that showed it as a predisposing factor for stroke, especially when accompanied by atherosclerotic risk factors (4,5). However, some uncertainties are still presented. First of all, VAH has no standard definition; currently, VA diameters ranging from 2 to 3 mm or asymmetry ratios of ≥1:1.7 have been identified in different studies. Moreover, the role of VAH as a stroke risk factor remains controversial, while its etiology and pathogenesis are unclear (6).

PCS may present with a wide range of clinical signs due to the alterations in the vertebrobasilar system and the clinical severity of the stroke itself. This situation makes the diagnosis difficult for vascular neurologists (1,6). Studies that suggested an association between VAH and PCS are mainly prevalence-based and provide data in the context of relationships between risk factors and PCS (7-11). A limited number of studies demonstrated the clinical severity of VAH and PCS (12-14). Therefore, our study aimed to evaluate the relationship between VAH and PCS and determine the extent of their clinical association.

Methods

Patients

We retrospectively screened all patients with an acute ischemic stroke who are admitted to our clinic between January 2016 and June 2019. Among the patients with a definite acute ischemic stroke diagnosis with diffusion-weighted imaging, patients with PCS and computed

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tomography angiography (CTA) taken within 1 week of admission were included in the study. Patients with bilateral VAH, vertebral artery dissection, total occlusion, and hemorrhagic infarction and patients with lacking information about the initial National Institutes of Health Stroke Scale (NIHSS) and modified Rankin Scale (mRS) score were excluded from the study, thus a final total of 178 patients were included. The study was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital Local Ethics Committee (approval number: 1855, 24.05.2019).

The demographic characteristics and vascular risk factors [diabetes mellitus (DM), cardiac disease, hyperlipidemia, smoking, and arterial hypertension] of patients were recorded. The ischemic lesion patterns were radiologically grouped as territorial, embolic (>1.5 cm in diameter or a single lesion that affects a vascular site with multiple acute lesions), and lacuna (isolated lesion with a diameter of ≤1.5 cm). Additionally, posterior circulation ischemic lesions were divided into the following five groups based on anatomy: bulbus, pons, mesencephalon, cerebellum, and occipital (Table 1).

Clinical Assessment

Stroke severity was measured by the NIHSS score (range: 0-42) and mRS-a neurological functional disability scale-ranging from 0 to 6 at 90 days after stroke.

Vessel Analysis

A Toshiba Aquilium 64 CT Scanner (Toshiba Medical Systems Corporation, Shimoishigami, Japan) was used for all head and neck CTA scans (120 kV, 494 mA, 0.5 mm thickness, 40 cm FOV, 25.9 cm reconstruction diameter, 512×512 matrix, and 500 ms exposure time). Bolus triggering was used for optimum enhancement with the administration of 350 mgI/mL contrast media at a rate of 4-5 mL/s. Multiplanar reformations, three-dimensional volume renderings, maximum-intensity projections, and curved planar reformations were post-processed from the source images obtained from the aortic arch to the vertex.

The CTA images of all patients were evaluated based on the VAs. VAH was defined as follows: diameter of ≤2.0 mm or a difference in diameter with the contralateral side that is >1:1.7 (3,10,11).

Statistical Analysis

For descriptive statistics, mean, standard deviation, median, minimum, and maximum values were used for quantitative variables, and frequency and percentage values were used for qualitative variables. The distribution of variables was measured using the Kolmogorov-Smirnov test. Independent samples t-test and the Mann-Whitney U test were used depending on distribution normality for the analysis of quantitative independent data. The chi-square test was used for the analysis of qualitative independent data and the Fisher's test when data did not meet the chi-square assumptions. All statistical analyses were performed using the Statistical Package for the Social Sciences version 22.0 software (SPSS Inc., Chicago, IL, USA). A p-value of ≤0.05 was considered significant.

Results

Of the 178 patients with acute PCS, 115 (64.6%) were female and 74 (41.6%) were diagnosed with VAH. No significant difference was found in gender (female/male: 51/23 vs 64/40, p=0.310) and age (65.4±10.6 vs 66.1±12.9, p=0.676) distribution of the groups with and without VAH. Among the patients with VAH, 44 (59.5%) had right-sided.

No statistically significant difference was found between the two groups in terms of vascular risk factors (hypertension, DM, hyperlipidemia, coronary artery disease, and smoking) (p>0.05).

The NIHSS score was 3.8±2.9 and mRS was 1.6±1.1 in patients with VAH, whereas 2.4±1.7 and 1.2±0.9 in the patients without VAH, respectively. The NIHSS (p=0.01) and mRS (p=0.018) scores were significantly higher in patients with VAH compared to patients without VAH.

In terms of the stroke patterns, the lacunar stroke pattern was significantly more common in patients without VAH (p=0.045), while other stroke patterns were similar in both groups (p>0.05). Posterior circulation infarct localization did not significantly differ in the patients with and without VAH (p>0.05) (Table 2).

Table 1. Characteristics of the study group

		Minimum-maximum	Mean ± SD/(n, %)
Age		28.0-89.0	65.8±12.0
Gender	Female	-	115 (64.6%)
	Male	-	63 (35.4%)
VAH	(+)	-	74 (41.6%)
	(-)	-	104 (58.4%)
Right VAH		-	44 (59.5%)
Left VAH		-	30 (40.5%)
Clinical assessment			
NIHSS		0.0-15.0	3.0±2.5
mRS		0.0-5.0	1.4±1.0
Risk factors			
Hyperlipidemia		-	116 (65.2%)
Diabetes		-	73 (41.0%)
Arterial hypertension		-	121 (68.0%)
Cigarette smoke		-	52 (29.2%)
Coronary heart disease		-	38 (21.3%)
Stroke pattern			
Territorial		-	82 (46.0%)
Lacunar		-	53 (29.8%)
Embolic		-	43 (24.2%)
Location of infarction			
Medulla oblongata		-	23 (12.9%)
Pons		-	74 (41.6%)
Mesencephalon		-	8 (4.5%)
Cerebellum		-	56 (31.5%)
Occipital lobe and thalamus		-	28 (15.7%)

SD: Standard deviation, VAH: vertebral artery hypoplasia, NIHSS: National Institutes of Health Stroke Scale, mRS: modified Rankin Scale

Table 2. Demographics, clinical characteristics, and clinical outcome of patients concerning VAH presence/absence

		VA hypoplasia (+) (n=74)	VA hypoplasia (-) (n=104)	p	
Age		65.4±10.6	66.1±12.9	0.676	m
Gender	Female	51 (68.9 %)	64 (61.5%)	0.310	X^2
	Male	23 (31.1%)	40 (38.5%)		
Risk factors					
Hyperlipidemia		48 (64.9%)	68 (65.4%)	0.943	X^2
Diabetes		26 (35.1%)	47 (45.2%)	0.179	X^2
Arterial hypertension		48 (64.9%)	73 (70.2%)	0.453	X^2
Cigarette smoke		23 (31.1%)	29 (27.9%)	0.644	X^2
Coronary heart disease		16 (21.6%)	22 (21.2%)	0.940	X^2
Clinical assessment					
NIHSS score		3.8±2.9	2.4±1.7	**0.010**	m
mRS score		1.6±1.1	1.2±0.9	**0.018**	m
Stroke pattern					
Territorial		37 (48.6%)	45 (44.1%)	0.310	X^2
Lacunar		16 (21.1%)	37 (36.3%)	0.045	X^2
Embolic		23 (30.3%)	20 (19.6%)	0.069	X^2
Location of infarction					
Medulla oblongata		11 (14.9%)	12 (11.5%)	0.514	X^2
Pons		32 (43.2%)	42 (40.4%)	0.703	X^2
Mesencephalon		2 (2.7%)	6 (5.8%)	0.330	X^2
Cerebellum		27 (36.5%)	29 (27.9%)	0.240	X^2
Occipital lobe and thalamus		8 (10.8%)	20 (19.2%)	0.128	X^2

^{m}: Mann-Whitney U test, $^{X^2}$: chi-square test (Fischer's test), VAH: vertebral artery hypoplasia, Boldface values indicate significant results (p<0.05).

Discussion

This study assessed the association between VAH and PCS by retrospective analysis of patient data and revealed some similarities and differences from studies on this subject in the last 20 years, which seems to be a trend in studies of this type. However, the most important output of our study was the worse clinical severity in patients who suffered from posterior ischemic stroke in the presence of VAH. Despite the limitations that are present in this study and many studies in this field (due to the inability to perform population-based analyses), this is an important finding that could help in clinical settings.

VAH is common in society; however, there are differences between the prevalence values. The incomplete consensus on VAH definition and the use of different measurement methods [magnetic resonance angiography (MRA), CTA, and ultrasonography] in studies may explain the reason for these differences. A review by Katsanos and Giannopoulos (6) revealed that VAH was two times more common in PCS than in anterior system stroke. A study with 129 patients with acute stroke by Mitsumura et al. (8) identified 44.4% of VAH cases in patients with PCS. Similarly, among the 750 patients with stroke evaluated by Kulyk et al. (13), 193 have PCS and 33.7% of this group had VAH. Another similar percentage comes from a study by Park et al. (11), who revealed that VAH was present in 45.6% of patients with PCS. Our study revealed that 41.6% of patients had VAH. We could not perform direct comparisons with these previous studies because anterior system strokes were excluded from our study. However, our findings, at least, seem to be consistent with previous studies in terms of the relationship between PCS and VAH.

Previous studies have predominantly demonstrated the relationship between prevalence and risk factors (7-11). VAH has been studied in a limited number of studies in terms of clinical outcome, and these have not proposed any association with VAH and stroke severity (12-14). Kulyk et al. (13) revealed that mRS was similar in patients with and without VAH. Yang et al. (14) compared the NIHSS scores in patients with PCS (with and without VAH) and revealed no relationship. A study with 815 patients that had had an acute ischemic stroke, by Sauer et al. (12), revealed no significant difference between the median NIHSS and mRS scores in patients with and without VAH. However, when we look at the details of this study, comparisons were performed in the whole patient group (anterior and posterior) rather than separately (12). Our study revealed that the NIHSS score was 3.8±2.9 and the mRS score was 1.6±1.1 in patients with VAH. Both scores were significantly higher compared to those without VAH. These findings may provide a new perspective for the clinical severity of PCS with different clinical findings.

Considering the imaging-based studies that examine the relationship between PCS and VAH, Doppler ultrasonography (7,13,14) and MRA (5,9,13,14) are revealed as the most popular methods used. Doppler ultrasonography is a rapid and noninvasive technique for the assessment of vertebral arteries, but it may fail to identify aplasia, hypoplasia, occlusion, or dissection (15). CTA has been shown to have higher sensitivity and positive predictive value in detecting intracranial vessel stenosis and occlusion compared to MRA (16). Our study was performed with the CTA measurement method and we think that it gave more objective results in this sense compared to the other studies.

Different results have been obtained regarding the embolic stroke patterns in patients with VAH. Perren et al. (7) revealed that the embolic stroke pattern was more frequent in patients with VAH. Quite conversely, Sauer et al. (12) revealed that the embolic stroke pattern was less frequent in patients with VAH. Data is limited on this topic, as previously mentioned, and even available data seems to be biased; however, most were probably based on the clinical characteristics of patients, imaging modalities, and genetic/phenotypic differences. Our study revealed that the lacunar stroke pattern was less frequent in patients with VAH, and no differences were found regarding other stroke patterns. This situation can be explained by the possibility that risk factors contributing to the etiopathogenesis of lacunar stroke were more common among patients without VAH.

Many imaging studies have demonstrated that VAH may independently predispose patients to regional hypoperfusion in the posterior circulation (17). Other evidence from relevant research revealed that VAH may lead to ischemic events in the posterior circulation, especially when accompanied by other atherosclerotic risk factors (4,16,18). In our study, the evaluation of risk factors regarding the relationships revealed that none of the vascular risk factors were associated with a significant difference among the groups.

Study Limitations

Our study has some limitations. The number of patients was low to draw a generalized conclusion. However, there is very little conclusive data on this topic and available studies have not focused on the relationships between VAH and only PCS. Anterior group strokes were not included in the study by design, thus no comparison could be made concerning VAH frequencies. In a study, a 42% decrease of flow was detected in the posterior inferior cerebellar artery (PICA) territorial area of the ipsilateral VAH (3). Case reports and some studies revealed a relationship between VAH and ipsilateral PCS, especially PICA strokes (11). However, we did not evaluate the side of hypoplasia and the side of stroke. Additionally, long-term outcomes should be observed to better assess the clinical outcome and severity.

Conclusion

Our study results suggest a significant relationship between VAH and clinical severity of stroke in patients with PCS. Detailed prospective and clinical studies with larger groups will be useful to determine the relationship between VAH and clinical outcomes.

Ethics Committee Approval: The study was approved by the University of Health Sciences Turkey, İstanbul Training and Research Hospital Local Ethics Committee (approval number: 1855, 24.05.2019).

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