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Clinical study

Headache features of cerebellar ischemic strokes: Clinical and radiological-experiences of a single center

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ABSTRACT

The prevalence of headache in stroke has been reported between 8% and 34%. Determining the prevalence, features, and effects on prognosis of cerebellar ischemic strokes that presented with headache solely and/or with other cerebellar signs were the aims of our study. All patients diagnosed with cerebellar ischemia were included. Electronic medical records were reviewed. Patients have been followed up for 6th month. Descriptive statistics were generated. A total of 4763 patients were evaluated retrospectively, 200 patients had cerebellar ischemia and 22 patients of these cerebellar ischemias (11%) had a headache at initial presentation. Ataxia, dysarthria, dysmetria were the most common neurological findings. There was no significant difference whether ischemic lesion single or multiple and whether above or below 1.5 cm diameter. Ischemic lesions generally were in cortical/ juxtacortical layer. According to vascular perfusion areas, 54.5% patients' ischemia was located in PICA (posterior inferior cerebellar artery) territory. Patients presenting with a headache, predominantly had left hemispheric (vermian > hemispheric > pedincular) involvement. Although these patients generally had high modified Rankin Scale scores at the first evaluation, they had low NIHSS (National Institutes of Health Stroke Scale) scores (0–5), and nearly all patients recovered, with low mRS at the 6-month follow-up. Cerebellar ischemic strokes with headache presentation are significantly prevalent in patients with left hemispheric, cortical/juxtacortical, PICA perfusion territory ischemias and are associated with low morbidity unless there was a conscious disorder. We believe this is one of the first studies that evaluated the clinical and radiological parameters of cerebellar stroke patients with headache.

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1. Introduction/background

Headaches are a common phenomenon in cerebrovascular disease [1]. In previous studies, the prevalence of headache in stroke has been reported between 8% and 34%. In half of these patients' first stroke manifestations was headache [2–4]. Even though headaches are common in stroke, the underlying mechanisms are incompletely understood [3]. It is assumed that the trigeminovascular system's activation in the intracranial vessels is the cause of this symptom [5,6]. Headaches are more frequent in vertebrobasilar than in anterior circulation strokes, and cerebellar localizations are the most common ones [3,4,7].

In the current study, our main objective was to evaluate the features of cerebellar ischemic infarctions with a headache on demographic, clinical, radiological, etiological, and prognostic parameters.

To evaluate these features, the prevalence of headache in cerebellar ischemias, coexisting cerebellar clinical signs, neuroradiological patterns of ischemic lesions, and NIHSS and mRS of patients were evaluated at administration and 6th month follow-up period.

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2. Material and methods

2.1. Data collection and ethical approval

This study included patients diagnosed with cerebellar ischemic stroke between January 2007 and March 2018 at the Neurology Department of Gazi University Faculty of Medicine. Patient data were obtained from the electronic patient registry. The data of 4763 patients with ICD diagnostic code I67.9 (Cerebrovascular Diseases, unspecified) were screened and 200 patients with cerebellar infarction were detected. Within these patients, 22 patients with initial headache symptoms were included in the study. Ethics committee approval was granted by the Ethics Committee of Gazi University in December 2020 (Approval Number: 2020-832).

2.2. Study design

Patient age, gender, symptoms, and neurological findings on admission were recorded and evaluated. Sixteen-detector row Computed tomography (CT; [BrightSpeed Elite 16 Slice CT Scanner]; General Electric, Milwaukee, WI, USA), magnetic resonance imaging (MRI; 1.5 and 3-Tesla Magneton Aera; Siemens, Erlangen, Germany), MR angiography, echocardiography and doppler ultrasonography (Logic S8 and S9; General Electronic) were performed. Parenchymal, bilateral and unilateral involvement, infarction area, arterial mapping (according to the vascular perfusion area delineated by Tatu et al.), hearth rhythm [based on electrocardiogram (ECG), and Holter findings], brain edema, and comorbidities were analyzed [6]. Antiaggregant and anticoagulant use before the stroke was also assessed, in addition to smoking habits. Stroke etiology was determined according to the ASCOD classification (A, atherosclerotic; S, small vessel disease; C, cardioembolic; O, other defined causes; D dissection) [8].

2.3. Follow-up

Stroke severity was scored using the National Institute of Health Stroke Scale (NIHSS) at the time of admission to the emergency department, and discharge. To determine prognosis, the modified Rankin Scale (mRS) scores of all patients were calculated on admission and discharge, and after 6 months, based on electronic inpatient and outpatient clinical records [9–12].

2.4. Statistical analysis

Descriptive statistics were generated. Categorical variables are expressed as numbers and percentages (%). If the expected frequency was less than 5 in at least one of the cells in 2 × 2 cross tables, the categorical variables were evaluated using Fisher's exact test, and the continuity-corrected chi-square test was used when the expected frequency was between 5 and 25. In all other cases, Pearson's chi-square test was performed. If the expected frequency was less than 5 in at least one cell, categorical variables were evaluated with the likelihood ratio test; otherwise, they were examined using Pearson's chi-square test. The significance of group differences was examined using the Mann-Whitney *U* test when the number of independent groups was two; for comparisons of more than two groups, the Kruskal-Wallis test was used. If the Kruskal-Wallis test was significant, the factors responsible for the difference were determined using Conover's test. Data were analyzed using IBM SPSS Statistics 17.0 (IBM Corporation, Armonk, NY, USA). Results were considered significant at $p < 0.05$.

3. Results

A total of 4763 consecutive patients, diagnosed with ischemic cerebrovascular disease, evaluated retrospectively during the study period. A majority of these patients had anterior cerebral circulation ischemia. In posterior cerebral circulatory ischemic strokes, 200 patients had cerebellar ischemia (4,19% of our ischemic stroke data between 2007 and 2018) and 22 patients of these cerebellar ischemias (11% of all cerebellar ischemic stroke patients) had a headache at initial presentation. The follow-up period was 180 days. At baseline, patients with cerebellar strokes with headache (CSWH) patients' mean age was 65.4 (minimum 32, maximum 87) years. Six (27.3%) of the patients were women, 16 (72.7%) were men. In terms of accompanying neurological examination findings, gait ataxia and/ or truncal ataxia, dysarthria, dysmetria were the most common ones. When the radiological features of these cases were evaluated, single cerebellar infarction was observed with a rate of 54.6% and multiple cerebellar infarctions were seen with a rate of 45.4%. Multiple patterns included both unilateral cerebellar ischemic lesions and bilateral cereballar lesions. In the present study, we also evaluated infarct patterns in terms of cerebellar histological layers. Cortical/ juxtacortical ischemic lesion rate was 63.6%, deep white matter involvement was 0% and combined involvement were 36.3%. When the infarct sizes were examined, large ischemic lesions above 1.5 cm were 59%, 1.5 cm, and below were 41%. According to vascular perfusion areas, 54.5% patients' ischemia was located in PICA territory, 27.2% were in SCA, 4.5% were in AICA and 13.6% were in both three perfusion areas. Detailed baseline characteristics are summarized in Table 1.

The ischemic lesions of the cases were classified in terms of cerebellar parenchymal anatomy such as vermian, hemispheric, and peduncular regions. Lesions presented in multiple regions counted separately since left and right involvement can be seen at the same time. In 23 of the lesions, hemispheric involvement (9 right hemisphere, 14 left hemisphere) was detected. There were 26 ischemic vermian area (9 right vermian, 17 left vermian), peduncular involvement was present in 4 lesions (1 right cerebellar peduncle, 3 left cerebellar peduncles). According to these findings, headache is seen predominantly in left cerebellar involvement significantly ($p < 0.05$). Fig. 1 demonstrates parenchymal involvement with the bar graph.

Hypertension, diabetes, and coronary artery diseases were the most comorbid conditions. There was one patient who has a hypercoagulative condition genetically. One patients' etiology was iatrogenic (endoscopic sinus surgery). There was no vasculitis or malignancy induced hypercoagulopathy. Patients had predominantly atherosclerotic etiology (50%). Others etiologies were cardioembolic (27.2%) and dissection (22.7%).

The mean ASPECT score was 8 (6–10). Four patients had a brainstem compression in their acute stroke period. Only one had decompressive posterior occipital craniectomy, others were treated efficiently with anti-edema medication 'mannitol'.

Although they generally had high modified Rankin scales at first evaluation, they had low NIHSS (0–5) scores. Nineteen patients had 0–3 NIHSS and others had 4–5 NIHSS. At initial evaluation, 18 patients had high mRS 4–5, 4 patients had mRS 0–3. Six patients had mRS 4–5, 16 patients had mRS 0–3 at the discharge period. Two patients had mRS 4–5, 20 patients had mRS 0–3 at 6th month follow-up. No mortality was present. Changes in mRS during our evaluation were demonstrated in Fig. 2. All ataxic patients have been taken into rehabilitation programs at an inpatient period and continued in follow up if necessary.

Three patients had solely headache symptoms at the initial evaluation. They all had a single cerebellar lesion, and all of them

Table 1
Baseline characteristics of cerebellar ischemic stroke patients that presents with headache.

Cerebellar Stroke presenting with Headache	Number (percentage) (N:22)
Gender	
Women	6 (27.3%)
Men	16 (72.7%)
Clinical presentation other than headache	
Gait and/or Truncal Ataxia	11 (50%)
Dysarthria	4 (18.2%)
Dysmetria, dysdiadokokinesia	4 (18.2%)
Normal Neurological Examination	3 (13.6%)
Ischemic Lesion Pattern (Number)	
Single	12 (54.6%)
Multiple	10 (45.4%)
Ischemic Lesion Pattern (Histological layer)	
Cortical/ Juxtacortical (solely)	14 (63.6%)
Deep White Matter (solely)	0 (0%)
Both	8 (36.3%)
Ischemic Lesion Pattern (size, cm)	
≤1.5	9 (41%)
>1.5	13 (59%)
Vascular Perfusion Areas	
PICA	12 (54.5%)
AICA	1 (4.5%)
SCA	6 (27.2%)
Both (PICA + AICA + SCA)	3 (13.6%)
Etiology	
Atherosclerosis	11 (50%)
Cardioembolism	6 (2.2%)
Dissection	5 (22.7%)
Vertebral Artery Occlusion Rates	
Atherosclerosis (11 patients)	4 (36.3%)
Cardioembolism (6 patients)	2 (33.3%)
Dissection (5 patients)	5 (100%)

had a cortical/ juxtacortical pattern with hemispheric involvement. Medial PICA territory was affected in 2 cases and the other was located in medial SCA territory. Three of these patients had mRS 0–1 at administration to the emergency room (ER) and follow up period.

4. Discussion

This study evaluated the prevalence and clinical impacts of cerebellar ischemic stroke patients with a headache from a single ischemic stroke database retrospectively. We found an 11% prevalence of headache as an initial symptom of cerebellar ischemia. This manifestation generally has been seen with other cerebellar clinical signs especially with ataxia and dysarthria, but also headache can be seen solely as in our 3 patients. Also, we found that headache was seen mostly with left cerebellar ischemic involvement (especially left vermian). CSWH patients had cortical/juxtacortical ischemic lesions and predominantly PICA vascular territory was affected. However, patients had high modified Rankin scales scores at initial evaluation, they had low NIHSS (0–5) scores. On the other hand, approximately all had shown a great improvement at discharge and 6th month follow- up. Together these findings suggest that examination of a headache patient in the ER seems important to detect subtle cerebellar ischemia.

There are limited previous studies regarding headache features of cerebellar ischemic stroke patients; however, the prevalence of headache in our study was comparable to prior investigations, which have evaluated the headache prevalence in both anterior and posterior circulation ischemic stroke patient datas [2–4]. As in previous stroke studies our small CSWH group of patients, men were more affected than women (F/M: 3/8) [13]. These headaches frequently co-existed, particularly with dysarthria, ataxia, dysmetria, and dysdiadokokinesia [1,6,14]. But also headaches can be the only initial symptom of a cerebellar stroke as in other types of strokes [1,7,13]. When the radiological features were evaluated, there was no significant difference whether ischemic lesion single or multiple and whether above or below 1.5 cm diameter. Significantly left cerebellar ischemias especially in vermian lesions were present in our CSWH patients ($p < 0,05$) [15–17]. Vermian ischemias the dominant lesions in our study group. Hemispheric and peduncular involvement has been detected in a decreasing manner respectively. The most common neurological condition accompanying headache in vermian infarcts is ataxia, which is consistent with our current knowledge, considering the cerebellum physiology [14,18]. Headaches in strokes are associated with infarct size or compressive effect [4,6,7]. The cortical/juxtacortical ischemias were generally small in size (<1,5 cm) and were in a non-compressive pattern. Trigeminovascular activation or cross-diaschisis mechanisms and insular cortex involvement could play a role in the pathogenesis of this headache, probably due to the complex networks of the brain [4,19–25].

In 19 patients headache corniced with the onset of cerebellar signs whereas in 3 patients the only symptom was a headache at initial evaluation. Most of our patients described their headaches in the form of stabbing or throbbing patterns. In all of these patients, the pain was localized at the posterior of the head and neck ipsilateral to their ischemic lesions as has been delineated in previous studies [3,26,27]. Headache resolved in all of our patients within the first month of acute ischemic stroke. In more than half of the patients, pain relief was achieved within the first

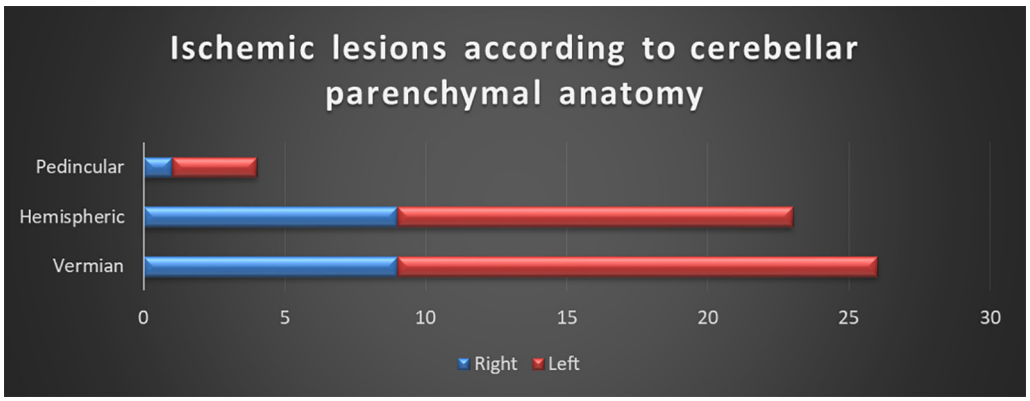


Fig. 1. Bar graph showing the ischemic lesion locations according to cerebellar parenchymal anatomy. Predominantly left cerebellar ischemias were seen, followed in decreasing order by vermian, hemispheric, and peduncular ischemias.

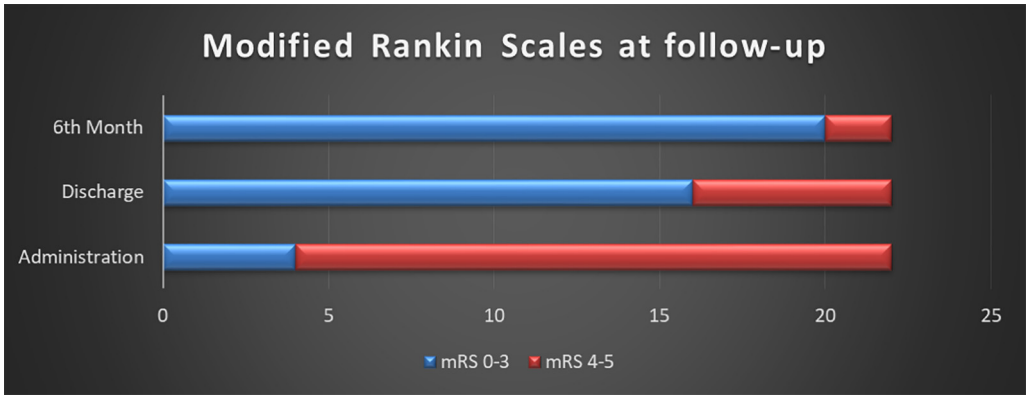


Fig. 2. Bar graph showing the modified Rankin Scale (mRS) scores at follow-up. At the initial visit, 18 patients had high mRS scores of 4–5, four had mRS 0–3. At discharge, six patients had mRS 4–5, and 16 had mRS 0–3. At the 6-month follow-up, two patients had mRS 4–5, and 20 had mRS 0–3.

week with antiplatelet drugs and paracetamol was needed in some cases. Anti-edema treatment was initiated to 13 patients who had an ischemic lesion above 1.5 cm and, in these patients, pain relief was achieved. In the follow-up imaging which was performed 6 months after the initial event in patients with dissection, we discovered that the dissected vertebral artery was occluded in all patients. Besides dissection (5 cases), 2 cardioembolic and 4 atherosclerotic vertebral artery occlusions were detected in our patients. Patients with vertebral artery occlusion had a longer duration of headache (5–7 days) than the rest of the group and their headaches were localized to the ipsilateral occluded vertebral artery. The mechanism of this headache can be parenchymal edema or perturbation of overlying meninges and/or vascular structures. In patients with large vessel occlusion, augmented blood flow from collaterals may initiate headache due to activation of the trigeminal nerve terminals in the vessel wall [14,27–29]. Patients who present with symptoms of impaired consciousness may also have suffered from a headache, but this cannot be evaluated due to lack of enough cooperation. Therefore, we excluded all patients with impaired consciousness from the study. Although one patient presenting with impaired consciousness was included in the study because he was able to express himself partially due to his mild confusion state. Therefore, the number of our patients' population was lower than we have expected.

In previous studies, headaches observed with stroke or seen as the first sign of stroke were evaluated in a limited number of studies [7]. In these studies, anterior or posterior circulation stroke, arterial or venous infarction, atherosclerotic or cardioembolic etiology, hemorrhagic or ischemic stroke, large artery or small artery involvement, and gender differences were examined [1–3]. Besides, the nature, duration, localization, and spread of headaches, and whether their type was more similar to migraine or other primary headaches were evaluated. In the results of these studies, it was noted that headache was more prominent in women, posterior circulation strokes, hemorrhagic strokes, cardioembolic strokes, cortical infarcts, venous thrombosis than arterial strokes, and large artery occlusion in arterial events. In addition to the similarity of the results of large artery involvement and cortical ischemia, in our data, atherosclerotic etiologies are observed more frequently than cardiac embolism [2,3,7].

On the other hand, although there are unclear data about these headaches and different results were observed in different studies, it was emphasized that it was more pronounced in the first 72 h in terms of duration, stabbing in the region suitable for the ischemic area localization, especially mimicking tension headache [3]. There is not enough data about the severity of pain, its characteristics, and the frequency of being unilateral or bilateral [2,3,28]. This situation is thought to be due to the inadequate evaluation of the quality of headaches during acute stroke periods, which is one of the limitations of our study [2]. If these headaches are very severe, sudden, and have a characteristic that has not been experienced before, brain imaging is already considered [30,31]. On the contrary, it is possible to miss the diagnosis of stroke in cases where a patient with a mild headache with a nonspecific character or has already experienced a headache of a similar character.

The present study is limited by its retrospective nature and is a small single-center population. The prevalence of cerebellar ischemic strokes with headache presentation may be under detected due to the presence of patients with impaired consciousness and lack of some information of some patients in the electronic data system. Also, detailed headache characteristics weren't be determined in these patients. Nevertheless, we have found a similar prevalence of headache in cerebellar strokes between the previous headache stroke studies. While the impacts of headache presentation in cerebellar ischemic strokes on morbidity and mortality were evaluated, we did not evaluate the quality of life measures.

5. Conclusion

Patients who had a headache as an initial manifestation of cerebellar ischemic stroke lonely or with other cerebellar symptoms have an 11% prevalence in our stroke data and have some important aspects other than the characteristics of pain. Concordant and different to previous studies, we found that headache was more common in cortical/juxtacortical involvement, atherosclerotic etiology, PICA arterial perfusion area, vermis involvement, especially left cerebellar ischemia, and in the male gender. Patients with vertebral artery occlusion had a longer duration of headache than the rest of the group. Moreover, even though patients had high morbidity initially, they had shown a good improvement at follow-up evaluation. We believe this is one of the first studies that evaluated the clinical and radiological parameters of cerebellar stroke patients with headache presentation. Larger series and more detailed studies are needed to define the basic mechanisms and clinical integrity of headache features of cerebellar strokes.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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