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Small volume of the posterior cranial fossa and arterial hypertension are risk factors of hemifacial spasm

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ABSTRACT

Objectives: So far, there are only two studies evaluating the relation between the small volume of the posterior cranial fossa (VPCF) and the occurrence of HFS, both on Asian population. The aim of the study was to determine small VPCF and arterial hypertension (AH), as risk factors for hemifacial spasm (HFS) and their relation to neurovascular conflict (NVC) in Polish Caucasian-origin patients.

Materials and methods: The study included 60 patients with idiopathic HFS and 60 healthy volunteers matched by sex and age. AH was defined according to WHO. The VPCF measured the volume of the prepontine, prespinal and both cerebellopontine angle cisterns in MRI scans.

Results: There were no significant differences between occurrence of AH and the VPCF of patients and controls but the mean VPCF in women was significantly smaller than in men, In the multivariate regression analysis model only NVC was the statistically significant. In the subgroup of >50-year-old patients the most dominant risk factor was NVC (OR 71.09; 95% CI 21.08–239.77; $p = 0.0000$), followed by the AH duration (OR 1.07; 95% CI 1.00–1.16; $p = 0.047$). In the subgroup of <50 years, NVC was also the dominant risk factor, followed by the lower VPCF (Walad test: OR 0.4; 95% CI 0.16–1.04; $p = 0.045$).

Conclusion: There was no significant difference in VPCF and in frequency of AH diagnosis in HFS patients and age- and sex-related controls, but the logistic regression analysis showed that small VPCF and AH duration are risk factors of HFS in younger and older patients respectively.

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1. Introduction

The most common cause of hemifacial spasm (HFS) is a neurovascular conflict (NVC) between the artery and the facial nerve at the root entry zone (REZ) of the brainstem. The number of patients who disclose this conflict have grown together with the sensitivity of high-resolution magnetic resonance imaging (MRI), up to 94–98% [1,2]. However, NVC is also seen in the 6–25% of MRI scans in normal population [3–6], and in 15% of HFS patients on the contralateral, asymptomatic side [2,7]. It suggests other factors having influence on the occurrence of HFS symptoms. The role of smaller volume of the posterior cranial fossa (VPCF) and of arterial hypertension (AH), as risk factors of HFS, are discussed. Posterior cranial fossa (PCF) narrowness creates conditions where the intracranial structures could exert pressure on each other, thereby surrounding vessels could compress the facial nerve. It could explain why there is a greater prevalence of HFS among females, compared to males, and in Asians compared to Caucasians, and in patients with small PCF. HFS has been also reported in Paget's disease and in the petrous bone hypoplasia with the reduction of the cerebellopontine angle cistern volume [8], and in patients with the contralateral facial nerve neurinoma [9]. So far, there are only two studies evaluating the relation between the size of PCF and the occurrence of HFS, both on Asian population. Kamiguchi et al. [10] found significantly narrower cerebello-pontine angle cistern, and Chan et al. [11] significantly smaller (about 11%) VPCF (without the fourth ventricle) in patients with HFS as compared to the control group.

AH was identified as a possible risk factor in the first published studies [12–14], but it has not been confirmed by the next, larger and better controlled studies [2,15].

The aim of the study was to determine small VPCF and AH as risk factors for HFS and their relation to NVC in the cohort of the Polish Caucasian-origin patients.

2. Materials and methods

Patients diagnosed as primary HFS registered in the Movement Disorders Out-patient Clinic, University Hospital, Krakow, Poland, in 2004–2010 years, were identified. Patients with secondary HFS caused by compressive (*e.g.*: tumor, arteriovenous malformation, Paget disease) or non-compressive lesions (*e.g.*: trauma, inflammation, stroke, multiple sclerosis) were excluded. All others were invited to the study. At the screening visit, patients giving informed consent were interviewed and examined by neurologists. The diagnosis of primary HFS was confirmed and patients with secondary AH (renal disorders, thyroid disease, pheohromocytoma, Conn's syndrome, Cushing's syndrome, drug-induced, *etc.*), with a history of severe head trauma, cerebrovascular and other brain diseases, and cerebellar atrophy on standard neuroimaging, were excluded.

The control group was recruited from patients who complained of hypoacusia and/or tinnitus without pathological findings in laryngological and neurological examination.

The diagnosis of HFS was made according to the occurrence of unilateral, involuntary, clonic or/and tonic muscle contraction in the region innervated by the facial nerve. AH was defined according to the WHO/International Society of Hypertension Writing Group [2003] criteria in patients with earlier AH diagnosis, who were receiving antihypertensive medication and in patients with the systolic blood pressure ≥140 mmHg and the diastolic blood pressure ≥90 mmHg on 3 separate visits over a month. Blood pressure was measured with a pressure gauge in both upper limbs after 20-min rest. Each measurement was performed twice [16].

The standard MRI examination in all involved patients and control group subjects (GE Signa HDxt 1.5T) was followed by 3D FIESTA (TE/TR//FA/FOV/slice thk/NEX: 2,4/5/55/22/1 mm/2) and 3D T1 SPRG (TE/TR//FA/FOV/slice thk/NEX: 2,6/23/20/22/1 mm/2. All MRI scans were reviewed by one radiologist (MH) unaware of the subjects' medical history. The presence of NVC was checked bilaterally.

The VPCF was measured using Osirix software that counted the CSF volume, based on the ROI area, the thickness and number of the individual layers. The measure was limited to the region from the REZ of the trigeminal nerve to the REZ of the vagus nerve of the medulla oblongata, and included only the fluid space of precerebellar cistern, prespinal cistern and cerebellopontine cisterns. In order to minimize the influence of the cerebellum atrophy, the CSF volume from backward of the pontocerebellar cisterns, laterally and backward of the cerebellum hemisphere and in the fourth ventricle were not considered for the measure. The region of interest (ROI) was automatically marked on each layer in the 3D sequences (Fig. 1) and corrected manually by the radiologist, if necessary.

2.1. *Statistical analysis*

Numerical variables are expressed as mean ± SD. Qualitative variables are described as the absolute value of cases in the distinctive group. The variables distribution was checked by the Shapiro–Wilk test. Statistical significance was assessed by χ^2 test between the quantitative variables, with the Yates's or Fisher's correction, if necessary. Student's *t*-test was performed to evaluate data, and to follow a normal distribution, for other variables the Mann–Whitney test was used. To determine the correlation between numerical variables, correlation analysis was performed. Pearson correlation

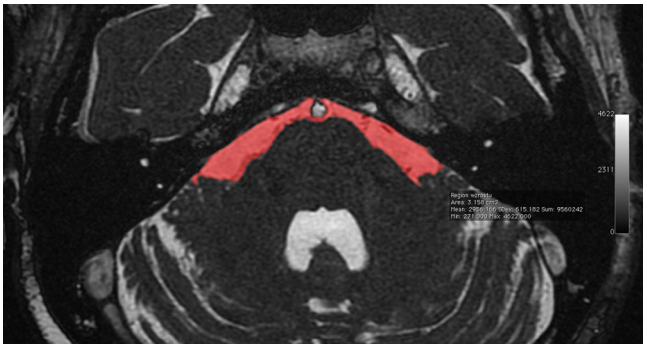

Fig. 1 – An example of ROI views of MRIs, *i.e.* the cerebellopontine cisterns, precerebellar cistern and prespinal cistern.

coefficient was calculated for normally distributed variables and the Spearman's rank correlation coefficient for a non-parametric measure. For the assessment of risk factors logistic regression models were applied. Walad test was used to estimate the relationship between independent variables. p-values <0.05 were considered statistically significant. Statistical analysis was performed using commercially available software (STATISTICA v. 6.0, StatSoft Inc version 9.2 Poland) licensed to the Jagiellonian University.

3. Results

115 of 129 registered primary HFS patients were invited to the study and 60 of them agreed to participate in the study and followed the inclusion and exclusion criteria. There were 42 (70%) women; the mean age was: 58.3 ± 9.1 years, and the mean duration of HFS symptoms was 9.2 ± 6.9 years. The control group consisted of 60 subjects; 62% women, the mean age was 60.3 ± 10.9 years.

VPCF defined as the volume of the prepontine, prespinal and cerebellopontine angle cisterns on both sides in the HFS patients and controls are shown in Table 1. There were no significant differences between the patients and controls. The mean volume in women was significantly smaller than in men ($t = 6.2$; $p = 0.0000$), both in the HFS patients ($t = 4.2$; $p = 0.00009$), and in the control group ($t = 4.4$; $p = 0.00006$).

AH was diagnosed in 37 (61.6%) of the HFS patients and in 27 (45.0%) of the controls (the difference is not statistically significant). The mean duration of AH in the HFS patients was slightly, but not significantly longer than in controls (11.3 ± 8.4 *vs* 8.1 ± 7.7 years, $p = 0.13$). The diagnosis of AH in 25 (41.7%) patients preceeds HFS onset, in 8 (13.3%) it stated after the HFS symptoms occurred, and in 4 (6.7%) patients both diseases occurred simultaneously.

The NVC with VII nerve on the symptomatic side was found in 57 (93.4%) of HFS patients and in 4 (6.7%) controls ($p = 0.000$). The NVC occurred in the 36 (97.3%) HFS patients with AH and 21 (91.3%) cases without AH ($p = 0.325$). Among the control group NVC occurred in 1 (3.7%) case with AH and 3 (9.09%) without AH ($p = 0.386$).

The mean VPCF was significantly lower in the HFS patients without AH, compared to patients with AH (4800 ± 1200 mm^3 *vs* 5500 ± 1400 mm^3, $p = 0.04$) and controls (4800 ± 1200 mm^3 *vs* 5600 ± 1200 mm^3, $p = 0.01$). In the group of women without AH the mean VPCF in patients was also significantly lower than in controls (4300 ± 1000 mm^3 *vs* 5300 ± 1200 mm^3, $p = 0.009$) (Table 2).

Table 1 – Comparison of PF volume in patients with HFS and in the control group.

	The CSF volume in the analyzed area [mm^3] (mean ± SD)		p value
	HFS	Control group	
Women	4700 ± 1200	4900 ± 1200	$t = -0.05$; $p = 0.9$
Men	6300 ± 700	6300 ± 900	$t = -0.68$; $p = 0.49$
All	5200 ± 1300	5400 ± 1300	$t = -1.00$; $p = 0.3$

Table 2 – Comparison of the CSF volume in the investigated area among HFS patients with and without AH.

HFS patients	CSF volume in the HFS patients [mm^3]	CSF volume in the investigated area in the control group [mm^3]	Statistically significance (t-Student test)
With AH	5500 ± 1300	5200 ± 1400	$t = -0.8$; $p = 0.4$
Women	5100 ± 1300	4500 ± 1300	$t = 1.5$; $p = 0.15$
Men	6500 ± 600	6100 ± 1100	$t = 1.0$; $p = 0.3$
Without AH	4800 ± 1200	5600 ± 1200	**$t = -2.5$; $p = 0.01$**
Women	4300 ± 1000	5300 ± 1200	**$t = -2.7$; $p = 0.009$**
Men	6000 ± 800	6500 ± 1000	$t = -1.1$; $p = 0.3$

For the analysis of HFS risk factors, age, gender, VPCF, diagnosis and duration of the AH, and the NVC with VII nerve were put to the conditional logistic regression model. Only duration of AH (OR 1.07; 95% CI 1.002–1.151; $p = 0.03$) and NVC with VII nerve (OR 77.0; 95% CI 24.0–246.4; $p = 0.0000$) were found to be significant risk factors for the HFS, but in the multivariate regression analysis model only NVC (OR 517.4 95% CI 19.7–13558.8, $p = 0.00035$) was the statistically significant. The results in the subgroup of >50 year old HFS patients, the results of the regression analysis were similar. The most dominant risk factor was NVC (OR 71.09; 95% CI 21.08–239.77; $p = 0.0000$), followed by the AH duration (OR 1.07; 95% CI 1.00–1.16; $p = 0.047$). In the subgroup of <50 year, NVC was also the dominant risk factor, followed by the lower VPCF (Walad test: OR 0.4; 95% CI 0.16–1.04; $p = 0.045$).

4. Discussion

The results of the study do not confirm previous reports showing lower VPCF in HSF patients than in controls [10,11]. VPCF measured in this study as the summary of the volume of the prepontine, prespinal and both cerebellopontine angle cisterns in MRI scans do not differ in HFS patients and controls. The direct comparison between our and previous studies is difficult because of significant differences in methodology of VPCF measure. Kamiguchi et al. [10] assessed the VPCF in CT scans using two different markers: petrous angle (measured between two lines drawn from the median point of the posterior surface of the clivus to the posteromedial surface of the bilateral petrous bones at the level of the internal auditory meatuses) and the pons diameter index. Chan et al. [10] made the volumetric analysis of PCF by marking the dural contours as the external boundary and the outline of the brain structures in the PCF as the inner boundary of PCF (excluding the fourth ventricle) in 3D MRI scans. In our opinion the method used in this study, focused on selected cisterns in the close neighborhood of nerve VII REZ, is more accurate for the study of the effect of NVC, and eliminates the individual differences of pons and cerebellum volume related to the possible atrophy. It should be noted that the reduction of PF volume rate found by Chan et al. [10] was rather mild, only – 11.4% of mean volume in the tested area.

The next negative result of the study is the statement that AH in all HFS patients is not significantly more frequent than

in controls (62% *vs* 45%). The result is contradictory to the first published studies on this topic [12–14], but consistent with the last two publications [2,15].

The most interesting finding of the study is the result of the conditional logistic regression analysis showing lower VPCF is a risk factor of HFS in younger (<50 years) patients, and AH duration is a risk factor in older patients (>50 years). It suggests the involvement of VPCF and AH in the pathogenesis of HFS, even if any significant difference in the VPCF and AH comorbidity between HFS patients and controls do exist. We propose the hypothesis that the reduced VPCF and duration of AH, are independent factors involved in HFS pathogenesis in different periods of age. AH is an age-related disease and its pathological effect on the arterial wall also needs some time to cause the thickness of the vessels. For this reason arteriosclerotic changes causing the NVC are more likely to occur in older age. On the other hand, the reduced VPCF is related mostly to genetically determined factors, and should affect younger people.

The independence of VPCF and AH as risk factors of HSF in age-different populations is also supported by our observation that HFS patients without AH had significantly lower VPCF in comparison to HFS patients with AH and controls, especially in women.

The limitation of our study is concerns a relatively small group of patients in multivariate logistic regression analysis. However, HFS is a rare disease, and the number of investigated patients (60) in this study is higher than involved in previous studies of Kamiguchi et al. (34 patients) [10] and of Chan et al. (41 patients) [11].

In conclusion, we did not find a significant difference in VPCF and in frequency of AH diagnosis in HFS patients and age- and sex-related controls, but the logistic regression analysis showed that small VPCF and AH duration are risk factors of HFS, first in the younger, and the second in older patients.

Conflict of interest

None declared.

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None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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