

Vertebral Artery Hypoplasia May Contribute to Abnormal Vestibular Evoked Myogenic Potentials

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Abstract- Congenital vertebral artery hypoplasia (VAH) is an uncommon embryonic variation of the posterior circulation. The clinical relevance and hemodynamic impact of VAH have been under debate. We tried to localize the topographic domain of vertebral artery hypoplasia with vestibular evoked myogenic potential (VEMP) studies.

From January 2005 to October 2005, we reviewed the magnetic resonance angiographic records of 250 health check-up outpatients (108 men and 142 women; mean age, 30.8 ± 14.0 years; range, 25 to 55 years). There were 26 subjects with a hypoplastic VA. We performed a case-control study by recruiting another 26 healthy subjects without hypoplastic VA as a control group. VEMP testing was performed in each subject for comparison.

The results revealed that 88.47% of the healthy subjects with a VAH demonstrated abnormal VEMPs either unilaterally or bilaterally, which was statistically higher than control group without a VAH ($p=0.019$). Given that hypoplastic VA was exclusively right-sided in these patients, the majority of whom had an ipsilateral delayed response or absence of VEMP. We therefore hypothesize that VA hypoplasia might contribute to brain stem lesion or interruption of sacculo-collic reflex.

Key Words: Vertebral artery hypoplasia, MR Angiogram, Hypoperfusion, Vestibular evoked myogenic potentials

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INTRODUCTION

Congenital vertebral artery hypoplasia (VAH) is an uncommon embryonic variation of the posterior circulation. The frequency of this congenital variation has been reported to range from 2% to 6% based on autopsy find-

ings and angiograms⁽¹⁻³⁾. The clinical relevance and hemodynamic impact of VAH have been under debate⁽⁴⁻⁶⁾. For example, overall vertebral artery flow volume has been reported to be adequate in asymptomatic carriers⁽⁴⁾. In contrast, VAH has been proposed to be a risk factor for lower brain stem infarction. Little is known whether

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the topographic domain of VAH is a regional anatomic or a systemic contributory factor.

The vestibular evoked myogenic potential (VEMP) test evaluates the sacculocollic reflex, which descends through the lower brainstem^(7,8). We were able to localize the topographic domain of VAH with VEMP tests⁽⁹⁾. We hypothesized that the VAH may cause the lower brainstem damage even in the healthy subjects. Therefore, we performed a case-control study and compared the results of VEMP tests between healthy subjects with and without a hypoplastic VA.

METHODS

Patients selection

We reviewed the records of consecutive 250 magnetic resonance imaging (MRI) health check-up outpatients based on the health center registration (108 men and 142 women; mean age, 30.8 ± 14.0 years; age range, 25 to 55 years) during the period between January 2005 to October 2005. These 250 subjects received whole body MRI health examination including cerebral angiography.

The exclusion criteria were psychiatric illness (n=3), diabetes mellitus (n=20), epilepsy (n=2), hypertension (n=26) (diastolic pressure above 95 mm Hg), cardiovascular disease (n=16), and MRI evidence of ischemic stroke (n=12).

The inclusion criteria was healthy subjects with a MRA evidence of VAH. The detection of VA hypoplasia was based on a VA <2 mm in diameter in the cervical MR angiogram (0.3 Telsa, AIRISII, Hitachi Medical Corporation). Finally, 26 subjects were selected as the experimental group. All fulfilled the inclusion/exclusion criteria and had an exclusively right-sided hypoplastic VA.

Control group

Control group were recruited from participants of the remaining 224 subjects, and comprised 26 age- and sex-matched subjects (12 men and 14 women). The control group had a mean age of 33.5 ± 11.6 years (range, 25 to 45 years) and fulfilled the criteria of healthy subjects without a hypoplastic VA. The cardiovascular risk

factors were not different between the experimental and control groups.

VEMP tests were performed on the controls and on the 26 subjects. The tests were carried out in a semi-dark, quiet room by a technician who was blinded to the study protocol. The study protocol was approved by the Institutional Review Board (IRB) of the Tao-yuan General Hospital, and written informed consent was obtained from all patients or their relatives before the participation in the study.

Vestibular-evoked myogenic potentials

VEMP tests were performed in 52 subjects in a quiet room with the presence of two researchers and/or the parent(s). A single-channel recording of the evoked potential was obtained with Ag/AgCl surface electrodes, namely a noninverting electrode placed on the mid-sternocleidomastoid muscle, an inverting electrode on the ipsilateral upper sternum, and a ground electrode on the contralateral side of the neck. Electrode impedances were kept at less than 5 kOhms. During recording, the subjects were instructed to lift their head 30° from a supine position or to keep the head at 30° from the horizontal plane while propped on the elbows in a recumbent position. Background electromyographic activity was continuously monitored visually for tonic contraction. A total of 150 monaural alternating clicks of 0.1-msec duration were presented using calibrated EAR 3A insert earphones at 5 Hz. The signal was amplified and band-pass-filtered from 10 Hz to 3 kHz using the Bio-Logic Navigator (IL) with a recording epoch of 53 msec. VEMPs (Bio-Logic Systems Corp., Mundelein, IL) were recorded for each subject at 90, 85, and 80 dB normalized hearing level for both ears. From each tracing, the peak latencies of wave p13 as well as n23, and peak-to-peak (p13-n23) amplitude were measured for each ear at each intensity. A 90 dB stimulus intensity was used for final report.

In this study, we use the control group data as the criteria for defining delayed VEMP. The mean latencies of peak p13 and n23, and the amplitude p13-n23 of the normal control subjects at our laboratory (mean \pm SD) were 12.1 ± 2.2 milliseconds for p13 latency, 24.8 ± 2.8

milliseconds for n23 latency, and $102.3 \pm 18.7 \mu\text{V}$ for p13-n23 amplitude. Hence, latencies of peak p13 and n23 exceeding 16.5 and 30.4 milliseconds (mean ± 2 SD), respectively, were defined as delayed responses.

Statistical analysis

The X^2 test was used to compare the difference of p13 and n23 latency between patient groups.

RESULTS

Vestibular-evoked myogenic potentials

Among the 52 sides of the 26 subjects of experimen-

tal group, except for 1 side that showed no response, VEMP tests disclosed delayed responses in 22 subjects, including unilateral delay in 20 and bilateral delay in 2 subjects (Fig. B). The remaining 3 subjects (11.53%) showed normal vestibular evoked myogenic potentials bilaterally. In contrast, in the control group, VEMP testing disclosed delayed response in three subjects (11.53%), including unilateral delay in two and bilateral delay in one subjects. In other words, 88.47% of the subjects with VAH demonstrated abnormal VEMPs either unilaterally or bilaterally. This was significantly higher than the percentage of abnormal VEMPs in the subjects without VAH ($p=0.019$).

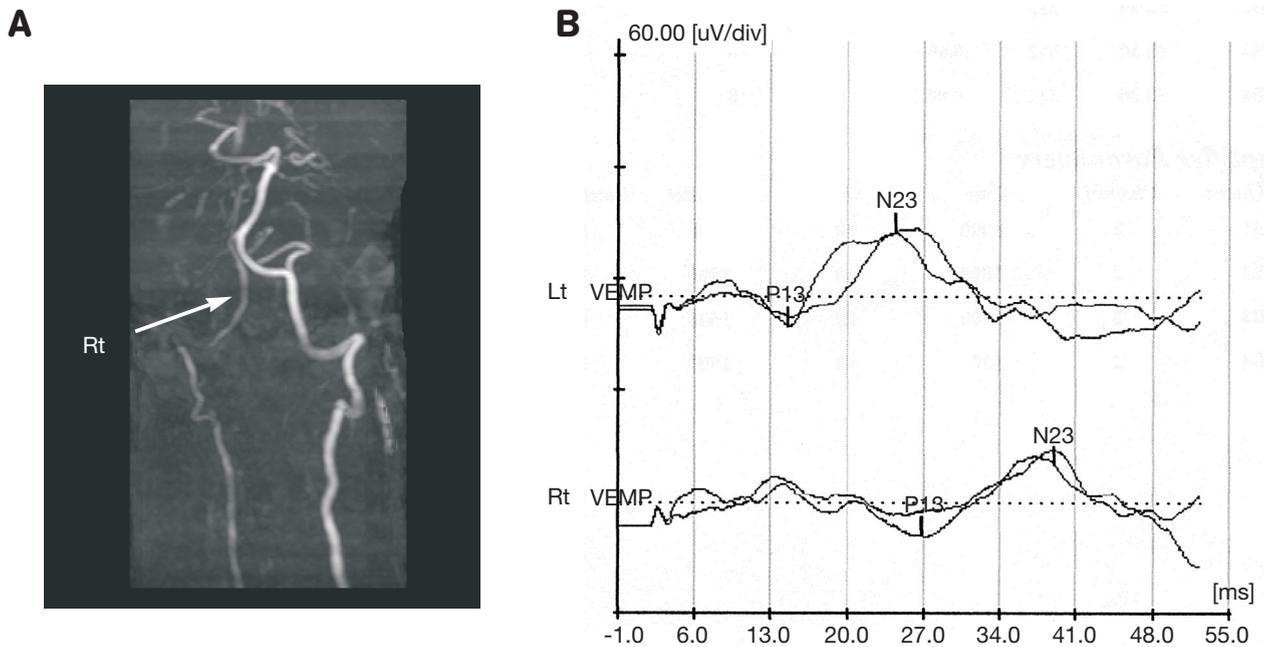


Figure. (A) The magnetic resonance angiogram in a woman suggests a diagnosis of VA hypoplasia on the right side (arrow). (B) The corresponding vestibular evoked myogenic potentials show an ipsilateral delayed response.

Table 1. Baseline demographic data

	Tested group Subjects with VAH	Control Subjects without VAH
Number of patients	26	26
Females/males	14/12	14/12
Mean age (years)	33.2 ± 11.2	33.5 ± 11.6

VAH: vertebral artery hypoplasia.

Table 2. Mean latencies of p13 and n23

Group	No.		p13	n23 (ms)
Subjects with a VAH	26	Rt ear	18.3±2.5*	33.8±2.9*
		Lt. ear	12.0±1.3 (p: 0.02)	25.1±2.6 (p: 0.018)
Subjects without a VAH	26	Rt ear	11.9±2.7 (p: 0.019)	24.8±2.9 (p: 0.02)
		Lt. ear	12.2±1.5 (p: 0.02)	24.7±2.8 (p: 0.017)

VAH: vertebral artery hypoplasia. The 26 VAH were all located on right side.

Mean latencies of p13 and n23 were significantly longer in the right ear of the subjects with VAH than those in the left ear and those in the subjects without a VAH (Table 2). Given the exclusive right-sided hypoplastic VA in our group of subjects with VAH, the majority (69.23%, N=18) had a concurrent ipsilateral delayed response or absence of VEMP. (Figs. A - B)

DISCUSSION

VAH was detected among 10.4% of the healthy subjects which was significantly higher than the previous reports (2 to 6%). How could the larger number of vertebral artery hypoplasia be explained? A higher incidence of VAH was described in Asia (15.7-20.2%) from small-scale studies^(10,11). Sample size would be one possible explanation. In any case, based on this small scaled study, we draw an association between VAH and ipsilateral abnormal VEMP. The majority (88.47%) of the subjects with VAH demonstrated abnormal VEMPs either unilaterally or bilaterally. The incidence was significantly higher than the percentage of abnormal VEMPs in the subjects without VAH (p=0.019). Mean latencies of p13 and n23 were statistically longer in the right ear of the subjects with ipsilateral (right-sided) VAH. These data altogether indicated that VAH may lead to ipsilateral VEMP abnormalities, which included delayed response or even absence of ipsilateral VEMP. In topographic considerations, VEMP tests chiefly evaluate the saccolcollic reflex, which descends through the lower brainstem where the intracranial vertebral artery inclines. Vertebral artery runs upward medial to the front of the medulla oblongata and supplies the brain stem from the vestibular nerve to the anterior root of the first cervical

nerve, where saccolcollic reflex embedded. It is thus reasonable to postulate that even in asymptomatic healthy subjects, VAH may contribute to functional deficits in the corresponding territory.

The prolongation of mean latency of p13 and n23 imply a demyelination process of the vestibulospinal tract⁽⁸⁾. Segmental demyelination is probably secondary to ischemic axonal dystrophy⁽¹²⁾. VAH may lead to repetitive hypoperfusion injury to corresponding brainstem regions^(5,6). Although one may infer a brain stem lesion from a delayed VEMP, absence of VEMP would indicate interruption of the sacculo-collic reflex, not necessarily a brain stem lesion. Nevertheless, we postulate that a delayed response or absence of ipsilateral VEMP can be attributed to “hypoperfusion” of the hypoplastic VA. This assumption is supported by the findings in our previous report, namely VA hypoplasia leading to “ipsilateral” brain stem/cerebellar ischemic stroke through regional hypoperfusion⁽⁴⁾. VA hypoplasia and vertebrobasilar insufficiency have been shown to selectively damage the saccolcollic/ vestibulospinal pathway, because of its high energy requirement and lack of collateral circulation^(13,14). It has been posited that interruption of blood flow for 5 minutes could produce spotty degeneration of the saccolcollic pathway⁽¹⁵⁾.

Some confounding factors did exist in the present study. We did not exclude migraineurs in the present study. A higher frequency of hypoplastic vertebral artery in migraineurs has been documented. Liao et al. described an abnormal VEMP with prolonged p13 and n23 latencies in migraineurs⁽⁷⁾. Because of the high prevalence of migraine disorder, it could be a significant confounding factor. Moreover, when interpreting the prolonged p13 and n23 latencies, one should take into

consideration the recent finding by Allena et al. that a shorter rather than a longer latency may happen with brain stem lesions⁽¹⁶⁾. Our hypothesis of “regional demyelination by VAH-related brain stem hypoperfusion” would not be fully validated before more comprehensive studies. On the other hand, Allen et al. also described abnormal vestibulo-collic reflexes abnormal in migraine. VAH-related brain stem hypoperfusion injury may provide a tentative pathophysiologic basis for that observation in view of a higher incidence of VAH in migraineurs.

Finally, the sample size of our study was relatively small (N=26). Given the low frequency of VA hypoplasia, sampling bias may have been enhanced. Also, an alteration of VA diameter on stress condition would exist⁽¹⁷⁾. Thus there is not a unanimous consensus on MR angiographic diagnosis of VAH with the use of diameter criteria. A large-scale study with refined inclusion/exclusion criteria (e.g. with migraineurs taken into consideration) is necessary to verify the reproducibility of our results. Despite these limitations, we believe that VA hypoplasia associated with abnormal VEMPs is a real entity that deserves more attention.

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