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Clinical commentary

Primary trigeminal neuralgia is associated with posterior fossa crowdedness: A prospective case-control study

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ABSTRACT

Neurovascular conflict (NVC) has been postulated to be the underlying cause of trigeminal neuralgia (TN). Does the posterior fossa crowdedness increase the chance of NVC? The aim of this study was to quantitatively measure the posterior fossa crowdedness in patients with TN and to perform a comparison with healthy controls. We conducted a prospective case-control study of 46 patients diagnosed with primary TN and 46 sex- and age-matched healthy controls. All subjects underwent high-resolution three-dimensional MRI, and the 3D Slicer software was used to measure the posterior fossa volume (PFV) and hindbrain volume (HBV). The posterior fossa crowdedness index (PFCI) was calculated as HBV/PFV × 100%. The results showed that patients with TN had a larger HBV (155.4 ± 23.2 cm^3 versus 152.9 ± 13.5 cm^3, P = .16) and a smaller PFV (182.7 ± 18.3 cm^3 versus 186.1 ± 11.7 cm^3, P = .42) as compared to control subjects, but these values were not significantly different. The mean PFCI was significantly higher in patients with TN than in controls (85.1% ± 3.4% versus 82.2% ± 5.3%; P = .03). Women had a more crowded posterior fossa than men (85.8% ± 2.1% versus 84.1% ± 2.6%; P = .023) in patients with TN. The correlation analysis showed that a higher PFCI was associated with younger age (P = .02), woman (P = .014), and TN disease (P = .001). From this study, we conclude that patients with TN have a more crowded posterior fossa than healthy subjects. Women, younger age and TN disease are associated with a higher PFCI. The posterior fossa crowdedness may be a risk factor of NVC, and thus more likely to result in the genesis of TN.

1. Introduction

Trigeminal neuralgia (TN) is a rare, episodic painful disorder that is unilateral, brief electric shock-like, provoked by light touch and limited to the distribution of one or more divisions of the trigeminal nerve [1,2]. Neurovascular conflict (NVC) at the trigeminal nerve root entry zone (REZ) of the brainstem has been postulated to be the underlying cause of TN [2,3]. However, the specific aetiology of NVC remains unclear. Furthermore, NVC has been demonstrated in healthy test subjects as well [4,5], and TN can occur in patients without vascular compression [6], suggesting that NVC alone is insufficient to produce TN.

It has been suggested that morphological and volumetric changes in posterior fossa may play a role in the genesis of NVC [7,8]. Several cases of TN have been associated with Paget's disease [9], distorted petrous bone [10], Chiari's malformation [11], achondroplasia [12], and Dandy-Walker malformation [13], diseases that include crowded posterior fossa due to lesions or malformations. Furthermore, there is a female dominance in TN [14], at the same time, women reportedly have a more crowded posterior fossa than men [15]. Moreover, though epidemiological studies performed in Asia remain scarce, relevant studies suggest that the prevalence of TN may be different between Asians and whites, and they attribute this to the morphologic difference of skull [16,17].

These observations led us to hypothesize that posterior fossa crowdedness (PFC) may be a risk factor for NVC, thus resulting in the genesis of TN. To address this problem, we conducted a prospective case-control study to quantitatively measure the degree of PFC in patients with TN in comparison with age- and sex matched control subjects.

2. Materials and methods

2.1. Patients and control subjects

The study included patients clinically diagnosed with idiopathic TN, who received treatment at the neurosurgery department of

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West China Hospital from September 2014 to January 2015. Idiopathic TN was diagnosed according to the criteria of the second edition of the International Classification of Headache Disorders [18]. Patients diagnosed with secondary TN or bilateral symptoms were excluded. Controls were healthy age- and sex-matched volunteers who provided written informed consent. This study was approved by the West China Hospital Ethics Committee.

2.2. Magnetic resonance imaging

All patients and control subjects were examined with the same magnetic resonance imaging (MRI) scanner (Philips Achieva, 3.0T). A standard protocol of conventional axial T1WI, axial T2WI, and a special three-dimensional sequence focused over the posterior fossa: 3D-T2-DRIVE (TR, 2000 ms; TE, 200 ms; matrix, 256 × 168; ACQ voxel MPS, 0.59/0.89/1.60 mm; REC voxel MPS, 0.29/0.29/0.80 mm; thickness, 0.5 mm) were performed. The image was jointly interpreted by neurosurgeons and neuroradiologists. Subjects with structural abnormalities were excluded.

2.3. Measurement of posterior fossa crowdedness

The posterior fossa volume (PFV) was defined as the space encircled by tentorium cerebelli, occipital bone, clivus, petrous bone and foramen magnum. Hindbrain volume (HBV) was defined by encircling the brain tissue inside the posterior fossa area, including the fourth ventricle. The MRI images were transferred to a personal computer, and 3D Slicer software (version 3.6.3, U. S.) was used for segmentation and measurement (Fig. 1). All work was performed by a radiologist blinded to group assignment and experienced with the software. The posterior fossa crowdedness index (PFCI) was calculated as HBV/PFV × 100%.

2.4. Test-retest reliability

Test-retest reliability in determining the PFCI was repeatedly measured in 12 patients with measurements taken one week apart by the same neuroradiologist who was blind to the clinical information.

2.5. Statistical analyses

Student's t-test was used for comparisons between the patients and controls. Pearson correlation test was used to examine the test-retest reliability and the correlations of various factors to posterior fossa crowdedness. Multiple regression analysis was used with PFCI as the dependent variable and with sex, age, TN/control as independent variables. Associations were considered statistically significant when $P < .05$. SPSS software was used for statistical analyses (version 19.0). The mean was expressed ±SD throughout.

3. Results

3.1. Test–retest reliability

Test–retest reliability for PFCI was good after the measurements were repeated one week apart (r = 0.83, p < .001).

3.2. Demographics and PFCI measurements

There were 92 study subjects, comprising 46 TN patients and 46 healthy controls, with 26 women (56.5%) and 20 men (43.5%) in each group. The mean age of patients with TN and controls were 46.5 ± 9.3 (range 23–69) and 46.3 ± 9.5 (range 22–69) years.

Patients with TN had a larger HBV (155.4 ± 23.2 cm^3 versus 152.9 ± 13.5 cm^3, P = .16) and a smaller PFV (182.7 ± 18.3 cm^3 versus 186.1 ± 11.7 cm^3, P = .42) as compared to control subjects (Table 1), but these values were not significantly different. The mean PFCI was significantly higher in patients with TN than in controls (85.1% ± 3.4% versus 82.2% ± 5.3%; P = .03) (Fig. 2A). Women had a more crowded posterior fossa than men (85.8% ± 2.1% versus 84.1% ± 2.6%; P = .023) in patients with TN (Fig. 2B).

3.3. Predictors of PFCI

The correlation analysis showed that age was negatively correlated with the PFCI (r = −0.35; p = .017) in patients with TN. The scatterplot demonstrated that PFCI was declined with age in this series (Fig. 3). The multivariate linear regression analysis revealed that a higher PFCI was associated with younger age (P = .02), woman (P = .014), and TN disease (P = .001).

4. Discussion

The pathophysiological cause of TN is still unknown and current studies mainly focus on neurovascular compression of the trigeminal nerve REZ, microvascular decompression (MVD) leads to NVC elimination and successful pain relief, strongly supporting this theory [2,3,19]. However, there has been ongoing debate on the actual predisposing factors in TN. It is unclear why there are females dominance in this disease, and it's also confusing why TN can occur in patients without vascular compression, while some people do not develop this disease even though they have vascular compression on imaging.

Previous studies have indicated that patients with Chiari's malformation have an underdeveloped small posterior fossa, normal developed hindbrain and a higher crowdedness index [20,21]. In addition, large numbers of case reports have described the simultaneous presentation of TN and Chiari's malformation [22]. Surprisingly, the only suboccipital decompression leads to resolution of pain in most of the cases [22]. The mechanism by which Chiari's malformation could cause TN was not clear, and the authors hypothesized that TN symptoms could be caused by vascular compression at the REZ, which could be affected by anatomic factors related to the Chiari's malformation, such as a small posterior fossa [22]. These observations indirectly imply that a small posterior fossa volume may be a risk factor of NVC.

Various parameters have been used for estimating posterior fossa morphology, including length (1D) [8,20], angle or area (2D) [23] and volume (3D) [24,25]. However, these measures are highly subjective and are strongly influenced by imaging technique. Advances in magnetic resonance technology have made it possible to accurately analyze volumetric parameters of the region of interest (ROI). Two morphometric studies of the posterior fossa volume in patients with TN have been previously published, however, both have failed to find a difference in posterior fossa size between patients with TN and controls [26,27]. We think that both of the studies have some limitations, on one hand, the limited number of subjects used may make it hard to reflect the difference. On the other hand, both of the previous studies were focused on the measurement of the posterior fossa volume, but they had failed to take account of the crowdedness. This evaluation measure (posterior fossa volume) did not fully account for the individual differences, and it may be easily influenced by the individual's body type and head circumference.

We conducted a case-control MRI volumetric study, and a new measurement, the PFCI, was used to estimate the effective space of posterior fossa. This crowdedness index measure can avoid interference from individual differences, and can more accurately

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