Is Migraine Related to Medial Meningeal Artery and Spinous Foramen Caliber?

Migren ile Medial Meningeal Arter ve Spinöz Kanal Çapı İlişkili Mi?

Spinous Foramen Caliber in Migraine

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Özet

Amaç: Migren, tüm başağrısı hastalıkları içinde doktora en fazla başvuru nedenlerinden birisidir ve günümüzde halen migren tanısı için özel bir laboratuvar testi veya radyolojik inceleme yoktur. Migren ağrısında altta yatan mekanizmanın medial meningeal arter vazodilatasyonun neden olduğuna dair geniş bir inanç vardır. Öte yandan son zamanlarda pek çok hipotez vazodilatasyonun rolünü azaltmaktadır. Atak sırasında medial meningeal arterde dilatasyon gelişiyorsa kronik dönemde içinden geçtiği forameni de genişletebilir. Çalışmamızda bu fikirden yola çıkarak migren tanısı olan hastalarda kontrol grubuna göre medial meningeal arter çapı ile spinöz foramen alanında farklılık olup olmadığının araştırılması amaçlandı. Gereç ve Yöntem: Çalışmaya migrenli 36 hasta ve kontrol grubu olarak gerilim tipi baş ağrısı olan 26 hasta alındı. Hastalara çok kesitli beyin BT (bilgisayarlı tomografi) anjiografi tetkiki yapıldı. Migrenli olgular ile kontrol grubu olgularının tümünde her iki taraf medial meningeal arter ve spinöz kanal alanı ölçüldü. Bulgular: Migren hastaları ile kontrol grubunun medial meningeal arter çapı ve spinöz kanal alanı ölçümleri arasında istatistiksel olarak anlamlı farklılık saptanmadı. Tartışma: Çalışmamızda migren patofizyolojisinde dura materi besleyen damarlardaki vazodilatasyonun etken olduğunu gösterecek bulgu saptanmadı. Bu sonuç migren patofizyolojisinde ve etyolojisinde farklı hipotezlerin araştırılması gerektiğini göstermesi açısından önemlidir.

Anahtar Kelimeler

Migren; Meningeal Arter; BT Anjiografi

Abstract

Aim: Although migraine is one of the headache disorders for which people most often consult a doctor, it still does not have a specific diagnostic laboratory or radiologic test. Vasodilation of the medial meningeal artery is widely believed to cause migraines. However, some current hypotheses decrease the role of the vasodilation. If the medial meningeal artery dilates during attacks, in the long term it can expand the foramen pass through. Based on this idea, our study investigated whether there is a significant difference between the medial meningeal artery and spinous foramen sizes of migraine patients compared with a control group. Material and Method: Thirty-six migraine patients and 26 tension-type headache (TTH) patients as the control group were involved in the study. Patients were scanned with brain CT (computed tomography) angiography. The medial meningeal artery and spinous foramen sizes of both groups were measured. Results: There was no statistically significant difference between the measurements of migraine and tension-type headache patients. Discussion: In our study we could not find any evidence to show vasodilation of the dura mater's vasculature as a factor of migraine pathophysiology. This result indicates the need to continue investigating the different hypotheses for migraine pathophysiology.

Keywords

Migraine; Meningeal Artery; CT Angiography

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Introduction

Migraine, whose prevalence was found as %11,7 by Lipton et al., is a common disease in population [1]. A specific laboratory test or radiological investigation is still not currently available for the diagnosis of migraine. An episodic, unilateral, severe, and throbbing headache is its characteristic property [2]. The disease may be associated with autonomic symptoms, and aura, a focal neurological symptom, may occur in one-third of the patients [3].

For many years, the dura mater and its vasculature have been at the center of the hypotheses trying to explain the pathophysiology of migraine [4,5]. According to the vascular theory, the middle meningeal artery (MMA), which is the primary vasculature of the meninges, plays the most important role in migraine pathophysiology; the general belief about the mechanism of migraine headache is the vasodilation of the meningeal blood vessels [6-8].

With the improvement of technology, it has been possible to visualize extremely thin vessels by Magnetic Resonance Angiography (MRA) and Computed Tomographic Angiography (CTA), and to make reliable measurements [9-11]. Additionally, the spinous foramen, which is the site of the entry of the MMA into the cranium, can also be visualized with the CT angiography.

In the present study, we used multi-slice CT angiography to investigate whether the diameter of the MMA and the area of spinous foramen differed in the patients with migraine.

Material and Method

Although the tension-type headache (TTH) is the most commonly experienced primary headache in the population [12], the role of dural vascular causes in its pathophysiology has not been widely investigated [13,14]. Therefore the cases with TTH have been included in the control group in our study.

Selection of the Patients

A total of 64 patients diagnosed with migraine and TTH were included in the study. The criteria for inclusion in the study were as follows: (i) being in the age range of 18 to 58 years; (ii) being diagnosed with migraine or tension-type headache according to the diagnostic criteria of the International Classification of Headache Disorders (ICHD-II) defined by the International Headache Society (IHS); (iii) a disease course of more than two years; (iv) the frequency of pain being at least two episodes per month; (v) an indication of CT with contrast due to reasons such as a change in the severity of headache or an increased frequency of episodes. The criteria for exclusion were as follows: (i) uncertainty of the diagnosis of migraine or TTH regarding the other diseases associated with headache; (ii) being diagnosed within the previous three years; (iii) recently used vasoactive drugs; (iv) allergy for iodinated contrast material; (v) a previous head-neck surgery.

The study was approved by the local medical ethics committee, and the patients were informed prior to the study (approval number: 923/2014).

CTA

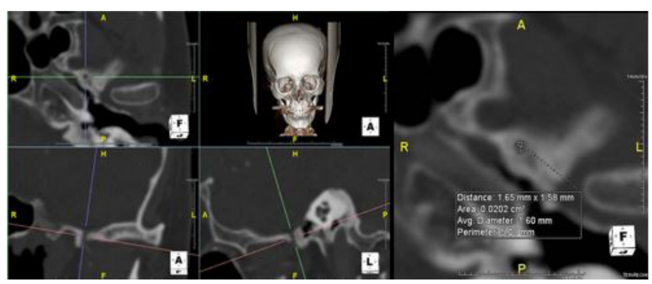
The patients were scanned using a CT scanner with 64 detectors (Aquillon 64, Toshiba Medical Systems, 2011, Japan), and with the following CT scan parameters: collimation 64x0.5, gantry rotation time 0.5 sec, slice thickness 0.5 mm, step value 0.64, 120 kV, and 450 mA. Fifty ml of non-ionic, iodinated contrast material including a high iodine concentration (iodine concentration 350 mg/ml) was administered intravenously through the antecubital vein via a 18- to 20-G catheter and using an automatic pump (Ulrich Medical's technical version, 2004, Germany), at a rate of 4 ml/sec. Forty cc of serum physiologic was administered following the contrast material. Computed Tomographic Angiography was applied using the bolus tracking method, and the application was initiated when the density in the internal cerebral artery (ICA) was 90 to 100 Hounsfield Units (HU).

Evaluation of the Images

The CTA images were evaluated with the Aquarius (iNtuition Edition v. 4.4.11.82.6784, California, USA) software on the orthogonal and oblique planes, and using multi-planar reconstructions (MPR), volume rendering (VR), and maximum intensity projection (MIP) images.

The area of the spinous canal and the diameter of the middle meningeal artery were measured bilaterally in both groups. The left and the right sides were compared for each patient and between groups. The measurements were made when the patients were not in the course of an episode.

The spinous canal has been commonly visualized as a canal with ovoid shape that extends from anterior to posterior and from medial to lateral. Area measurements were made on the axial sections at the narrowest site of the canal, after the coronal and sagittal MPRs had been made in concordance with the canal's own axis (Picture 1). The measurements were made on the internal surface of the canal, by the aid of the region of interest (ROI). The diameter of the middle meningeal artery was measured at the site that was about 2 to 3 mm proximal to its level of entry into the spinous canal. On the coronal oblique MPR images which were perpendicular to the long axis of the artery, the out-to-out measurements were made at the area filled with contrast (Picture 2).

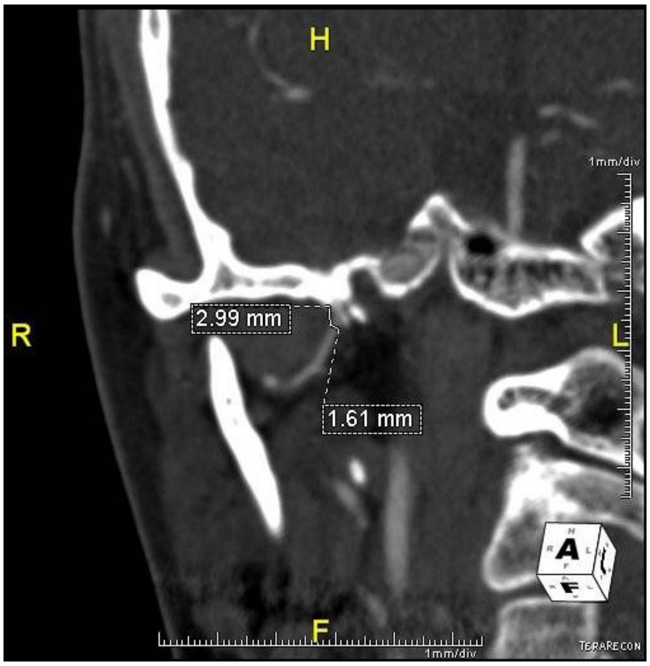


Picture 1. The reformatted images used for the measurement of the spinous canal area: the coronal, sagittal, and axial reformatted sections which are parallel to the long axis of the canal, and an example of the measurement of the canal performed on axial image.

Statistics

The data of the study were analyzed using the SPSS 15.0 (Statistical Package for Social Sciences, 15.0, SPSS Inc., Chicago, USA) statistical software.

For the continuous variables, the Mann-Whitney U test and the T-test were used in comparison of the independent groups, and



Picture 2. The measurement of the diameter of the right-side middle meningeal artery at the site nearly 3mm proximal to its entry into the spinous canal.

the dependent groups were compared using the Wilcoxon test. The Chi-square test was used in comparing the discrete variables between the groups.
The area of the canal and the arterial diameter were compared in terms of gender using the independent samples test.
A p value <0.05 was accepted to be statistically significant. The descriptive statistical values were expressed in numbers and average percentages.

Results

The two patients who were observed to have atherosclerosis in the ICA after the CT angiography were excluded from the study. The study proceeded with a total of 62 patients. The patients were separated into two groups: 26 cases (41.9%) had TTH, and 36 cases (58.1%) had migraine-type headache. Of the 62 patients, 5 had aplasia of the right spinous canal, and 4 had aplasia of the left spinous canal; therefore the statistical analyses of the right-side measurements included the data of a total of 57 patients, and those of the left-side measurements included the data of a total of 58 patients.
The mean ages of the cases with TTH and migraine headache were 37.42 (18-56) years and 34.19 (18-58) years, respectively; this difference was not found to be significant (p>0.05).
Of the 26 cases with TTH, 22 were female (84.6%) and 4 were male (15.4%); of the 36 cases with migraine-type headache, 32 were female (88.9%) and 4 were male (11.1%). The distributions of genders were similar in the two groups (p >0.05).
The mean durations of the disease in the cases with migraine and TTH were found as 9.3 (2-28) years and 4.6 (2-16) years, respectively.
The area of the right spinous canal in the 25 TTH cases was (mean) 2.182 mm2 (0.51-3.67); this value was measured as (mean) 2.545 mm2 (1.22-6.19) in the 32 migraine cases. The area of the right spinous canal did not differ significantly between the groups (p =0.296).
The area of the left spinous canal in the 25 TTH cases was (mean) 2.484 mm2 (0.39-4.00); this value was determined as (mean) 2.525 mm2 (1.01-5.22) in the 33 migraine cases. The area of the left spinous canal did not differ significantly between the groups (p =0.54).
The results of the measurements regarding the area of the spinous canal are shown in Table 1.

Table 1. Spinous foramen calculations

		Number of foramens	Mean	Standart Deviation	Median	Minimum	Maximum
TTH	R	25	2.18	0.73	2.18	0.51	3.67
	L	25	2.48	0.76	2.47	0.39	4.00
MTH	R	32	2.54	1.04	2.26	1.22	6.19
	L	33	2.52	1.00	2.28	1.01	1.86
Total		115	2.44	0.93	2.23	0.51	6.19

*p >0.05 (right = 0.29; left = 0.54)

Abbreviations: TTH: Tension type headache; MTH:Migraine type headache; R: right; L: left

The diameter of the right-side middle meningeal artery was measured as (mean) 1.358 mm (0.77-2.32) in the 25 TTH cases; this value was found as (mean) 1.401 mm (1.01-1.86) in the 32 migraine cases. The diameter of the right-side middle meningeal artery did not differ significantly between the groups (p =0.571).
The diameter of the left-side middle meningeal artery was measured as (mean) 1.344 mm (0.93-2.03) in the 25 TTH cases; this value was (mean) 1.394 mm (0.75-2.14) in the 32 migraine cases. The diameter of the left-side middle meningeal artery did not show significant difference between the groups (p =0.571).

Discussion

The migraine headache is one of the most common reasons among all headache diseases for consulting a doctor. The World Health Organization has considered it among the diseases leading to the greatest disablement. It has been known that about 17.5% of women and 5.6% of men experience migraine headache [1]. Besides its unfavorable effects during episodes, it also has chronic effects such as low performance in school and professional life, and social problems. Nevertheless a specific laboratory test or radiological investigation is still not available currently for the diagnosis of migraine.
Although the pathophysiology of migraine is still not exactly understood, for many years, the middle meningeal artery and the venous system have been at the center of the pathophysiology hypotheses [4,5]. There is a common belief that the underlying mechanism of the migraine headache is the vasodilation of the intracranial blood vessels [15]. In the study of Asghar et al. [16] performed more recently with MR angiography, headache on the same side has been shown to regress with the decrease of the unilateral vasodilation in the MMA in the patients who were administered the vasoconstrictor agent sumatriptan (5HT 1B/1D receptor agonist) during migraine pain. Similarly, in a study of Villalon et al. [6] the level of serotonin, which is a vasoconstrictor and central neurotransmitter, has been shown to decrease during a migraine episode, and the headache has

been eliminated with the intravenous infusion of serotonin during the episode. In the same study, ergotamine and other anti-migraine agents have been shown to cause vasoconstriction in the external carotid circulation. This study concludes that the cerebral and meningeal vasodilation is the primary triggering cause of the migraine headache [6].

There are also studies claiming that the meningeal and cerebral vasodilation exists secondary to the release of vasoactive neuropeptides resulting from the activation of the trigeminovascular system, rather than acting as a primary trigger of pain in migraine pathogenesis. In these studies, vasodilation is claimed to play a role in the persistence and worsening of headache [17]. A third consideration claims that the vasodilation is only a harmless audience in the pathogenesis of migraine pain [18,19]. The common point of all three considerations is the existence of vasodilation in migraine headache. However, these hypotheses have mostly been developed due to studies conducted with experimental animals. The reason why there is limited number of studies conducted with humans is because, until recently, invasive methods have been required to make these findings. However, non-invasive sectional imaging methods such as MRA and CTA have been improved, now making it possible to visualize the thin vessels such as the MMA in a sensitive manner [9,10].

More recently, many hypotheses have decreased the role of vasodilation. In the study of Schoonman et al. [20] conducted with 3T MR angiography, an artificial migraine episode was initiated in migraine patients through the infusion of NTG, and the MMA diameters were measured before and during the episodes; the results showed no significant differences. In a study investigating the human MMA microscopically, the dural extravascular tissue surrounding the meningeal arteries was demonstrated to be too rigid to allow a marked expansion of the vessels. It has also been reported that the meningeal arteries are located within grooves at the internal tabula of the calvarium and that 3/4 of their surroundings are composed of bony tissue. As a result, marked vasodilation is impossible [21].

In the chronic phase, the dilation of the arteries may lead to the widening of the canals that they pass through [22]. If any vasodilation had existed during a migraine episode, it might have caused widening of the spinous foramen that the vessel passes through, and this might be considered an indirect finding. To consider this hypothesis, in our study we measured the areas of the spinous canals in the cases experiencing migraine episodes for an average of 9 years. The multi-sectional CT is the most convenient method for visualizing and reliably measuring the spinous canal. When compared to a control group, if a widening is determined in the diameter of the spinous canal that is located at the site of migraine headache, this may indirectly demonstrate the existence of vasodilation in migraine etiopathogenesis. So, the CT may be regarded as a method that helps in the diagnosis of migraine according to the ICD criteria, in cases where initial diagnosis is unclear. Exposure to ionizing radiation is the most important disadvantage of CT; however, this risk can be minimized by investigating only the base of the head.

Knowing whether vasodilation is a mechanism included in the pathophysiology of migraine is extremely important for the development of therapeutic agents. The triptans and ergots are the most effective anti-migraine agents used today. Being potent vasoconstrictors [23], they cause risks for myocardial and cerebral ischemia in patients with vascular diseases [24]. If it is proven that vasodilation does not play a role in pathophysiology, new and safer medications can be developed for these patients [20].

Our study measured both the diameter of the MMA and the area of spinous foramen. The mean value of the MMA diameter was found as 1.38±0.28 on the CT angiography, which was similar to the results of the studies in the literature conducted with MRA [20,25].

The measurements of the MMA diameters and the areas of spinous canal did not show differences in the TTH cases compared to the control group. These results indicate the necessity of considering hypotheses other than vasodilation in the pathogenesis of migraine.

The most important limitation to this study was the measurement of the parameters when the patients were not in the phase of a migraine episode. The difficulties experienced in the admission of the patients to the hospital during an episode, and in the application of procedures during routine intensive work, make it impossible to perform the visualization procedures in the course of an episode. In the literature, similar studies have been conducted during migraine episodes triggered by NTG; however it is not definite that the attacks provoked by NTG are similar to the spontaneous migraine attacks [20]. Not performing the vascular measurements during episodes might have led to the exclusion of changes in diameter that might exist during an attack. This is why we also included the measurement of the spinous canal area in our study.

Conclusion

The area of the spinous canal, which may be indirectly affected by the meningeal arterial dilation that is considered to have an important role in migraine pathophysiology, does not differ in the patients with migraine compared to the group with headache due to non-vascular etiopathogenesis.

We also did not find an increase in the meningeal arterial diameter. This result supports the increasing number of studies reporting that meningeal vasodilation does not play a role in the etiopathogenesis of migraine headache. The present results need to be supported by further studies conducted with a wider series, also including investigations performed during migraine episodes.

Competing interests

The authors declare that they have no competing interests.

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