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Optic canal size in idiopathic intracranial hypertension and asymmetric papilledema

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ABSTRACT

Objective: Asymmetric papilledema (AP) is a rare condition in idiopathic intracranial hypertension (IIH). As the pathophysiology of papilledema developement in IIH remains unclear, the study of AP could clarify some etiologic aspects. We aimed to evaluate bony optic canal size in IIH patients with AP.

Patients and methods: All IIH patients based on modified Dandy criteria in our referral tertiary eye hospital underwent neuro-opthalmologic exams and grading of papilledema according to modified Frisén scale. Very asymmetric papilledema (VAP) defined as a ≥2 grade difference between the two eyes. Clinical features, cerebrospinal fluid opening pressure (CSF OP), best corrected visual acuity, Humphery visual field, and brain magnetic resonance imaging (MRI) and MR venography was performed for all patients. Spiral orbital computed tomography (CT) scan which is the choice method for details of bony structures with axial, coronal and sagittal planes was done in patients with VAP.

Result: 59 patients with IIH were diagnosed that 18.6% of them (n = 11) had VAP. There was no IIH patient with strictly unilateral Papilledema. Presenting symptoms and CSF OP was not significantly different between patients with symmetric and asymmetric papilledema. In patients with VAP, bony optic canal size was not statistically significant different in axial, coronal and sagittal plane when comparing the eye with higher grade edema to the fellow eye.

Conclusion: Our study showed that bony optic canal size evaluated by orbital CT scan was not different in VAP in IIH patients. Finding the exact pathophysiology of AP need further studies.

1. Introduction

The most important complication of idiopathic intracranial hypertension (IIH) is visual loss. Recognizing underlying factors which damage nerve fibers in the presence of increased Cerebrospinal fluid (CSF) pressure can help to find strategies to prevent or delay visual loss.

PE is almost always bilateral in IIH patients. There are few reports of asymmetric PE which may provide opportunity to study the underlying mechanisms in development of PE and visual loss in IIH. Several factors such as optic nerve sheet anomaly or decreased elasticity of lamina cribrosa have been suggested to explain very asymmetric papilledema (VAP) [1], but its mechanism remains unclear.

Optic canal consists of two components including bone and meningothelial cells which cover the subarachnoid space of the optic nerve. Recently, Bidot et al concentrated on the role of bony optic canal size in the development of asymmetric papilledema in IIH. They used magnetic resonance imaging (MRI) to measure the bony optic canals size [2,3]. We decided to use computed tomography (CT) scan, which is a more appropriate method to evaluate the bony optic canal diameter in IIH patients with VAP.

2. Materials and methods

Our study was approved by Tehran University of Medical Sciences Research Ethics Committee.

The study was conducted at neuro-ophthalmology clinic of Farabi

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Eye Hospital that is the biggest tertiary referral center of eye and receives patients from all parts of country. All consecutive patients with new diagnosis of IIH based on modified Dandy criteria [4] from September 2015 to August 2017 were enrolled in the study. We included only patients with recent presentation and known cases or longstanding IIH patients (more than one month duration of disease) were excluded from study. Initial symptoms of patients including visual loss, transient visual obscurations (TVO), diplopia, tinnitus, and headaches were recorded. Best corrected visual acuity, intraocular pressure, slit lamp funduscopic examination, automated Humphery visual field testing (Carl Zeiss Meditec, Dublin, CA) were also evaluated. All cerebrospinal fluid opening pressures (CSF OP) were measured by a single neurologist (S.Y) with the same technique on the day of PE grading and orbital CT scan. VAP defined as a ≥2 modified Frisén grade difference between the two eyes [2,5].

2.1. Radiologic evaluation

Brain MRI with gadolinium and brain MR venography (MRV) were performed for all patients to confirm the diagnosis and rule out of other differential diagnosis. In addition, all patients with asymmetric papilledema underwent orbital CT scan. The CT examination included orbital cuts and was performed on a 16-detector-row scanner (GE Healthcare, Milwaukee, WI, USA) with 1-mm slice reconstructions. All CT examinations were reviewed by an experienced radiologist in orbital imaging (Sh. K) blinded to the neuroophthalmic examination.

Axial scans were performed parallel to the canthomeatal line. Coronal and sagittal reconstructions were also performed. In sagittal and axial views, optic canal diameter was measured in a plane where the walls of canal were well parallel. In coronal plane, the optic canal width and height were measured in a plane where the whole bony optic canal could be viewed (Fig. 1). Protrusion of the optic nerve head, diameter of optic nerve sheath complex (ONSC), and vertical tortuosity of the intraorbital optic nerve were also investigated.

2.2. Statistical analysis

All statistical analyses were performed with SPSS version 14 (SPSS, Inc., Chicago, IL).Frequency distribution of initial data was tested by Kolmogorov-Smirnov test for normality and non-parametric tests were used due to the absence of a Gaussian distribution.

Continuous and ordinal variables were compared between groups using the Mann–Whitney U test. Two-sided Fisher exact or Pearson chi-square tests were used to compare categorical variables. McNemar and Wilcoxon signed-rank tests were used for paired eyes with very asymmetric papilledema for continuous and categorical variables, respectively. These tests were 2 tailed, and significance was set at 5%.

Table 1
Demographics, symptoms, and signs in patients with idiopathic intracranial hypertension with symmetric and asymmetric papilledema.

Papilledema	Symmetric (n = 48) n(%)or Median (IQR)	Asymmetric (n = 11) n(%)or Median	*P* value
Demographics			
Age (years)	34(26-45)	45(40-47)	0.08
Sex, men	14(29.2)	0(0)	0.04
Symptoms			
Headache	20(41.7)	6(54.5)	0.44
Nausea and vomiting	2(4.2)	1(9.1)	0.47
Decreased vision	21(43.8)	9 (81.8)	0.02
Transient visual obscuration	8(16.7)	1(9.1)	1
Diplopia	5(10.4)	0(0)	0.57
Tinnitus	7(14.6)	4(36.4)	0.09
Signs			
CSF opening pressure (cm H_2O)	32.3(24.5-38)	31(22.8-45.6)	0.91

3. Results

During 2 years period of the study, 59 patients with IIH were diagnosed that 18.6% of them (n = 11) had VAP. All were Iranian and there was no IIH patient with strictly unilateral PE. The grade of edema was more severe in left eye in 9 patients. All patients with VAP were women. However, there was no significant difference in the age of patients in symmetric and asymmetric group. Patients with symmetric papilledema used to present with decreased vision more commonly compared with VAP group (Table 1). Otherwise, there was no significant difference in the presenting symptoms and CSF OP between two groups (Table 1). In patients with VAP, visual fields were worse in the eye with highest grade edema compared with the fellow eye (mean deviation, -4.8 vs -3.5 dB; P = 0.06).

Orbital CT scan with standard protocol of the study was performed for 9 of 11 patients with VAP. Two patients had been performed their CT in other centers which were excluded from radiologic analysis. In these patients with VAP, bony optic canal size was not statistically significant different in axial, coronal and sagittal plane when

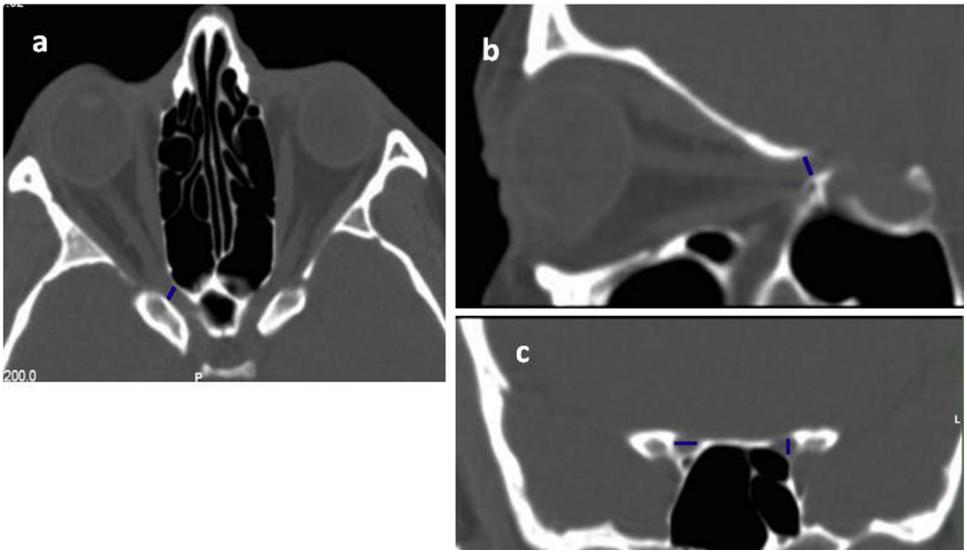

Fig. 1. Sites of optic canal measurements in axial (a), sagittal (b) and coronal (c) planes in very asymmetric papilledema patients with IIH.

Table 2
Comparison of ophthalmic and radiologic features between the eye with the higher grade papilledema versus the eye with the lower grade papilledema in IIH patients with very asymmetric papilledeam.

	Higher Grade Median (IQR) or n (%)	Lower Grade, Median (IQR) or n (%)	*P* value
Ophthalmic findings (n = 11)			
Modified Frisén grade	4(3.75-5)	3(2-3)	—
VA, logMAR	0.4(0.10-1.00)	0.10(0-0.30)	0.16
HVF, mean deviation	−4.8[(-32.5)- (-0.4)]	−3.5[(-6.6)-(-0.19)]	0.06
Radiologic Findings (n = 9)			
OPNSC diameter	7.5(6.4-7.75)	6.9(6.1-7.9)	0.11
Optic canal diameter in axial plane (mm^2)	3.7(3.2-3.9)	3.5(3.2-3.9)	0.96
Optic canal diameter in coronal plane (mm^2)	5.3(4.7-5.6)	5.1(4.6-6)	0.80
Optic canal diameter in sagittal plane (mm^2)	3.6(3.4-3.9)	4.2(3.4-4.4)	0.47
ON head protrusion	4(44.4%)	2(22.2%)	0.63
Optic Nerve Tortuosity	6(66.7%)	5(55.6%)	1

VA: visual acuity, HVF: humphery visual field, ONSC: optic nerve sheat complex.
The optic canal is a small bony canal at the apex of orbit and if there is asymmetry, it would be in scale of millimeters or less. Therefore, along with comparison of median of optic canal diameters, we decided to test the association of asymmetry of PE with that of optic nerve sheath complex (ONSC) and bony optic canal diameters by chi-square analysis. Ignoring the absolute differences, in this way, the side with higher grade edema was associated with larger ONSC (*P*-value = 0.02), however no such association was found for bony optic canal diameter (*P*-value = 0.9).

comparing the eye with higher grade edema to the fellow eye (Table 2).

4. Discussion

VAP is uncommon in IIH and rarely encountered in IIH studies. Heterogeneous prevalence of 3.6, 7 and 10 percent were reported for VAP in Bidot et al [2], IIH treatment trial [6] and Wall et al [7] studies, respectively. While the definition of VAP was the same in these studies (two modified Frisén grade difference or more). In our study, VAP was defined the same as former mentioned studies and a prevalence of 18.6 percent was detected. However, a prevalence of 23% has also been reported [1].

Details of symptoms and signs of IIH and CSF OP in VAP have been infrequently considered. In retrospective study of Bidot et al [2], patients with VAP were more likely asymptomatic (6/20, 27%) and had lower CSF OP compared with symmetric group. While in our study we had no asymptomatic IIH patients either with symmetric or asymmetric PE; because according to modified Dandy criteria of IIH [4], patients should have symptoms and signs of increased intracranial pressure.

Comparing IIH patients with symmetric and asymmetric PE, we found no significant differences in age, clinical symptoms and signs and CSF OP except for a subjective visual loss that was observed more in VAPs. Subsequently, visual acuity and visual field were not significantly different between the eyes with higher grade and lower grade PE. In previous studies, TVO was not associated with extent of disc edema and visual loss at presentation [4,6]. IIH treatment trial also found no relationship between perimetry mean deviation (PMD) and PE grading [6]. In addition in this cohort study, there was no statistically significant relationship between CSF OP and PMD. Regarding the small size of the bony optic canal, the differences between the two fellow optic canals would be in submillimeter scale. Therefore, we decided to perform another analysis ignoring the absolute differences. In this way, the side with higher grade edema was more commonly associated with larger ONSC which is in agreement with previous studies [8]. However no such association was found for bony optic canal diameter.

The potential role of bony optic canal size in development of PE has recently been considered [2,3,9]. To our knowledge, orbital CT scan which is the method of choice for showing anatomical details of bony optic canal has never been done in IIH patients. One study included 46 IIH patients and has not noted VAP [9]. They found that visual function was not associated with optic canal diameter. In another study, retrospective data of brain MRI in 7 patients with IIH and VAP have been reviewed and only one patient had CT scan. They found that bony optic canal was smaller on the side of the lowest grade edema [2]. Following this study, the writers evaluated the grade of PE with size of optic canal with MRI in 69 IIH patients (six of them had VAP) [3]. They concluded that poor visual function and severe papilledema or optic atrophy were associated with a larger optic canal. Consequently, they rationalized that smaller size of optic canal can be a factor in development of compartmentation of perioptic CSF and less transmission of CSF along optic nerve. In this study, in fact the writers pooled the data of all IIH patients to test the correlation between optic canal diameter and grade of PE. It seems that by this method, individualized variation of optic canal size in population has not been considered. Indeed, it could be a source of confounding factor to merge the optic canal diameters of different patients. Moreover, as addressed by the writers, larger optic canal could be a consequence of longstanding edema resulting in bone remodeling and not the cause of greater optic disc edema.

Apart from diameter of bony optic canal, other factors may contribute in CSF dynamic around subarachnoid space of optic canal in IIH patients. For example, increased thickness of meningothelial layer may protect optic nerve from further transmission of CSF pressure to its intra-orbital segment and cause lesser grade edema. It is shown that oxidative stress and elevated pressure can influence on physiology of meningothelial cells in optic canal and leading to proliferation of meningothelial cells [10]. On the other hand, toxic substances to astrocytes such as lipocalin-like prostaglandin D synthase (L-PGDS) increase in the subarachnoid space of the optic nerve compared with lumbar CSF in IIH patients [11]. Xin X et al showed that L-PGDS could inhibit astrocyte proliferation in vitro [12].

We tried to overcome some of the limitations of previous studies with including only recently presented IIH patients (to prevent the effect of bone remodeling resulted from longstanding raised ICP), use of orbital CT scan for measuring optic canal size, measuring optic canal in different planes (axial, coronal and sagittal) and paired comparison of the eyes with high and low grade edema. However, our study had limitation. Using modern retinal imaging such as optical coherence tomography could add useful data.

In conclusion, our study showed that age, clinical symptoms and signs and CSF OP were not significantly different between IIH patients with symmetric and asymmetric PE. In addition, in IIH patients with VAP, the bony optic canal size was not different between two sides. Finding the exact pathophysiology of asymmetric PE need further studies.

Conflict of interest

There is nothing to declare.

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