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Research Article

Non-Invasive Techniques in the Diagnosis of Pseudotumor Cerebri

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Abstract

Aim: To analyze non-invasive techniques in diagnosis of Pseudotumor Cerebri (PTC).

Methods: Twelve cases diagnosed with PTC (group 1), and 10 healthy controls (group 2) were included in the study. All patients were examined for visual acuity, anterior segment and fundus. Ocular Ultrasonography (USG) was used to measure the anteroposterior diameter of the globe. Orbital and cranial Magnetic Resonance Imaging (MRI) was performed. The data were statistically analyzed, and $P<0.05$ was considered as statistically significant.

Results: Orbital MRI and USG findings showed statistically significant differences for anteroposterior diameter of the globe, optic nerve thickness, perioptic cerebrospinal fluid space, sella height, posterior scleral flattening, and papillary protrusion ($P<0.05$). Anteroposterior diameter of the globe on USG was found smaller in group 1 compared to group 2, but the difference was not statistically significant.

Conclusion: Measurement of anteroposterior diameter of globe is an important parameter in the differential diagnosis of papilledema. MRI can be used as a noninvasive technique in the diagnosis and follow-up of PTC patients.

Keywords: Pseudotumor cerebri; Ocular ultrasonography; Magnetic resonance imaging

Introduction

Pseudotumor Cerebri (PTC) is associated with a high intracranial pressure in absence of any intracranial space occupying lesions or hydrocephalus. It is characterized by headache and optic disc edema. Temporary loss of vision and double vision may also be seen. Neurological symptoms are usually absent, but sixth nerve palsy may rarely appear. PTC is usually seen in young or middle- aged women, and its etiology is not known most of the time [1-5].

In patients with papilledema, radiological imaging is used to rule out a neurological emergency. Intracranial structures may be seen in detail on radiological imaging. Some radiological imaging findings that were not considered to be important in the past are now accepted as significant findings [1-5].

In this study, transverse and anteroposterior diameters of globe, optic nerve thickness, and perioptic Cerebrospinal Fluid (CSF) space were measured on orbital MRI images. The anteroposterior diameter of the globe was also measured with orbital A-scan Ultrasonography (USG). Posterior scleral flattening, vertical tortuosity and papillary protrusions were analyzed on sagittal and axial USG images. The results were compared with the MRI findings.

Methods

PTC patients followed in Neuro-ophthalmology Department of Ankara Numune Education and Research Hospital constituted PTC group (group 1, n=12). The patients with normal orbital-cranial MRI findings acted as the controls (group 2, n=10). All participants provided their informed consents. The study was conducted in accordance with the principles of Declaration of Helsinki.

PTC was diagnosed according to modified Dandy criteria: 1) Symptoms and signs that may be associated with a high intracranial pressure (headache, papilledema, etc.). 2) Documented increased CSF opening pressure higher than 25 cm H_2O, with normal CSF composition. 3) No abnormal neurological findings except a sixth nerve palsy. 4) Absence of any space occupying lesions on neuro radiological imaging [1-4].

Complete ophthalmological examination including visual acuity, color vision, pupillary reflexes, eye movements, and fundus examination were done in all patients. B-scan ocular USG was performed to examine the optic nerve for presence of optic disk drusen and optic nerve sheath expansion. A-scan ocular USG was performed to determine the anteroposterior diameter of the globe. Humphrey automated static perimetry was used for visual field testing. Pattern Visual Evoked Potential (PVEP) was measured in accordance with ISCEV standards in our Electrophysiology Department, using Metrovision, MonPack visual electrophysiology device. All patients were consulted with Neurology Department, and they had Lumbar Punctures (LP). CSF pressure was evaluated according to the Dandy criteria [1].

Radiological imaging included orbital and cranial MRI. Transverse and anteroposterior diameters of the globe, optic nerve thickness, and perioptic CSF space were measured on axial and coronal orbital images. Posterior scleral flattening, vertical tortuosity,

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Table 1: Orbito-cranial MRI findings and comparison of qualitative parameters between two groups.

	PTC*		Control		
	PTC* (n**)	PTC (%)	Control (n)	Control (%)	p
Ventricular contraction	2	8.3	0	0	0.292
Subarachnoid contraction	0	0	0	0	-
Posterior scleral flattening	18	75	2	10	0.001
Papillary protrusion	5	20.8	0	0	0.039
Vertical tortuosity	15	62.5	8	40	0.137

Table 2: Comparison of quantitative parameters between two groups and statistical analysis.

	PTC	Control	P
Transverse diameter	23.13±5,31	23.52±0,89	0.841
Anteroposterior diameter	21.85±1.01	23.16±0.89	0.000
The thickness of the optic nerve	2.86±1.10	3.70±0.71	0.001
Perioptic CSF space	4.16±2.61	0.95±1.06	0.000
Sellar height	9.31±1.83	7.23±0.41	0.000
Sella-pituitary height	4.70±2.17	2.05±1.28	0.000
Anteroposterior diameter (USG)	22.58±1.77	22.66±1.12	0.071

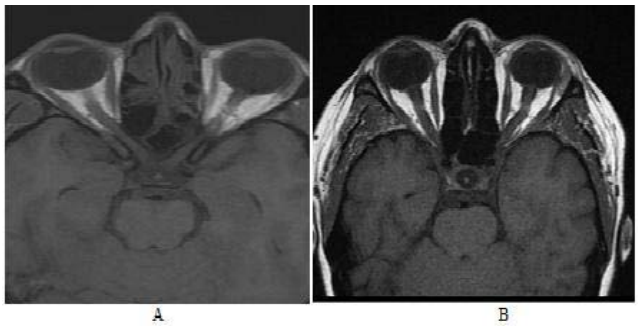

Figure 1: A) Normal optic nerve in control group B) Vertical tortuosity of left optic nerve in PTC group.

papillary protrusions, and "empty sella" were analyzed on the sagittal and axial views. The same radiologist performed all radiological assessments.

Brain and orbital MRI of all participants were done with a 1.5-T MRI system (Signa Excite, GE Medical Systems, Milwauke, Wis.), using a standard head coil. Orbit was analyzed on axial T1-weighted [repetition time/echo time (120S20/14 ms; section thickness/section interspacing 2.5mm/1mm) and axial T2-eighted (4340/112; 2.5/1] images. The matrix size was 256x224 and FOV was 16cm.

Vertical tortuosity was analyzed on both sagittal and axial planes (Figure 1). Optic nerve curving was analyzed on the sagittal plane. The transverse diameter of the globe was measured on the axial plane, perpendicular to each other from outside to outside of the sclera (medial-lateral), and outside of the sclera to the anterior border of the cornea (anterior-posterior). Optic nerve and perioptic CSF space were analyzed immediately posterior to the globe. CSF space was measured from outside to outside, on axial plane (Figure 2). For sella measurements, a line was drawn from the upper ridge of the

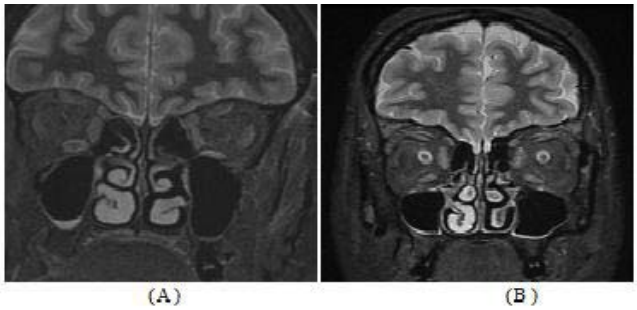

Figure 2: A) Optic nerve sheath image in control group B) Figure 2BIncreased CSF space in the optic nerve sheath in PTC group.

sellar dorsum to planum sphenoidale (sella's upper limit), and the distance between the base of the sella and this line (sellar height) was measured. The height of the pituitary gland and the height of sella were measured, and the values obtained were subtracted. The outline of the sclera was analyzed for loos of arc shape and flattening, in order to analyze scleral flattening and papillary protrusions. Presence of swelling of the optic nerve head into the vitreous space was also searched for.

All data were statistically compared. Student's t and Mann-Whitney U tests were used for statistical analysis. Statistical significance was set at $P < 0.05$.

Results

All patients in group 1 were females, and they were between the ages of 19 and 55 years (mean 33.5±15.6 years). Group 2 consisted of 8 women and 2 men, and their ages ranged between 25 and 58 years (mean 38.2±13.2 years). There were no statistically significant differences between the groups in terms of age or gender ($P > 0.05$).

The ventricular and subarachnoid contraction rates were not significantly different between two groups. The differences between the groups were statistically significant for posterior scleral flattening and papillary protrusions. The rate of vertical tortuosity was higher in group 1 when compared to group 2, but the difference between the groups was not statistically significant (Table 1).

Comparison of quantitative MRI parameters between the groups revealed that there were statistically significant differences for anteroposterior diameter, optic nerve thickness, sella height, and sella pituitary height between two groups. Two groups were similar for the transverse diameter of globe. Anteroposterior globe diameter measured by USGs was smaller in PTC group compared to the control group, but the difference between two groups was not statistically significant (Table 2).

Discussion

Headache and papilledema may appear due to life-threatening clinical conditions. Therefore, the etiological factors should be investigated quickly and thoroughly. The diagnosis of PTC or benign intracranial hypertension syndrome can be set after ruling out other pathologies such as hydrocephalus and intracranial masses. CSF examination is one of the most important interventional procedures for the diagnosis of central nervous system pathologies. On the other hand, radiological imaging is one of the most important noninvasive

diagnostic tools. Radiological imaging is also necessary to rule out the risk of herniation. Previously it was thought that orbital and cranial MRI were not useful for diagnosis, but nowadays they are considered as quite valuable to support the diagnosis in patients who are not eligible for LP for any reason. In recent years, parameters such as the flattening of the posterior sclera, empty sella turcica, and vertical optic nerve tortuosity have been considered as significant findings [6-12].

PTC is most frequently seen in obese, young or middle-aged, female patients [2-5], which was the case in our study.

Previous MRI and Computed Tomography (CT) studies that investigated the role of cross-sectional brain imaging in PTC concluded that there were structural signs which were helpful in establishing this diagnosis [6-10]. Weisberg analyzed several signs (small ventricles, non-visualized cisterns, prominent cisterna magna, empty sella and enlarged optic nerves) on CT in 28 patients [7].

Later controlled studies compared a variety of findings on CT and MRI. Several studies found significantly wider Optic Nerve Sheath Diameter (ONSD) in PTC patients compared to the controls [6-8]. Brodsky reported perioptic nerve sheath expansion in of 45% of the patients, and noted that an increase in CSF signal might be seen besides thinning of the optic nerve [8]. Others noted that an enlarged, elongated subarachnoid space around the optic nerve was more common in PTC patients compared to the healthy controls; however the difference between the patients and the controls was not statistically significant [9]. Similar to our study, Beckerman et al. reported that presence of papilledema was detected in patients presenting as a slightly less valuable diagnostic sign compared with ONSD [13].

Flattening of the posterior aspect of the globe was significantly more prevalent in PTC patients [7-9]. The extreme form of flattening, and protrusion of the head of the optic nerve were significantly more common in PTC patients, similar to our findings. Those changes are supposed to be due to the effect of increased perioptic CSF pressure on the elastic sclera. Brodsky and Vaphiades stated that they could predict presence of elevated intracranial pressure in 90% of cases with PTC, and absence of elevated intracranial pressure in all controls [8,14,15].

Recent studies showed that the degree of empty sella turcica was more severe in PTC patients [7,11-14]. Empty sella develops as a result of acute or chronic intracranial CSF pressure alterations. The gaps in sella turcica may develop due to the full or partial control of CSF pressure where the pituitary gland expands to fill the sella turcica again. In our study, empty sella was seen in 75% of the patients. A quantitative MRI analysis of the pituitary morphology demonstrated a significant decrease in "pituitary gland to sella turcica area ratio" in patients with PTC [11,12].

Increased tortuosity of the optic nerve is one of the important findings in patients with papilledema and a high intracranial pressure. A high CSF pressure does not cause orbital proptosis, but compresses muscles and ligaments between the orbit and the globe. In our study, vertical optic nerve tortuosity was seen in 62.5% of the PTC patients, but comparison with the control group did not yield a statistically significant difference. Brodsky observed vertical tortuosity of the optic nerve in 40% of the patients [8]. Vertical tortuosity is easily detected, but it can be interpreted as a non-specific finding in normal subjects. Therefore, the axial and sagittal images should be analyzed together [8, 15-18].

Ultrasonographic measurement of optic nerve sheath diameter (ONSD) shows a good level of diagnostic accuracy for detecting intracranial hypertension. Sonographic ONSD evaluation may be useful as an additional tool to identify patients with a high intracranial pressure, as in PTC. This method can be used to monitor the efficacy of treatment. The degree of ONSD response to LP differs in subjects with PTC possibly due to defective CSF circulation in the optic nerve sheath, and this condition is defined as optic nerve compartment syndrome [19-24]. In PTC patients, the anterior-posterior diameter of the globe was measured by both MRI and USG, and the results were found to be compatible in statistical analysis.

LP is the most frequently used diagnostic method in the diagnosis and follow-up of PTC. LP is an invasive method that causes patient discomfort, and it may lead to complications such as development of intraspinal epidermoid tumors and back pain [1,2,15]. Therefore, USG and MRI findings may be used in the differential diagnosis when the patients are not eligible for LP.

The anteroposterior diameter of the globe measured with USG is an important parameter in the patients who have papilledema on ophthalmologic examination. Although previously considered as a nonspecific imaging modality, MRI may be used as a non-invasive diagnostic method in the diagnosis and follow-up of PTC.

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