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The Role of Optical Coherence Tomography in Early Detection of Retinal Nerve Fiber Layer Damage in Pituitary Adenoma

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ABSTRACT

Background and objectives: *This study aimed to evaluate the ability of optical coherence tomography (OCT) to differentiate eyes without obvious visual disturbances following pituitary adenomas (PAs) from normal eyes, in order to identify factors that could predict early diagnosis and timely treatment and prevent structural damage of visual pathway in patients with saddle area tumors.*

Material and methods: *The present study was carried out between 2014–2018. Participants were divided into three groups: 23 subjects (44 eyes) in the PAs with visual field involvement (VFI) group, 10 (20 eyes) in the PAs with normal visual field (NVF) group and 22 subjects (44 eyes) in the control group. All patients received diagnostic magnetic resonance imaging (MRI), automated perimetry, visual acuity, OCT and ophthalmological assessments. Also, the degree of visual field (VF) deficit and thickness of peripapillary retinal nerve fiber layer (pRNFL) were measured by OCT and then considered for statistical analysis as predictors of early diagnostic visual involvement in the PAs.*

Results: *All patients in the NVF and control groups (a total of 64 eyes) had normal VF. In the VFI group there were 16 eyes with complete hemianopia. Bitemporal hemianopia occurred in 20 eyes and eight eyes with concentric VF narrowing. Assessment of pRNFL thickness with OCT demonstrated the average and*

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all quadrants of pRNFL thickness in the VFI group were significantly thinner than the pRNFL thickness in the other groups (P<0.001). The pRNFL thickness in the inferior and nasal quadrants and the average value in the NVF group were significantly thinner than the control group (P<0.05).

Conclusions: *If a patient has band atrophy, there is an irreversible damage and the main goal is to diagnose a nerve damage using OCT before band atrophy.*

Keywords: optical coherence tomography, pituitary tumor, visual field, band atrophy, predictive factors.

INTRODUCTION

Various types of tumors can occur in the parasellar area, including pituitary adenomas, craniopharyngiomas, meningiomas, Rathke cysts and optic pathway gliomas (1). Lesions in optic pathways are usually caused by pituitary adenomas (PAs), leading to bitemporal visual field loss due to chiasmal compression (2). When tumors progress to a large extent, they may create chiasmal syndrome. Even if tumors are so large, clinical visual symptoms along with chiasmal compression might not be observed (3). Visual field defect does not occur in 30% of patients (4, 5). The degree of structural and functional damages, including retrograde degeneration to retinal nerve fiber layer (RNFL), retinal ganglion cell and their axon, affect the degree of postoperative recovery to some extent (6-9). Early diagnosis and timely treatment prevent the structural damage of the visual pathway. Axonal loss in the optic nerve usually shows itself along with thickness of peripapillary retinal nerve fiber layer (pRNFL) (10). Imaging technologies can easily help in quantification of axonal loss through RNFL and macular thickness assessment and plays an important role in the diagnosis and follow up of anterior visual pathway disease (11-14). The loss of pRNFL in eyes with chiasmal compression, accompanied by topographic correlation, can be identified by optical coherence tomography (OCT) regarding location and severity between the degree of RNFL thickness and VF defects in compressive optic neuropathies (3, 15-17). Rapid, non-invasive, and in vivo cross-sectional imaging of internal tissue microstructure is a big advantage of OCT done by measurement of echo time delay of back-scattered infrared light made possible by an interferometer and a low coherence light source. It evaluates optic nerve damage quantitatively in patients with saddle area tumors (18, 19).

Since nerve pathways involvement is so complicated, it is essential to diagnose optic involvement early. In order to determine optic involvement, we investigated OCT diagnostic value in contrast with funduscopic results. This study aimed to evaluate OCT ability to differentiate eyes without obvious visual disturbances of PAs from normal eyes.

MATERIAL AND METHODS

This cross-sectional study was conducted in the Ophthalmology and Neurosurgery Department of the hospitals of Iran University of Medical Sciences during 2014-2018, after having obtained the approval of the ethics committee of Iran University of Medical Sciences and the informed consent from all participants.

Subjects (33 cases and 22 controls) were selected for the present study based on the following inclusion criteria: diagnosed PA via MRI and evidence of optic chiasm compression, having general good condition, consent to take part in the study, having no previous treatment of tumor or other brain tumors, intracranial infection, demyelinating lesions or cerebrovascular disease, having no ophthalmological eye disorders found on detailed ophthalmological evaluation, and corrected visual acuity over 8/10 by standard Snellen chart. Demographic data, including age, sex, primary diagnosis, duration of the disease, as well as visual complaints like diminution of vision were all recorded.

Ophthalmology assessment

In this study, exact and detailed ophthalmological examination was done using slit lamp bio-microscopic examination by +90D lens to examine the disk, especially for the band atrophy presence.

Also, documentation was provided with Fundus photography documentation.

Automated perimetry

To conduct standard automated perimetry, 24-2 Swedish Interactive Threshold Algorithm (SITA) on the Humphrey Field Analyzer II instrument (Carl Zeiss Meditec) with a size III stimulus (Goldmann perimetry) on a 31.5 apostilb background was needed. We compared the mean scores of VF defects belonging to the three groups. Then, we analyzed pattern standard deviation (PSD) and mean deviation (MD). Besides, we calculated and analyzed the mean visual sensitivity of the temporal hemifield in 1/Lambert scale due to the fact that visual field loss in chiasmal compression was more significant in the temporal field. Since visual field sensitivity was recorded for each point by means of the decibel (dB) [10 log(1/Lambert)], 1/Lambert scale at each test location was measured by dividing the decibel unit by 10 and then it was unlogged. In this test, each eye of a patient must be fixated on central point separately. Meanwhile, different intense lights will be flashed in the peripheral field of vision. The patient must press a button in order to acknowledge the flashing light. Visual field testing can be unreliable if either the fixation loss is less than 20%, or false positive or false negative errors are less than 15%.

Optical coherence tomography

After pupil dilation, spectral domain OCT (RS 3000 Advance Nidec Co., Japan) performed the RNFL thickness analysis. Images of fundus surface were taken by the confocal laser scanning ophtalmoscope with a near-infrared light source and a wavelength of 785 nm. Retina cross-sectional images were taken by the optical interferometer using an infrared light source and a wavelength of 880 nm. Capture mode of OCT image was on disc circle mode (layer distance 3.45 mm; 1024 scans). In order to have the OCT image, the patient's fundus was scanned circularly around the optic disc in the order ''Temporal", ''Superior", ''Nasal" and ''Inferior", respectively. We have also calculated the average and per quadrant thickness of pRNFL.

Statistical analysis

Statistical analysis was performed using SPSS version 23 software (Statistical Package for the Social Sciences for Windows, Inc., Chicago, Illinois, USA). Continuous variables were presented as mean±standard deviation (SD), and categorical variables were expressed as frequency and percentage. Normality of data was tested with Shapiro-Wilk and Kolmogorov-Smirnov tests. Mann-Whitney U test was used to compare nonparametric values. $P<0.05$ was considered significant.

RESULTS

A total of 55 participants (108 eyes), including 23 subjects in the PAs with visual field involvement (VFI) group, 10 subjects in the PAs with normal visual field (NVF) group, and 22 in the control group, were investigated in this study

TABLE 1. General characteristics of the three groups

Variable		VFI	NVF	Control
Age (mean±SD*) (years)		50.95±9.28	48.10±6.90	51.09±9.31
Sex (female/male)		12/11	5/5	11/11
N (eyes)		44	20	44
Visual field test (mean±SD)	Mean deviation, dB	-11.78±6.13	-0.01±0.59	0.00±0.56
	Pattern standard deviation, dB	9.01±5.69	1.46±0.30	1.47±0.29
	Temporal visual field, 1/L	45.50±218.08	1216.29±242.39	1222.24±228.49
pRNFL thickness (μm) (mean±SD)	Average	66.32±12.81	87.51±3.83	91.01±5.90
	Inferior quadrant	96.68±13.20	120.46±2.81	123.54±5.88
	Superior quadrant	85.34±11.51	109.27±3.88	111.59±7.16
	Nasal quadrant	50.89±9.99	64.99±4.96	69.50±7.13
	Temporal quadrant	46.58±10.62	64.01±6.00	66.22±6.43

*SD=standard deviation

Variable		VFI	Control	P value
Visual field test	Mean deviation, dB	-11.78±6.13	0.00±0.56	<0.001
	Pattern standard deviation, dB	9.01±5.69	1.47±0.29	<0.001
	Temporal visual field, 1/L	45.50±218.08	1222.24±228.49	<0.001
pRNFL thickness (μm)	Average	66.32±12.81	91.01±5.90	<0.001
	Inferior quadrant	96.68±13.20	123.54±5.88	<0.001
	Superior quadrant	85.34±11.51	111.59±7.16	<0.001
	Nasal quadrant	50.89±9.99	69.50±7.13	<0.001
	Temporal quadrant	46.58±10.62	66.22±6.43	<0.001

*Mann-Whitney U test

TABLE 2. Peripapillary RNFL and visual field changes in the VFI and control groups

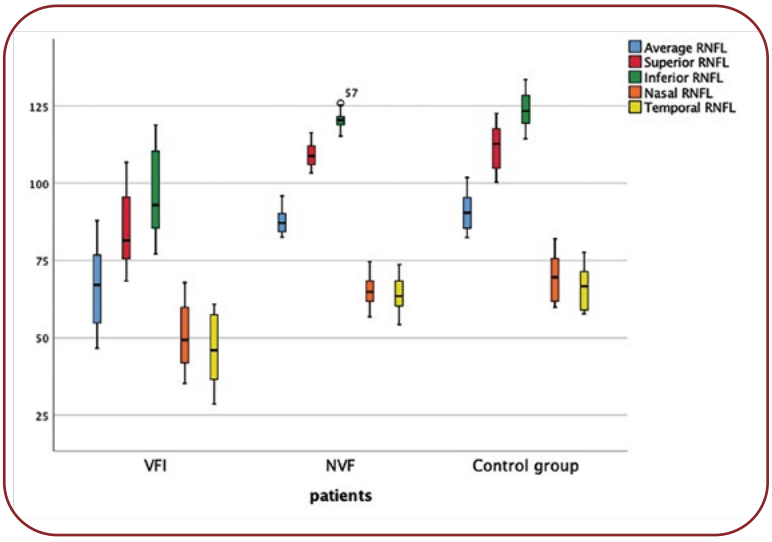

FIGURE 1. Box plot analysis the mean and all quadrants of pRNFL thickness in the three groups

Variable		NVF	Control	P value
Visual field test	Mean deviation, dB	-0.01±0.59	0.00±0.56	0.965
	Pattern standard deviation, dB	1.46±0.30	1.47±0.29	0.862
	Temporal visual field, 1/L	1216.29±242.39	1222.24±228.49	0.685
pRNFL thickness (μm)	Average	87.51±3.83	91.01±5.90	0.028
	Inferior quadrant	120.46±2.81	123.54±5.88	0.041
	Superior quadrant	109.27±3.88	111.59±7.16	0.178
	Nasal quadrant	64.99±4.96	69.50±7.13	0.032
	Temporal quadrant	64.01±6.00	66.22±6.43	0.277

*Mann-Whitney U test

TABLE 3. Peripapillary RNFL and visual field changes in the NVF and control groups

(two patients in the PAs with VFI group had one eye blinded). Age distribution and sex distribution of cases and controls were equal in the three groups (Table 1). Also, the mean thickness of pRNFLwas measured by OCT and visual field tests (Table 1).

Visual field defects

Normal visual field was found in 64 eyes (20 from cases and 44 from controls) (59.2%), while 16 (14.8%) eyes had complete hemianopia, 20 (18.5%) eyes bitemporal hemianopia and eight (7.4%) eyes concentric visual field narrowing.

Variable		NVF	Control	P value
Visual field test	Mean deviation, dB	-0.01±0.59	0.00±0.56	0.965
	Pattern standard deviation, dB	1.46±0.30	1.47±0.29	0.862
	Temporal visual field, 1/L	1216.29±242.39	1222.24±228.49	0.685
pRNFL thickness (μm)	Average	87.51±3.83	91.01±5.90	0.028
	Inferior quadrant	120.46±2.81	123.54±5.88	0.041
	Superior quadrant	109.27±3.88	111.59±7.16	0.178
	Nasal quadrant	64.99±4.96	69.50±7.13	0.032
	Temporal quadrant	64.01±6.00	66.22±6.43	0.277

*Mann-Whitney U test

TABLE 4. Peripapillary RNFL and visual field changes in the NVF and VFI groups

Comparison of pRNFL thickness in different groups

Box plot charts showed that the mean and all quadrants of pRNFL thickness in the VFI group were significantly thinner than the corresponding pRNFL thickness in the remaining groups (Figure 1). As shown in Table 2, the mean and all four quadrants pRNFL thickness around the optic disc in the PAs with visual field involvement (VFI) group significantly decreased compared with the normal controls ($P<0.001$). In the PAs with normal visual field (NVF) group, the pRNFL thickness in the inferior and nasal quadrants and the mean value were significantly thinner than the normal controls, as shown in Table 3 ($P<0.05$). Also, the pRNFLin the PAs with visual field involvement (VFI) group were significantly decreased compared with the PAs with the normal visual field (NVF) group ($P<0.001$) (Table 4).

DISCUSSION

Pituitary adenomas cause compression of the optic chiasm, leading to compromised visual function. Visual field defect is the most important neuro-ophthalmological finding in the pituitary tumors (50–96%). Bitemporal hemianopia is the result of the classic abnormal perimetry caused by the tumor growth. Meanwhile, the cross nasal fibers in the chiasm are compressed by the growth of the tumor (20-22, 25). However, tumor size, location and/or growth direction do not affect 30% of patients in terms of visual field abnormalities (21, 23, 24, 26). In addition, visual field defects cannot be caused by a short duration or the slight compression of the optic chiasm. Such defects occur when at least 30-50% of retinal ganglion cells (RGCs) are affected (24, 25). Peripapillary retinal nerve fiber layer (pRNFL) thickness has been proposed as a structural marker of axonal loss in the optic nerve. If the optic nerve or the optic tract in the brain is damaged, retrograde degeneration appears in pRNFL (10). Degeneration of optic nerve fibers happens due to RNFL thinning (10).

A horizontal band across the disc known as bowtie or band atrophy (BA) is occupied by the optic atrophy (27). According to recent studies, the mean values related to the RNFL of eyes with BA cloud be distinguished by OCT from those of normal controls in the two groups of patients (3, 16). Some studies indicate that RNFL loss in eyes with band atrophy of optic nerve, which occurs as a result of chiasmal compression, can be identified by OCT (10, 15-17, 28). In this research, the high-speed high accuracy FD-OCT determined the pRNFL thickness in both groups of patients with PAs and control subjects. This study showed a decreasing trend of RNFL thickness in all four quadrants in the VFI group in comparison with normal controls ($p<0.001$) (Table 2). Also, Moon CH et al reported that preoperative measurements of RNFL thickness in PA patients were considerably decreased in comparison with control group, which was consistent with our findings. Another research, conducted by Kanamori A, demonstrated that RNFL thickness measurements around the optic dis, done by OCT, showed characteristic RNFL loss in eyes with band atrophy (16, 29). Furthermore, we studied and checked the RNFL thickness in the superior, nasal, inferior and temporal quadrants and VF changes. Based on this study, considerable reduced RNFL thickness was observed in all quadrants in patients with VF defects (complete bitemporal hemianopia and concentric narrowing) in comparison with the PA

patients having normal visual field ($p<0.001$) (Table 4). Cennamo and Auriemma reported that OCT may have a role in the early diagnosis and management of patients with pituitary tumours (30).

The strength of our study was represented by a significant difference in some parts of pRNFL thickness (mean, nasal, inferior) in patients who had PA with normal visual field in comparison with the control group ($p<.05$) (Table 3). This proved that the optic nerve was involved too soon, which was missed by slit lamp examination but was sooner observed and diagnosed using OCT. This is the first report on RNFL thickness in patients with normal visual field compared with normal group decreased by OCT.

CONCLUSION

The present study shows that, when a patient has band atrophy there is an irreversible damage, and the main goal is to diagnose a nerve damage using OCT before band atrophy. When OCT shows a decrease in RNFL thickness, this must be considered an alarm sign without disorder in visual field or visual acuity. Neurosurgeons should classify such disorders as "neurology deficit" and rather take action to treat the patients instead of just waiting to observe changes in visual field or band atrophy in funduscopic exam. ❑

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