Evaluation of retinal nerve fiber layer thickness in patients of pituitary adenomas with and without optic chiasmal compression

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Research article

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Abstract

Background: Numerous studies have demonstrated loss of circumpapillary retinal nerve fiber layer (cpRNFL) thickness in patients with chiasmal compression using optical coherence tomography (OCT). This study aimed to evaluate the cpRNFL and ganglion cell compound (GCC) thicknesses in patients suffering pituitary tumors with and without chiasmal compression.

Methods: forty-four patients with pituitary adenoma (PA) (twenty-one without chiasmal compression and twenty-three with chiasmal compression) and eighteen controls were enrolled. cpRNFL and GCC thickness were measured in both patients and controls by SD-OCT.

Results: three groups (PAs with optic chiasmal compression, PAs without optic chiasmal compression and controls) were closely matched in terms of mean age, sex and IOP (p=0.173, p=0.184 and P=0.343, respectively). The average cpRNFL and GCC thickness was significantly different among three groups (cpRNFL : 94.1±12.5μm, 106.4±7.3μm, 110.7±6.9μm, respectively; GCC: 85.8±6.9μm, 93.8±5.0μm, 97.2±5.6μm, respectively). The cpRNFL was analyzed in different regions, and significant difference was found in nasal upper and nasal lower between PAs without optic chiasmal compression and controls.

Conclusion: Even there is no evidence of compression at the chiasm on magnetic resonance imaging (MRI), GCC and cpRNFL thinning could still be detected in patients of pituitary tumor by SD-OCT. The loss of RNFL is more severe in patients with chiasmal compression.

Backgrounds

Pituitary adenoma (PA) is an intracranial tumor with an estimated prevalence of 16.7%[1] and the cause of approximately 25% of all surgical resections for CNS tumors[2–4]. Visual impairment is the most common complaint, with visual loss occurring in 32–70% of patients[5]. Typical neuro-ophthalmic features include progressive bilateral slow and asymmetric deterioration in visual field defects and optic disc changes. Damage to the optic chiasm, changes in the retinal nerve fiber layer (RNFL) and the deterioration of visual function are closely related. RNFL has gradually become an area of research focus in patients suffering PA. Spectral domain Optical coherence tomography (SD-OCT) demonstrates the ability to acquire cross-sectional imaging of the retinal layers noninvasively with high resolution. It has been applied to analyze changes in the thickness of retina layers caused by pituitary adenoma. Visual function and the thickness of retinal layer are closely related[6,7]. Loss of RNFL thickness in patients with chiasmal compression can be identified by OCT [8–10]. With our growing understanding of the relationship between pituitary tumors and optic chiasm, we found that the impairment was not only caused by direct compression to the optic chiasm but also might be caused by disturbances in blood flow of the optic chiasm. Whether pituitary tumors without optic chiasm compression may cause damage in circumpapillary RNFL (cpRNFL) is unknown. We performed this study to measure the thickness of cpRNFL and ganglion cell compound (GCC) by OCT in patients suffering pituitary tumors with and without chiasmal compression.

Methods

This was a cross-sectional study. The procedures followed the tenets of the Declaration of Helsinki, and all participants signed a written informed consent. Patients with PA confirmed by pituitary magnetic resonance imaging (MRI) and postoperative histological findings in Beijing Tiantan Hospital between March 2017 and September 2017 were consecutively selected for this study. A few days before surgery, all participants underwent a thorough ophthalmological examination which included best-corrected visual acuity, intraocular pressure (IOP) measurements, slit lamp biomicroscopy, fundus photography, perimetry (Octopus) and OCT scanning. All subjects were more than 18 years old. Whether there was a chiasm impingement was clearly proved by pituitary MRI. Exclusion criteria for the study were: any previous cranial or ocular surgery; IOP higher than 21mmHg; high myopia (more than –6.0 D); relevant ophthalmic diseases like macular disease or glaucoma.

Fourier-domain optical coherence tomography (FD-OCT)

A commercially available RTVue–100 (Optovue Inc., Fremont, CA, USA)) was used to measure the RNFL and GCC thickness. The ONH protocol was used to obtain cpRNFL measurements, which were taken along a combination of radial and circular scans centered on the optic nerve head. The cpRNFL measurement was generated from a 3.45 mm circle around the ONH. Thickness data was calculated automatically after optic disc was outlined manually. cp RNFL was divided into 8 sectors: superio-nasal (SN); nasal upper (NU); nasal lower (NL); infero-nasal (IN); infero-temporal (IT); temporal lower (TL); temporal upper (TU); and ST (supero-temporal). GCC protocol was used to obtain GCC measurements, which consisted of 14 928 A-scans over a 6-mm-diameter area in the center of macula. GCC thickness was calculated as the distance between the internal limiting membrane and the outer edge of the inner plexiform layer. Average, superior, and inferior GCC thicknesses were calculated. OCT scans were performed by an experienced examiner who was masked from all the patient data. Images with a scan score index (SSI) of less than 30 were excluded.

Values are expressed as the mean ± standard deviation. Normality of the data was assessed with the Kolmogorov-Smirnoff test. One-way analysis of variance test was used to compare parameters among PAs with and without optic chiasmal compression and normal controls. A p value of less than 0.05 was considered statistically significant. SPSS version 23.0 (SPSS Inc., Chicago, IL) was used for statistical analysis.

Results

A total of 88 eyes of 44 patients with PA and 36 normal eyes of 18 controls were enrolled. Of the patients with PA, 23 patients showed optic chiasmal compression on MRI and 21 patients did not show optic chiasmal compression on MRI.

The PAs with optic chiasmal compression, PAs without optic chiasmal compression and control groups were closely matched in terms of mean age, sex and IOP ($p = 0.173$, $p = 0.184$ and $P = 0.343$,

respectively). The demographic and clinical characteristics are shown in table 1.

There is significant difference in average GCC and average cpRNFL between PAs with and without optic chiasmal compression. Average GCC and average cpRNFL are significantly lower in PAs with and without optic chiasmal compression than in control groups (table 2).

Table 3 shows cpRNFL thickness in different regions. The cpRNFL thickness of PAs with optic chiasmal compression lowers in every region when compared to controls. There is significant difference in NU and NL between PAs without optic chiasmal compression and controls.

The RNFL profiles of PAs eyes and control are plotted and shown in figure 1. Double hump patterns in the RNFL thickness profiles was demonstrated by SD-OCT. In these three groups, the peaks were located at the superotemporal (ST) and the inferotemporal (IT) regions, and the troughs were located at the nasal (NU+NL) and temporal (TU+TL) regions.

Discussion

A number of studies have researched the cpRNFL and GCC thickness of patients with pituitary adenomas and cpRNFL and GCC thinning was confirmed in those with chiasmal compression. Blanch et al.'s study[11] found a statistically significant decrease in GCC thickness in patients with early chiasmal compression before visual defects became apparent. Likewise, Beltrame et al. evaluated patients with pituitary macroadenomas with optic pathway compression. They found the thinner the RNFL was, the worse the visual acuity and visual field were[12]. In another two studies, authors reported a remarkable decrease in patients with chiasmal compression, and their results indicate that vision prognosis after surgical decompression of pituitary tumors could be predicted by preoperative RNFL. Patients with normal RNFL thickness show an increased probability for visual recovery[13,14].

In our study, we also found statistically significant decrease in cpRNFL and GCC thickness in patients with chiasmal compression when compared with controls. The decrease in cpRNFL was significant in all the sectors. It was in agreement with other studies [8–10].Meanwhile, there was statistically significant difference in cpRNFL and GCC thickness between patients with and without chiasmal compression. It revealed that the damage to the retinal ganglion cell was more severe in patients with chiasmal compression than patients without chiasmal compression. Glebauskiene B et al[15]. found significant RNFL thinning only in temporal quadrant in PA patients with suprasellar extension compared with the patients without suprasellar extension. In our study the cpRNFL reduction was significant in all sectors except for IN. We consider it to be because that the definition of PA without chiasmal compression was different from PAs without suprasellar extension. The different division of the cpRNFL region might be one of other reasons.

Meanwhile, cpRNFL and GCC thinning were found in PA patients without chiasmal compression. In addition, the present study demonstrated that the cpRNFL loss was particularly severe in NU and NL

sectors of optic nerve in patients without chiasmal compression, which was different in glaucoma: the inferotemporal and superotemporal RNFL thickness loss was more frequently found in glaucomatous eyes[16]. Our finding was not in agreement with the opinion that only chiasmal compression would cause visual pathway impairment. Our results were compatible with a prospective study carried out by Cennamo et al[17]. They found that up to 58% of patients suffering PA without chiasmal compression had GCC and cpRNFL loss, although their visual field and visual acuity was normal. In another study early impairment of visual pathway caused by PA without chiasmal compression in MRI was also detected by electrophysiological examination[18]. These tests can reveal abnormalities of a more widespread and insidious lesion of the visual pathway than expected based on tumor size and position.

The mechanism for cpRNFL and GCC impairment produced by PA is unclear. Most people attribute it to direct compression to visual pathway, which will cause axoplasmic flow disorder, conduction blockage, demyelinization and axonal fiber degeneration.[19–20] In our study we indeed found that damage to the retinal ganglion cell was more severe in patients with chiasmal compression than patients without chiasmal compression. In addition, there is another hypothesis been proposed as ischemic[21] damage of crossing nasal retinal fibers directly or indirectly. It was proven that distortion of vessels could be caused directly by tumors larger than 1 mm[22]. Intrasellar hypertension could also appeared because of an invasion by a space occupying lesion, which might lead to blockage of blood flow in optic chiasma[23]. Cennamo et al[17] postulated that the pituitary gland was secreting a vasoactive peptide that was causing ischemia and axonplasmic flow disorder. Other possibilities of the visual pathway abnormalities are changes in metabolites, trophic factors, or proteases associated with developing neoplasm in the immediate microenvironment[24,25]

There were some limitations in the present study. First, compression was defined as displacement of visual chiasm in contact with the tumor on MRI imaging. However, optic chiasm might be compressed by surrounding tissue when the tumor expanded, which was indirect and was not measurable. Second, due to the limited number of cases, we included both eyes of subjects, which might cause some bias in statistical analysis.

Conclusion

In conclusion, the presence of a pituitary adenoma, even in the absence of compression at the optic chiasm on MRI, may cause cpRNFL and GCC thinning, although the loss of RNFL is more severe in patients with chiasmal compression. SD-OCT can be used for early detection of chiasmal dysfunction, which could facilitate timely treatment of the condition and to prevent irreversible vision loss.

Abbreviations

cpRNFL: circumpapillary retinal nerve fiber layer

OCT: optical coherence tomography

GCC: ganglion cell compound

SD-OCT: spectral domain optical coherence tomography

PA: pituitary adenoma

MRI: magnetic resonance imaging

CNS: central nervous system

IOP: intraocular pressure

SSI: scan score index

Declarations

Ethics approval and consent to participate

The study protocol was reviewed and approved by the Ethics Committee of Ethics Committee of Tiantan Hospital of the Capital Medical University. Written informed consent was obtained from all participants prior to study enrolment.

Consent for publication

Not applicable

Availability of data and material

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

KL was responsible for the acquisition, analysis, interpretation of data and was a major contributor in writing the manuscript. LW, MW and SW participated in acquisition of data and revising it critically for important intellectual content. YQ's contribution was concept and design. All authors read and approved the final manuscript.

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Tables

Table 1 Characteristics of the study population

	PAs with optic chiasmal compression	PAs without optic chiasmal compression	Control	P-value
Participants, n	23	21	18	
Eyes, n	46	42	36	
Age, years	48.8±10.3	42.3±12.3	47.5±13.0	0.173
Female, n	12	15	14	0.184
IOP, mmHg	14.6	14.8	14.1	0.343

Table 2 GCC thickness and cpRNFL thickness in three groups (A: PAs with optic chiasmal compression; B: PAs without optic chiasmal compression; C: Control)

	PAs with optic chiasmal compression (A) (mean±SD)	PAs without optic chiasmal compression (B)	Control (C)	P (A vs B)	P (A vs C)	P (B vs C)
Average cpRNFL (μm)	94.1±12.5	106.4±7.3	110.7±6.9	<0.001	<0.001	0.049
Superior cpRNFL (μm)	96.6±12.5	109.8±8.6	113.8±8.4	<0.001	<0.001	0.093
Inferior cpRNFL (μm)	91.7±14.2	102.9±8.9	107.6±9.6	<0.001	<0.001	0.076
Average GCC (μm)	85.8±6.9	93.8±5.0	97.2±5.6	<0.001	<0.001	0.012
Superior GCC (μm)	85.5±7.8	94.5±5.3	97.3±5.9	<0.001	<0.001	0.064
Inferior GCC (μm)	86.2±6.8	93.0±5.1	97.2±5.7	<0.001	<0.001	0.003

Table 3 Eight regional RNFL thickness in in three groups (A: PAs with optic chiasmal compression; B: PAs without optic chiasmal compression; C: Control)

	PAs with optic chiasmal compression (A)	PAs without optic chiasmal compression (B)	Control (C)	P (A vs B)	P (A vs C)	P (B vs C)
SN (µm)	110.8±24.1	127.0±22.7	130.7±21.3	0.001	<0.001	0.480
NU (µm)	73.8±15.2	79.4±12.1	89.8±10.9	0.051	<0.001	0.001
NL (µm)	63.2±13.4	69.7±10.2	76.3±7.0	0.006	<0.001	0.009
IN (µm)	101.3±26.0	109.3±22.1	146.4±173.6	0.703	0.038	0.096
IT (µm)	128.0±21.8	146.2±15.4	151.3±20.1	<0.001	<0.001	0.258
TL (µm)	74.4±15.4	86.6±13.9	84.4±11.1	<0.001	0.001	0.496
TU (µm)	75.4±14.5	88.0±15.2	88.5±14.2	<0.001	<0.001	0.877
ST (µm)	126.4±22.1	145.0±16.2	146.2±18.1	<0.001	<0.001	0.773

superio-nasal (SN); nasal upper (NU); nasal lower (NL); infero-nasal (IN); infero-temporal (IT); temporal lower (TL); temporal upper (TU); ST (supero-temporal)

Figures

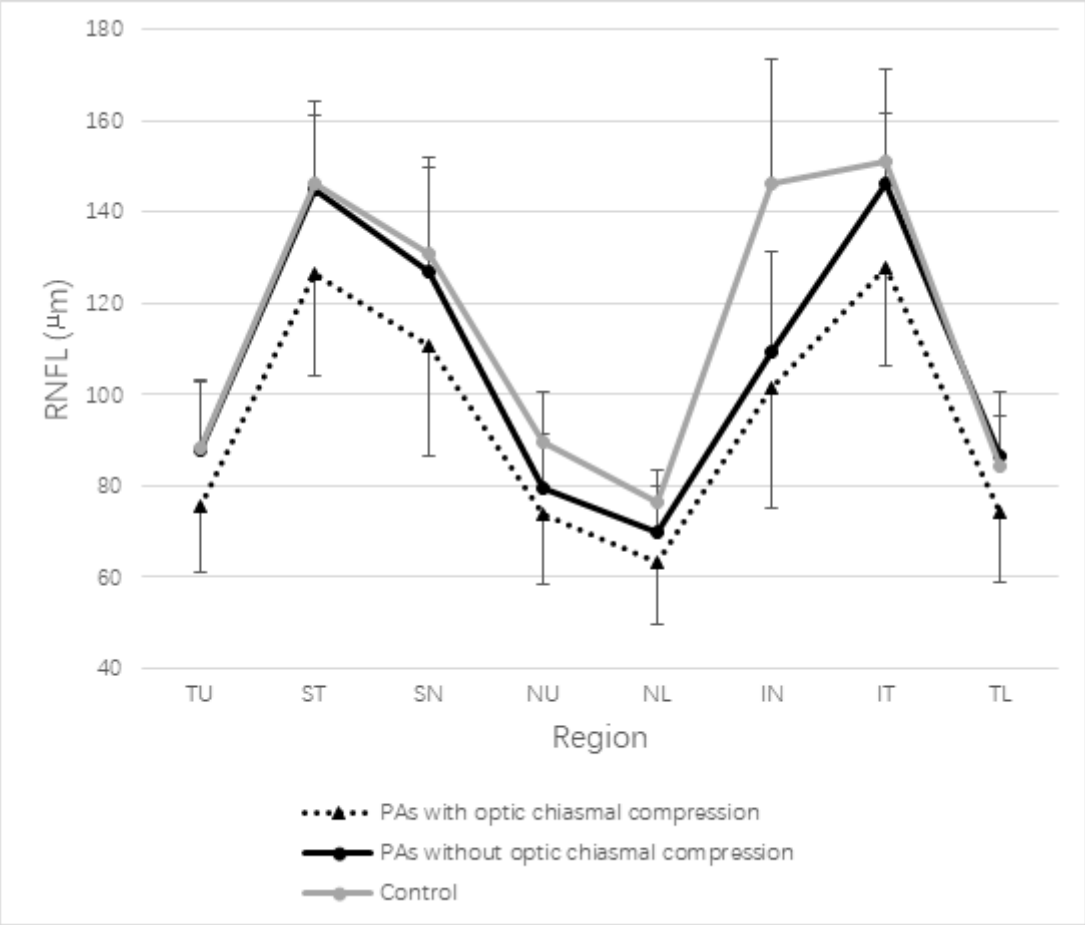

Figure 1

cpRNFL thickness profile of PAs with and without optic chiasmal compression and normal.