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Review article

Association of retinal nerve fibre layer thickness with quantitative magnetic resonance imaging data of the optic chiasm in pituitary adenoma patients

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ABSTRACT

To evaluate retinal nerve fibre layer (RNFL) thickness in patients with pituitary adenoma (PA) by optical coherence tomography and to compare it with magnetic resonance imaging (MRI) characteristics of pituitary extension.

154 eyes of 77 patients with PA were evaluated. Ophthalmologic evaluation was performed before surgical treatment. Average and per quadrant thickness of peripapillary RNFL (internal limiting membrane to nerve fiber layer/ganglion cell layer) were calculated. Optical coherence tomography was performed in a disc circle mode (layer distance 3.45 mm; 1024 scans). PA was confirmed by MRI scans. Characteristics of the optic chiasm in relation to the suprasellar adenoma were assessed.

Suprasellar extension of PA was diagnosed in 55 patients (71.4%). The optic chiasm thickness differed significantly in the groups with and without suprasellar PA extension ($p < .001$). A weak positive correlation was found between the height of the optic chiasm right side, middle part, left side and visual acuity ($r = 0.349$; 0.276; 0.307) ($p < .001$). RNFL thickness around the optic nerve disc measured preoperatively was reduced significantly in all four quadrants in PA patients compared with the control group ($p < .001$). RNFL thickness was reduced significantly only in the temporal quadrant in PA patients with suprasellar extension compared with the patients without suprasellar extension ($p = .009$). The temporal RNFL thickness showed the strongest positive correlation with the distance between optic chiasm and PA ($r = 0.401$, $p < .001$), while the superior, nasal and, inferior RNFL quadrants showed a weak ($r = 0.079$; 0.074; 0.113) or not significant ($r = 0.351$; 0.380; 0.180) correlation with the distance between the optic chiasm and PA. The chiasmal right side, middle part, left side heights correlated significantly with RNFL thickness in all quadrants ($p < .05$).

Our results indicate that suprasellar extension in PA patients causes visual disturbances.

1. Introduction

Pituitary adenoma (PA) is an intracranial tumor arising from the anterior pituitary with the reported prevalence rate of 16.7% [1]. The pituitary gland is located in a dural bag attached to the inferior aspect of the diaphragm of the sella and surrounded by venous spaces that correspond laterally to the cavernous sinuses [2]. PAs can easily expand laterally, because the medial wall of the cavernous sinus is a lateral part of the thin dural bag [2,3], so 6–10% of PAs can involve the cavernous sinus [4,5]. It is important to evaluate tumor's invasiveness, because it can influence management and prognosis of PA [6]. The optic chiasm is directly above the pituitary gland; and when the tumor grows beyond the sella, it frequently causes visual disturbances, such as decrease of visual acuity (VA) or visual field (VF) defects, due to chiasmal compression [7–14]. Thus, PA can be the cause of retinal nerve fibre layer (RNFL) thinning, which reflects axonal degeneration caused by compression of the anterior visual pathways, and can be objectively evaluated by optical coherence tomography (OCT) by quantifying RNFL thickness [15–20].

In our study, we investigated the association between the quadrant VA, VF, RNFL changes and chiasmal compression caused by PA.

To our knowledge, there are no studies that have explored the relationship among peripapillary RNFL thickness in the temporal,

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superior, nasal, inferior quadrants and the optic chiasm height, or correlation between RNFL thickness and the distance between the optic chiasm and PA.

2. Materials and methods

Permission (Number P2-9/2003) to undertake the study was obtained from the Biomedical Research Ethics Committee. The study was conducted in the Ophthalmology and Neurosurgery Departments of the Hospital of Lithuanian University of Health Sciences.

The subjects of this study were 77 cases of PA. The inclusion criteria were as follows: 1) determined and confirmed PA via MRI; 2) patient's general good condition; 3) patient's consent to take part in the study; 4) age $\geq$ 18 years; 5) no other brain tumors, intracranial infection, demyelinating lesions or cerebrovascular disease; 6) no ophthalmological eye disorders found on detailed ophthalmological evaluation.

Non-corrected and best-corrected visual acuity (VA) (measured in decimals from 0.1 to 1.0) were evaluated using Landolt rings (C optotypes) by Snellen test types at a 5 m distance from the chart. Intraocular pressure measurement, biomicroscopy and fundoscopy were performed in order to assess corneal and lenticular transparency and to evaluate the eye fundus. The subjects' pupils were dilated with 1% of tropicamide. Standard automated perimetry was conducted using a visual field analyzer (Humphrey Field Analyser, Model 745i, Carl Zeiss Meditec Inc. Dublin, CA, USA). The visual field test routinely assesses only the central 24–30 degrees, however, we performed Full Field Screening (135 points, 87 degrees temporally). In this test, the patient needs to fixate on a central point with each eye separately, while lights of various intensity are flashing in the peripheral field of vision. The patient has to acknowledge the flashing light by pressing a button. VF testing was considered unreliable if the fixation losses, false negative or false positive errors exceeded 20%.

3. Optical coherence tomography

RNFL thickness was analyzed with spectral domain OCT (*RS 3000 Advance Nidec Co*., Japan) after pupil dilation. Fundus surface images were captured with the confocal laser scanning ophtalmoscope using a near-infrared light source with a wavelength of 785 nm. Cross-sectional images of the retina were captured with the optical interferometer using an infrared light source with a wavelength of 880 nm. OCT image capture mode was a disc circle mode (layer distance 3.45 mm; 1024 scans): the patient's fundus was scanned circularly around the optic disc in the order "Temporal", "Superior", "Nasal", and "Inferior" to obtain OCT image. An average and per quadrant thickness of peripapillary RNFL were calculated as an internal limiting membrane (ILM) to the nerve fibre layer (NFL)/ganglion cell layer (GCL).

3.1. Brain imaging

All pituitary adenomas were analyzed based on MR imaging findings. The preoperative MRI investigations were performed with 1.5 T MRI scanners (*Siemens MAGNETOM Avanto*, 1.5 T *Philips ACHIEVA*) using a head coil and a standard pituitary scanning protocol, obtaining T1W sagittal and coronal and T2W/TSE coronal pre-contrast images, and T1W coronal and sagittal *Gadolinium-enhanced* MR images with the intravenous agent gadodiamide (*Omniscan, GE Healthcare*). The restrospective analysis of MRI data was conducted by an experienced radiologist. The coronal T2W/TSE sequence was chosen as a standard for the best optic chiasm resolution.

The optic chiasm thickness values were obtained by measuring the vertical diameter on the right side, left side and the middle part. The deformations or signal changes of the optic chiasm were evaluated and documented. The distance between the superior margin of the tumor and the inferior surface of the optic chiasm was measured as well.

The suprasellar extension and sphenoid sinus invasions by PA were classified according to the Hardy classification, modified by Wilson [6]. The degree of suprasellar and parasellar extension was graded as stages A–E.

3.2. Suprasellar extension

A: PA expanding into the suprasellar cistern
B: anterior recesses of the third ventricle obliterated
C: the floor of the third ventricle grossly displaced

3.3. Parasellar extension

D: an intracranial extension into the anterior, middle, or posterior fossa (intradural)
E: an intracranial extension into or beneath the cavernous sinus (extradural)

The degree of the sellar floor erosion was graded as grades I–IV. Grades I-II mean that the sellar floor is intact and are considered as non-invasive PA, grade III shows localized sellar perforation and grade IV shows diffuse destruction of the sellar floor, which are the signs of invasive PA.

The Knosp classification system was used to quantify invasion of the cavernous sinus: grade 0, no involvement of the cavernous sinus, represents the normal condition; grades 1 and 2, the tumor pushes into the medial wall of the cavernous sinus, but does not go beyond a hypothetical line extending between the centers of the two segments of the internal carotid artery (grade 1) or it goes beyond such a line, but without passing a line tangent to the lateral margins of the artery itself (grade 2); grade 3, the tumor extends laterally to the internal carotid artery within the cavernous sinus; grade 4, total encasement of the intracavernous carotid artery. According to the Knosp classification, only grade 3 and 4 pituitary tumors were considered to be invasive [21].

3.4. Statistical analysis

Statistical analysis was performed using the SPSS/W 23.0 software (Statistical Package for the Social Sciences for Windows, Inc., Chicago, Illinois, USA). Spearman's correlation was conducted to evaluate the relationships between RNFL quadrants thickness and the distance between the optic chiasm and adenoma, the optic chiasm height and visual acuity, RNFL quadrants thickness and the optic chiasm height. Normality of the distribution was tested with Shapiro-Wilk and Kolmogorov-Smirnov tests. Mann-Whitney *U* test was conducted to compare non parametric values. Differences were considered statistically significant when $p < .05$.

4. Results

Seventy-seven patients (154 eyes) diagnosed with pituitary adenoma by MRI were examined.

4.1. PA characteristics

Fourty six patients (59.7%) were diagnosed with invasive PA and 31 patients (40.3%) with noninvasive PA. Recurrant PA was found in 12 patients (15.6%).

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