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Opinion paper

Comparison of optical coherence tomography findings and visual field changes in patients with primary open-angle glaucoma and amyotrophic lateral sclerosis

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ABSTRACT

Recent studies revealing genetic connection of primary open angle glaucoma (POAG) and amyotrophic lateral sclerosis (ALS) have received particular attention. Exploring the evidence for common pathogenesis of these two progressive neurological disorders may assist in understanding the mechanism and searching for new treatment. Retinal nerve fiber layer (RNFL) defect and corresponding visual field (VF) impairment are well known neuropathy signs in glaucoma. In our study, thickness of certain retinal layer in ALS patients was analyzed to detect ganglion cell's soma and axon, and for first time visual field was examined for ALS. The correlation of retinal involvement and ALS progression were also investigated. The results were compared with those of POAG. The study may provide new knowledge for these two neurodegenerative diseases.

1. Introduction

Primary open-angle glaucoma (POAG) is characterized by slow and progressive degeneration of retinal ganglion cells (RGCs) that lead to retinal nerve fiber layer (RNFL) defect and visual function loss. Other than elevated intraocular pressure, multiple factors like genetic variations and environmental impacts are also considered to contribute to POAG's progression. POAG is regarded as a neurodegenerative disease and has been demonstrated to share some pathological features with other degenerative neurological disorders from central nervous system such as Parkinson disease and Alzheimer's disease [1,2].

Amyotrophic lateral sclerosis (ALS) is an untreatable, relentlessly progressive degenerative disorder of motor neurons in brain and spinal cord [3]. Since the mutations of two POAG-causative genes optineurin (OPTN) and TANK binding protein 1 (TBK 1) have been found to be associated with ALS pathogenesis [4–7], researchers tend to merge these two phenotypically distinct neuronal diseases into one common pathological mechanism [8–11].

Previous researches in ALS have suggested a more widespread pathology comprising non-motor alterations including corneal small fiber neuropathy and insufficient regeneration in peripheral sensory nerve fibers [12,13]. Involvements of the visual pathway and the retina which is known to be affected in glaucoma have also been reported. However, the results are heterogeneous [14–17]. Hubers and colleagues found significant thinning of the inner nuclear layer and the RNFL in ALS patients [18]; while Roth did not find any significant retinal variations in ALS patients [19].

Thickness changes of selective retinal layers are considered to be a reflection of the underlying neurodegenerative processes. Optical coherence tomography (OCT) is an imaging technique allowing in vivo observation of subtle retinal morphological variations as well as thickness measurement. It has been widely used to estimate the severity of optic neuropathy for POAG patients as well as to trace progression.

Here we analyzed ALS patients with OCT examinations and visual field tests, and compared those findings with POAG and healthy controls. We intended to provide new knowledge for the understanding of those two neurodegenerative diseases and their underlying mechanisms.

2. Methods

All patients were recruited at Peking University Third Hospital of Beijing, China, in a prospective manner from December 2016 to February 2017. Neurological assessments and eye examinations

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were obtained from 51 patients with clinically definite ALS and 26 age-matched POAG patients and 126 healthy individuals. Informed consent for the research was obtained from all participants. The study was approved by the Ethical Committee of Peking University Third hospital and was conducted in accordance with the Declaration of Helsinki.

2.1. ALS patients

ALS was diagnosed by board-certified neurologists specialized in motor neuron disease. ALS patients were receiving regular medicine treatment. Patients with coexisting neurodegenerative disorders or an ocular disease likely to demonstrate OCT changes (such as retinopathy and optic diseases), and patients who were unable to cooperate for ophthalmologic examinations were all excluded from the study. Severity of ALS was evaluated with ALS functional rating scores (ALSFRS), and sympathetic skin response (SSR) was also recorded to evaluate their sympathetic fibers function.

2.2. POAG patients

Subjects in POAG group were selected from Glaucoma clinic who were under medical treatment with regulated intraocular pressure (IOP) measurements (less than 20 mmHg). They were also screened to exclude central neurologic disorders and ocular diseases other than glaucoma that may affect OCT results.

2.3. Control group

The healthy control group was composed of people who applied for routine eye examinations. Patients who had ophthalmic pathologies other than refractive errors and those who had central neurological disorders were excluded.

IOP of all patients was measured using the Goldmann applanation tonometer. Central corneal thickness (CCT) measurements were done by Pentacam HR (Oculus, Wetzlar, Germany).

OCT (Zeiss Cirrus HD-OCT, Model 4000, Carl Zeiss Meditec, Inc.) scans were performed and peripapillary RNFL, macular thickness and ganglion cell layer plus inner plexiform layer (GCL + IPL) were measured in all cases. Optic nerve head was scanned to determine the RNFL thickness map. The temporal, superior, nasal and inferior quadrants of RNFL as well as the average thickness measurements were analyzed. Macular thickness was investigated for superior, inferior, temporal, and nasal quadrants in inner (3 mm diameter) and outer (6 mm diameter) regions as well as the central area (1 mm diameter). Results of GCL + IPL were also acquired.

Visual field (Octopus 900, HAAG-STREIT international) was examined for all participants and data of mean defect (MD), mean sensibility (MS) and square of loss variance (sLV) were obtained. Corrected vision acuity was examined before visual field test.

Statistical analysis was carried out using SPSS (Statistical Package for Social Sciences) Windows version 16.0. Data were presented as mean ± SD. The RNFL thickness, macular thickness, GCL + IPL thickness, and visual field indices were compared between the three groups using independent-samples *T* Test. The correlation of retinal structural changes with disease duration, severity and sympathetic function in ALS patients were evaluated using Pearson correlation coefficient and Spearman correlation. The p value less than .05 was considered significant.

3. Results

Detailed clinical characteristics and demographic features of all participants are summarized in Table 1. No statistically significant difference was revealed between the three groups regarding mean age and gender distribution ($p > .05$). The average duration of disease was 18.46 ± 6.16 months (6–72 mo) in patients with ALS, and their average ALSFRS was39.58 ± 10.41 (range, 10–48). The abnormal SSR cases in ALS group took up about 35.3%. The intraocular pressure (IOP) of all ALS was within normal limit. The central corneal thickness (CCT) measurements of ALS showed no significant difference from normal controls ($P > .05$).

3.1. RNFL

The peripapillary RNFL of glaucoma group was significantly thinner than in the ALS and control group. No significant RNFL thickness decrease was found in ALS patients compared with controls. The nasal quadrant of ALS peripapillary RNFL even had a statistically thicker measurement than the normal (Table 2).

3.2. Macular thickness and GCL-IPL

The average GCL-IPL thickness was statistically thinner in glaucoma's than in the ALS ($P < .05$). No significant difference was identified between the ALS and the controls.

Macular thickness in any region (inner, outer or central) and in any quadrants (superior, inferior, temporal and nasal) showed no significant difference between ALS and the healthy control though ALS had a slight decrease. POAG had thinner macular measurement than ALS, but their central macular thickness were of no significant difference (Table 3).

3.3. Visual fields

The ALS and the controls had similar MD ($p = .557$). The POAG's MD was significantly higher than the other two groups ($p = .001$ for POAG vs. ALS; $p = .002$ for POAG vs. normal). The MS and sLV in ALS were of no significant difference compared with POAG ($p = .841$ for MS and $p = .278$ for sLV), and both ALS and POAG had much lower results than the controls (MS: $p = .000$ for ALS vs. normal, $p = .005$

Table 1
The demographics and clinical features.

	ALS	POAG	Controls	p
Number	51	26	126	–
Male sex-no. (%)	25(49)	14(54)	68(54)	0.830
Age (years)[a]	55.04 ± 12.52	49.31 ± 17.96	54.24 ± 14.68	0.234
Disease duration (months)	18.46 ± 6.16 (6–72)	–	–	–
ALSFRS	39.58 ± 10.41 (10–48)	–	–	–
SSR Percentage of abnormal cases(%)	35.3	–	–	–
CCT (um)[b]	536.05 ± 32.07	–	537.93 ± 25.47	0.802

Data are shown as mean ± SD. $p < .05$ was statistically significant. ALSFRS, ALS Functional Rating Scores. SSR, sympathetic skin response. CCT, Central Corneal Thickness.
[a] ANOVA test.
[b] *t*-Test.

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