

Retinal Ganglion Cell Layer Thinning Followed By Retinal Nerve Fiber Layer Thinning In Patients with Uveitis

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Abstract

In the model of experimentally induced ischemia- reperfusion injury, retinal ganglion cells (RGC) expressing the gene AP-1 result apoptosis. The inflammation mediators, such as TNF- α , IL-1 β , etc. lead RGC to apoptosis, that may lead the thinning of the retinal ganglion cell layer (RGCL) followed by the optic nerve fiber layer (RNFL) thinning. In his study we observed retinal ganglion cell and optic nerve fiber layer thinning in patients with various uveitis, that the pathological features appear obliterative vasculitis, using the optical coherence tomography (OCT) imaging analyses.

Subjects were 182 eyes of 91 uveitis patients without glaucoma. Comparison were patients with normal tension glaucoma (NTG). Image analyses were conducted with 3D OCT-2000. As a result average RGCL thickness values in the patients with uveitis were significantly ($p < 0.01$) thinner than those in healthies. Cycle scan findings of RNFL around the optic disc in the patients with uveitis showed significant thinning especially at nasal side.

The retinal ganglion cell layer thinning followed by the retinal nerve fiber thinning in the patients with various uveitis was observed, and the thinning was similar to that in patients with glaucoma. The observation of RGCL and RNFL thickness may be useful for the diagnosis and the follow-up of uveitis.

Keywords: Retinal ganglioncell layer, Retinal nerve fiber layer, Optical coherence tomography apoptosis, Obliterative vasculitis

Abbreviations

RGCL: Retinal Ganglioncell Layer, RGC: Retinal Ganglion Cells, RNFL: Retinal Nerve Fiber Layer, OCT: Optical Coherence Tomography, NTG: Normal Tension Glaucoma, IPL: Inner Plexiform Layer.

Introduction

In the model of experimentally induced ischemia- reperfusion injury, retinal ganglion cells (RGC) expressing the gene AP-1 result apoptosis [1]. The inflammation mediators, such as TNF- α , IL-1 β , etc. lead RGC to apoptosis, that may lead the thinning of the retinal ganglion cell layer (GCL) followed by the retinal nerve fiber layer (RNFL) thinning. It's prospected that eyes in various diseases complicated with uveitis, that repeat remission and exacerbation then the pathological features appear obliterative vasculitis, may be also observed abnormal thickness of RDCL and RNFL. In this study, the RGCL and RFML thinning in patients with various uveitis were observed using the optical coherence tomography (OCT) imaging analyses, which have been conducted as routine examinations in patients with glaucoma.

Materials and Methods

Subject

Subject were 182 eyes of 91 uveitis patients (29 Male, 62 Female), those have no history of intraocular hypertension. The comparison were 68 eyes of 34 patients with normal tension glaucoma (NTG) (19 Male, 15 Female). The control were 52 eyes of 26 healthies (10 Male, 16Female). Uveitis patients were included Behcet's disease, sarcoidosis, systemic lupus erythematoses, chrone disease, chronic rheumatoid arthritis, sjogren syndrome, polymiositis, scleroderma, ulcerative colitis, heterochromic iridocyclitis, endotoxin-induced uveitis, etc. Most of these uveitis were inactive stage or relaxing state, and had no history of herpes-related symptom. Average age (average \pm S.D.) in uveitis was 65.5 \pm 13.8 year-old, NTG 64.9 \pm 15.4 year-old, and healthy control 66.6 \pm 14.7 year-old. There is no significant age difference among three groups.

Methods

The equipment used in optical coherence tomographical analysis was 3D OCT-2000 (Topcon, Tokyo). (Central wavelength of light source: 840nm, Diameter of circle scan: 3.4mm ϕ , 3D (V) scan in macula: 717 mm²). Ganglion Cell Layer thickness in macula (GCL) means those between ganglion cell layer and inner plexiform layer (IPL). Average thickness values in upper & lower fractions and

whole framework were evaluated, respectively. Average thickness values of RNFL around the optic nerve head divided into 12 sectors were measured and evaluated respectively clockwise in the right eyes, then anticlockwise in the left. We measured macular retinal thickness values in the framework, then compared values of average thickness and center thickness between uveitis and healthy control. Red fractions of significance map mean lower than 1% tile hazard ratio, compared with the same age, same gender and same race population.

In this study, “abnormal” means maps of RGCL with more than 3 red fractions, and 12 sectors around the disc of RNFL with more than one red sector. Statistical analyses were performed using χ^2 test and Mann-Whitney U test.

Results

The case1 was a 82 year-old male patient with polymyositis. There was RGCL thinning in red tiles (Figure 1). The case 2 was a 34 year-old male patient with SLE at first visit. The picture showed active uveitis and RGCL thinning (Figure 2). The case 3 was a 72 year-old female patient with dermatomyositis. The red tiles showed the thinning of RNFL and RGCL (Figure 3). The case 4 was a 78 year- old male patient with ulcerative colitis. The red tiles showed the thinning of RGCL (Figure 4). The thickness of macular RGCL in patients with uveitis was thinner than healthy control (Figure 5).

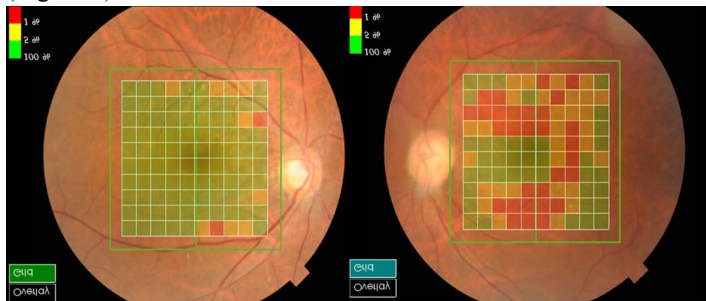


Figure 1: The case 1 was a 82 year-old male patient with polymyositis. There was RGCL thinning in red tiles.

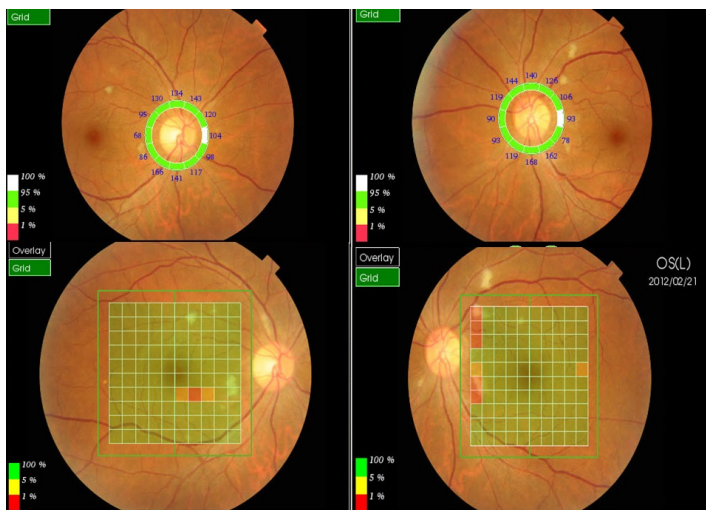


Figure 2: The case 2 was a 34 year-old male patient with SLE at first visit. The picture showed active uveitis and RGCL thinning.

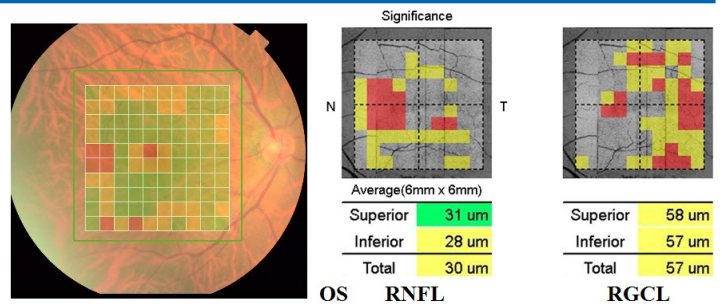


Figure 3: The case 3 was a 72 year-old female patient with dermatomyositis. The red tiles showed the thinning of RNFL and RGCL.

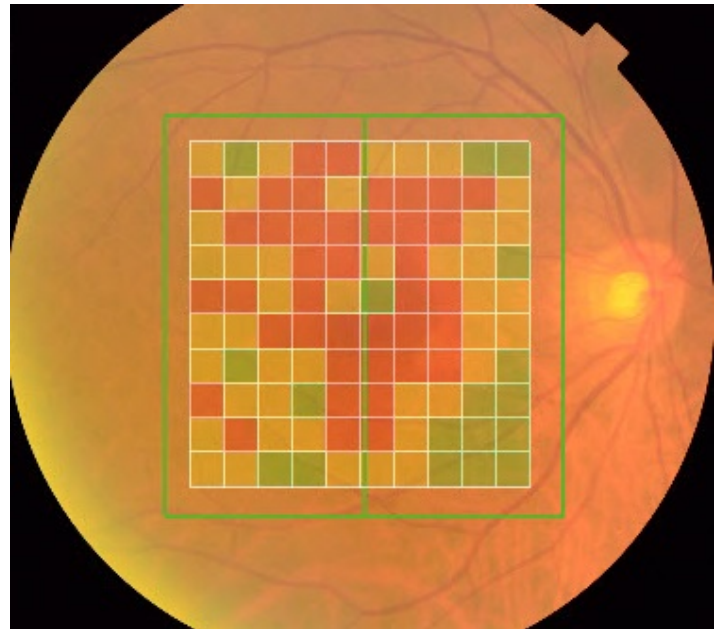


Figure 4: The case 4 was a 78 year- old male patient with ulcerative colitis. The red tiles showed the thinning of RGCL.

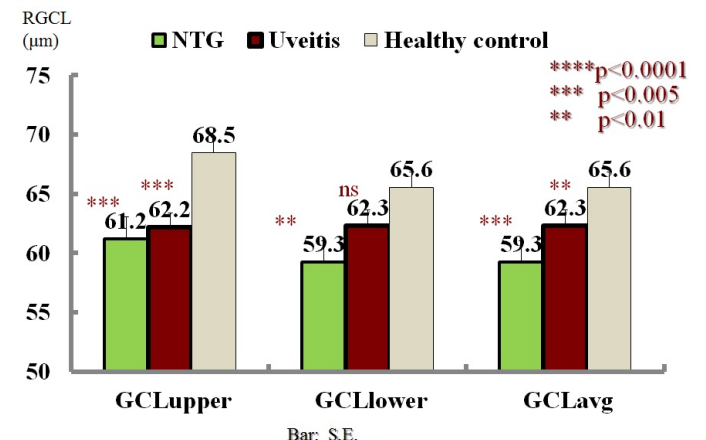


Figure 5: The thickness of macular RGCL in patients with uveitis was thinner than healthy control.

The thickness of peripapillary RNFL in patients with Uveitis was significantly thinner than healthy control at 11 to 7 o'clock, as well as NTG at 3 to 4 o'clock (Figure 6). The retinal thickness in patients with uveitis showed no significant difference.

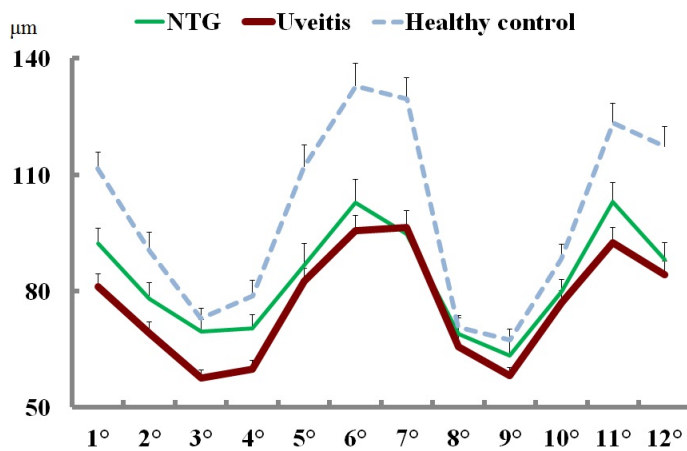


Figure 6: The thickness of peripapillary RNFL in patients with Uveitis.

The post hoc cell contribution tables among three groups showed whether maps of RGCL had more than 3 red tiles (abnormal) or not (Table 1), and 12 sectors around the disc of RNFL had more than one red sector (abnormal) or not (Table 2). The results showed that maps in patients with uveitis or NTG appeared significantly abnormal ones with red tiles or red sectors.

	Abnormal	Normal
NTG	5.059	-5.059
Uveitis	8.209	-8.209
Healthy control	-15.114	15.114
p<0.0001		

Table 1: The post hoc cell contribution tables among three groups showed whether maps of RGCL had more than 3 red tiles (abnormal) or not.

	Abnormal	Normal
NTG	4.908	-4.908
Uveitis	4.931	-4.931
Healthy control	-10.860	10.860
p<0.0001		

Table 2: Twelve sectors around the disc of RNFL had more than one red sector (abnormal) or not.

Discussion

TNF(tumor necrosis factor) and IL-1 β are pro-inflammatory cytokines as well as apoptosis-inducing factors [2]. It has been reported that an inflammatory cytokine IFN- γ produced by T cells is an apoptosis inducer for nerve cells [3]. An IFN- γ itself shows neurotoxicity [4]. IL-17 leads macrophages and astrocytes to promote the expression of inflammatory cytokines, factors such as TNF- α , IL-1 β and MMP-9 [5]. Cytokines, such as sIL-2R, IL-2, IL-4, IL-6 and IL-12, are also possible inducers of glaucoma optic neuropathy [6].

The acute or chronic inflammatory diseases are associated with systemic cytokine surge, may lead programmed cell death in ganglion cells. Recently, the development of optical coherence tomography of (SD-OCT) contributes to invasive periodical

examinations of optic nerve head and ganglion cell layer analyses, followed by early diagnoses and treatments.

In this study, the thinning of RGCL and RNFL was presented in patients with various uveitis. The thinning of RGCL begins from the early stage of uveitis, and with subsequence diseases for a long time cause the thinning of RNFL. It's an important point that the thinning may repeat the remission and exacerbation associated with the activation and remission of uveitis. The observation of RGCL and RNFL thickness may be useful for the diagnosis and the follow-up of uveitis. Further detail studies of the retinal ganglion cell layer thinning in uveitis are expected.

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