Retinal thinning correlates with clinical severity in multiple system atrophy

Tae Wan Kim[1,2], Jeeyun Ahn[1,2], Jee-Young Lee[3,4]
[1]Department of Ophthalmology, Seoul Metropolitan Government-Seoul National University Boramae Medical Center, Seoul, Korea
[2]Department of Ophthalmology, Seoul National University, College of Medicine, Seoul, Korea
[3]Department of Neurology, Seoul Metropolitan Government Seoul National University Boramae Medical Center Boramae Medical Center, Seoul, Korea
[4]Department of Neurology, Seoul National University, College of Medicine, Seoul, Korea

Introduction

Multiple system atrophy (MSA), which is called a atypical Parkinsonism, is a rapidly progressive neurodegenerative disorder relegating patients to total dependency within several years.[1]
Optical coherence tomography (OCT) is a non-invasive imaging technique which is easy to perform and capable of imaging the retina with high resolution.

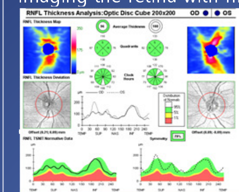

Figure 1. Retinal nerve fiber layer (RNFL) thickness analysis with Optical coherence tomography (OCT)

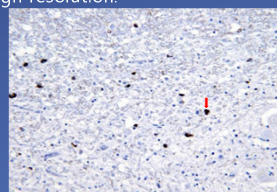

Figure 2. α-synuclein immunoreactive inclusions within glial cells in cerebellum in MSA patients

There are reports of the retina being involved pathologically in alpha-synucleinopathy such as Parkinson's disease (PD) and dementia with Lewy bodies (DLB).[2,3] OCT studies have shown retinal thinning in these disorders.[2,4]

In so far, there have been only few studies looking at changes in retinal layer thickness in MSA suggesting some degree of retinal thinning in MSA.[5-9]

Thus this study was planned to investigate retinal thickness changes in MSA patients according to the clinical severity, and also to the 2 subtypes of MSA.

Method

Study participants consisted of consecutively recruited MSA patients who visited the Boramae Medical Center (BMC) movement disorder clinic over a defined period and age-matched healthy controls receiving ophthalmological examinations for routine check-up during the same study period.
MSA patients were classified into two groups. One is MSA-P who presented Parkinsonian symptoms and the other is MSA-C who presented cerebellar ataxia.
Eyes with co-morbid ophthalmic pathologies capable of affecting retinal thickness or glaucomatous optic neuropathies, the presence of media opacity capable of inducing poor quality OCT images, and those incapable of undergoing OCT examination were excluded.
Patient demographic and clinical information such as age, gender, the Unified MSA Rating Scale (UMSARS) were collected.
High-resolution retinal imaging was acquired using spectral domain (SD)-OCT (Spectralis OCT; Heidelberg Engineering, Heidelberg, Germany and OPKO OTI Spectral OCT/SLO; Ophthalmic Technologies, Inc., Toronto, Canada).
Peripapillary RNFL thickness was evaluated using the Spectralis OCT machine. Mean retinal thickness was measured in the nine macular Early Treatment Diabetic Retinopathy Study (ETDRS) areas including a central 1-mm disc and inner and outer rings of 3 and 6 mm, respectively.

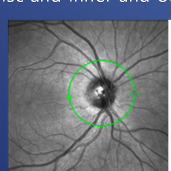

Figure 3. Scanning for retinal nerve fiber layer (RNFL) thickness analysis with Optical coherence tomography (OCT).

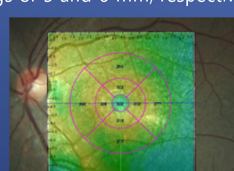

Figure 4. Mean retinal thickness measured in the nine macular Early Treatment Diabetic Retinopathy Study (ETDRS) areas.

This study protocol was approved by the Institutional Review Board of Seoul National University BMC and informed consent was obtained from all participants.

References

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Result

A total of 36 MSA patients and 71 healthy control subjects were enrolled in this study.
For the RNFL analysis, 15 MSA patients (28 eyes) and 27 controls (53 eyes) were included. Perifoveal retinal thickness analysis was done in 23 MSA patients (45 eyes) and 44 controls (78 eyes). Two MSA patients received scans from both the Spect ralis and OTI machines.

Table 1. Baseline patient demographics and ophthalmologic characteristics

	RNFL analysis				Perifoveal retinal thickness analysis			
	MSA (n=15)			Control (n=27)	MSA (n=23)			Control (n=44)
	All	MSA-P (n=10)	MSA-C (n=5)		All	MSA-P (n=18)	MSA-C (n=5)	
Age, yr	68.47 (7.34)	69.30 (4.86)	67.40 (7.16)	67.11 (7.19)	67.43 (7.37)	68.94 (6.48)	62.00 (8.86)	68.91 (10.67)
Gender (male), n (%)	10 (66.7)	8 (80.0)	2 (40.0)	14 (51.9)	11 (47.8)	9 (50.0)	2 (40.0)	17 (38.6)
Laterality (B/R/L), %	86.7/13.3	90.0/10.0	80.0/20.0	96.3/3.7	95.7/4.3	94.4/5.6	100/0.0	77.3/11.4/11.4
LogMAR BCVA	0.15 (0.19)*	0.16 (0.21)	0.13 (0.15)	0.06 (0.08)	0.16 (0.20)	0.16 (0.22)	0.16 (0.15)	0.09 (0.12)
Lens (phakic/pseudophakic), %	67.9/32.1	68.4/31.6	66.7/33.3	79.2/20.8	75.6/24.4	74.3/25.7	80.0/20.0	88.5/11.5
Spherical equivalent, diopters	0.81 (1.01)	0.88 (1.04)	0.68 (0.99)	0.20 (1.45)	0.35 (1.05)	0.38 (1.01)	0.25 (1.22)	-0.05 (1.62)
Axial length, mm	23.46 (0.54)	23.39 (0.57)	23.60 (0.49)	24.42 (1.37)	23.26 (0.66)	23.21 (0.71)	23.40 (0.49)	22.99 (0.56)
UMSARS-total		37.80 (30.10)	34.60 (15.07)			52.22 (22.49)	30.80 (19.83)	
GDS		2.20 (1.03)	3.40 (1.52)			3.11 (1.28)	2.00 (1.41)	

Data shown as mean (standard deviation) unless otherwise indicated.

Statistically significant values marked with "*" ($p<0.05$).

RNFL=retinal nerve fiber layer; MSA=multiple system atrophy; LogMAR=logarithm of the Minimum Angle of Resolution; BCVA=best-corrected visual acuity; UMSARS=Unified Multiple System Atrophy Rating Scale; GDS=Global Disability Scores

In the RNFL analysis, significant RNFL thinning was observed in the superior, inferior, superotemporal, inferotemporal sector, as well as the global average of the MSA compared to control (Figure 5-A).
The RNFL thinning was widespread in the MSA-P group whereas the MSA-C group did not show any significant RNFL thinning in comparison to control and the thickness variation was wide (Figure 6-A). There was an overall tendency of stepwise RNFL reduction from the control group to MSA-C and further on to MSA-P, although the nasal RNFL was an exception (75.89±14.75 for MSA-C and 72.43±10.08 for control).
As for perifoveal retinal thickness, there was significant retinal thinning in both the superior and inferior outer sectors of the MSA compared to control (Figure 5-B) As in the RNFL analysis, perifoveal retinal thinning was widespread and significant in the MSA-P group whereas the MSA-C group did not show any significant differences compared to the control group (Figure 6-B).
Although there was no significant correlation with RNFL thickness, there was a significant negative correlation between perifoveal retinal thicknesses at all sectors with the exception of the temporal outer sector and UMSARS (r = -0.539, P = 0.007 for the total macula, $-0.565 \le r \le -0.401$, $0.004 \le P \le 0.037$ for all other sectors) (Figure 5-C).

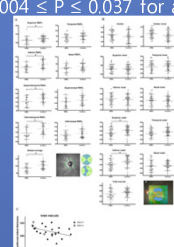

Figure 5. Scatter plots of RNFL thickness (A) and perifoveal retinal thickness (B) in MSA and controls subjects. (C) Scatter plots between the Unified MSA Rating Scale (UMSARS) and retinal thickness in the total macula showing significant negative correlation.

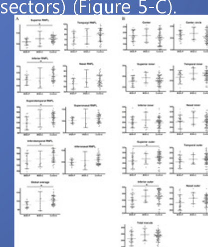

Figure 6. Scatter plots of RNFL thickness (A) and perifoveal retinal thickness (B) in MSA subtypes MSA-P, MSA-C and controls subjects.

Discussions

RNFL thinning was present in other sectors than the nasal sector, which has been reported previously.[5, 8] The proportion of MSA-C and MSA-P may be important when comparing the MSA group as a whole versus control since the degree of RNFL thickness difference was larger in the MSA-P subgroup. Another study conducted in only MSA-C patients also showed no significant thinning in the RNFL which was consistent with our results.[6]
As for perifoveal macular thickness, retinal thinning was significant in the superior and inferior outer sectors in our study whereas one previous study reported superior and nasal outer sector thinning.[7] We found that there is clinical correlation with retinal thickness, thus perifoveal OCT measurements may be dependent on the clinical severity of the subjects included.
In conclusion, RNFL and perifoveal retinal thinning was observed in MSA patients, and the latter correlated significantly with clinical severity. Further studies are warranted to investigate the clinical and functional consequence of retinal thinning in MSA and if such retinal changes can act as a biomarker to monitor the progression of disease.