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Clinical Features of Superior Segmental Optic Hypoplasia: Hospital-based Study

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Abstract

Purpose: To determine the clinical features of patients diagnosed with superior segmental optic hypoplasia (SSOH) and to compare the anatomical structures of SSOH to that of normal subjects quantitatively.

Methods: We examined the medical charts of 106 eyes of 59 patients with SSOH and 35 eyes of 35 normal subjects as controls. All of the eyes had been examined by spectral-domain optical coherence tomography (SD-OCT). Eyes with SSOH were classified as the definite type or the suspect type as determined by standard automated perimetry (SAP). The definite type had inferior visual field (VF) defects, while the suspect type did not have inferior VF defects. The findings of the SD-OCT images of 35 eyes with SSOH were compared to that of the 35 normal eyes.

Results: Of the 106 eyes with SSOH, 56 (52.8%) were classified as the definite type and 50 eyes (47.2%) were as suspect type. OCT showed that the average of the total retinal nerve fiber layer (RNFL) thickness was significantly thinner in the SSOH group than in the normal group ($P < 0.001$; Mann-Whitney U test). Sectorial analysis demonstrated that the RNFL was thinner than controls in all quadrants (all $P < 0.001$; Mann-Whitney U test). The comparison of the hourly sectors showed that the RNFL was thinner at 10, 11, 12, 1, 2, 3, 5, and 6 o'clock

sectors in the SSOH group than controls.

Conclusions: Approximately one-half of eyes with SSOH had a detectable VF defect. OCT showed that eyes with SSOH have a thinner RNFL in more expanded areas than controls.

Key words: superior segmental optic hypoplasia; optical coherence tomography; retinal nerve fiber layer; visual field defect

Introduction

Superior segmental optic hypoplasia (SSOH) is a congenital anomaly of the optic nerve head with a relative hypoplasia of the superior part of the optic nerve head and the retinal nerve fiber layer. It is characterized by 4 findings: pallor of the superior optic disc, thinning of the superior retinal nerve fiber layer (RNFL) corresponding to the optic disc pallor, superior entrance of the central retinal vessels, and superior peripapillary scleral halo [1-5]. The prevalence of SSOH in Japan and Korea is estimated to be 0.08 to 0.30% [6-8]. Yamamoto et al. [6] reported that the prevalence of SSOH is 0.3% in the Japanese based on a large-scale screening for eye diseases. This would be equivalent to one-tenth the prevalence of normal tension glaucoma (NTG) in the Japanese [9,10].

Although most patients with SSOH have an inferior altitudinal or sector-like visual field (VF) defect connected to the blind spot with relatively good best-corrected visual acuity (BCVA), some patients with optic disc satisfying the requirements of SSOH have atypical VF defects. This can lead to a misdiagnosis of SSOH, and thus it is essential to differentiate patients with SSOH from those with open angle glaucoma (OAG) including NTG. Unoki et al. [11]

examined 7 of 10 eyes with SSOH with time-domain optical coherence tomography (TD-OCT), and reported that the TD-OCT images revealed mild segmental hypoplasia that was not previously detected. Thereafter, investigators attempted to differentiate the SSOH of normal subjects [12,13] from that of glaucoma patients [14] by TD-OCT.

The introduction of spectral-domain OCT (SD-OCT), an OCT instrument with higher resolution and better imaging speed [15,16], has made it possible for clinicians to examine the retina and optic disc in greater detail. However, to the best of our knowledge, there are only a few reports comparing the circumpapillary retinal nerve fiber layer (RNFL) thickness of eyes with SSOH to that of normal controls by SD-OCT [17,18].

Thus, the purpose of this study was to classify patients diagnosed with SSOH based on the VF defects determined by standard automated perimetry (SAP) and to assess their structural characteristics quantitatively in the SD-OCT images.

Materials and methods

78 We examined the medical records of 106 eyes of 59 patients diagnosed with SSOH and 35
79 eyes of 35 healthy volunteers. All were examined between 2004 and 2015 in the Department
80 of Ophthalmology, Gifu University Hospital, Japan. The procedures used conformed to the
81 tenets of the Declaration of Helsinki, and they were approved by the Ethics Committee of
82 Gifu University Graduate School of Medicine.
83
84 All of the patients underwent a routine ophthalmological examinations including
85 measurements of the best-corrected visual acuity (BCVA), subjective refraction with a
86 refractometer (KP-8100PA, Topcon, Tokyo, Japan), slit-lamp biomicroscopy, intraocular
87 pressure (IOP) measurements with a Goldmann applanation tonometer (Haag-Streit AG,
88 Köniz, Switzerland), ophthalmoscopy, and optic nerve imaging with a SD-OCT device (SD-
89 OCT; Carl Zeiss Meditec, Dublin, CA, USA). If glaucoma or optic nerve hypoplasia was
90 suspected, perimetry with a Humphrey Field Analyzer (Humphrey Instruments, Dublin, CA,
91 USA) was performed with the central 30-2 Swedish Interactive Threshold Algorithm (SITA)
92 standard program.
93
94 We used the same diagnostic criteria of SSOH as those of the Tajimi Health Care Project [6];

a thinning of the optic nerve head rim most prominent in the superior nasal region with corresponding nerve fiber layer defects (NFLD) in the superior nasal region. All eyes diagnosed with SSOH were rated as definite SSOH type that had inferior visual field (VF) defects or suspect SSOH type that did not have inferior VF defects,.

After the introduction of SD-OCT in our department in 2008, the optic discs were assessed in 44 patients by the SD-OCT images. Thirty-five eyes of 35 patients with SSOH and 35 age-, sex-, refractive error-matched normal controls were studied in the same way. The exclusion criteria were: prior intraocular surgeries including laser treatment, other ocular diseases, disorders of the central nervous system, decimal BCVA $\leq$0.9, myopia of $\geq$ -6 diopters or astigmatism $\geq$3 D, and age $\leq$18 years. One eye of each subject was chosen for the analyses, and in patients with bilateral SSOH the eye with the poorer mean deviation (MD) was selected.

The optic disc cube scan image of the optic disc region in an area of 6 x 6 mm^2 (200 x 200 pixels) was analyzed. A circumpapillary RNFL thickness map was generated. A 3.46 mm diameter circle consisting of 256 A-scans, was then automatically centered around the optic

disc. The global, four-quadrants, and 12 hourly circumpapillary thicknesses of the RNFL were determined. The scanned images with signal strength ≥7/10 were used for the analyses, and values obtained from left eyes were converted into the right eye format.

Unpaired t-tests were used to determine the significance of the differences in the demographic data between patients with SSOH and normal subjects. The sex distribution in the two groups was evaluated with the chi-square test. Mann-Whitney U tests were used to compare the data between SSOH and control eyes. A P value of <0.05 was taken to be statistically significant. All of the statistical analyses were performed with the SPSS software (IBM SPSS statistics, version 23).

Results

The demographics and clinical findings of the 27 men and 32 women with SSOH are shown in Table 1. The mean age was 35.7 ± 15.7 (mean ± standard deviation) years with a range of 7 to 71 years. The mean IOP was 14.9 ± 3.4 mmHg with a range of 7 to 26 mmHg. The mean refraction error (spherical equivalent) was -3.63 ± 3.38 D with a range of -13.38 to +1.25 D.

The averaged MD was -2.51 ± 4.00 decibels (dB) with a range of -22.24 to +3.14 dB.

Six of the SSOH cases were diagnosed with open angle glaucoma including normal tension glaucoma. There were 2 cases that had a family history of diabetes mellitus, however both were limited to their mothers and were type I diabetes mellitus [2,5]. None of the patients had a family history of optic nerve hypoplasia.

Forty-two cases were the definite type in at least one eye, and the remaining 17 cases were the suspect type. Of the 42 definite cases, 14 cases were bilateral, and 20 cases were definite in one eye and suspect type in the contralateral eye, and the remaining 8 cases were unilateral. Of the 17 suspect cases, 13 were bilateral and 4 cases were unilateral.

The demographics data of 35 eyes with SSOH and 35 eyes of the normal controls are shown in Table 2. Among the 35 eyes with SSOH, 22 cases were the definite type and 15 cases were the suspect type. There were no significant differences in age, sex distribution, refractive error, and MDs between the eyes with SSOH and normal controls.

146 The average total RNFL thickness was significantly thinner in the SSOH patients than that of
147 the control group (P <0.001; Mann-Whitney U test). The RNFL thickness in the superior,
148 nasal, and inferior sectors were significantly thinner in the SSOH eyes than in the normal
149 control eyes (all except the nasal sector P <0.001; Mann-Whitney U test; Table 3). In the
150 hourly analyses, the RNFL was significantly thinner at the 10, 11, 12, 1, 2, 3, 5, and 6 o'clock
151 sectors than in the normal controls (all P <0.001; Mann-Whitney U tests; Table 3).
152

153 ## Discussion

154

155 Our results showed that approximately one-half of the 106 SSOH eyes were the definite type
156 (56 eyes, 52.8%) and one-half the suspect type (50 eyes, 47.2%). Twenty-two of the SSOH
157 cases (37.3%) were only the definite type, 17 cases (28.8%) were only the suspect type, and
158 20 cases (33.9%) had both types in their two eyes. Forty-two cases (71.2%) had definite type
159 in at least one eye. Although none of our cases had reduced BCVA, the severity of the VF
160 defects varied among the definite type of SSOH eyes.
161

162 Yamamoto et al. [6] estimated that the prevalence of SSOH was about 0.3% in the Japanese

163 population, and approximately two-thirds of the SSOH patients were the definite type. They
164 found 54 eyes of 37 cases with SSOH. Their results showed that approximately one-half of
165 the 54 SSOH eyes were the definite type (28 eyes, 51.9%) and one-half the suspect type (26
166 eyes, 48.1%). Eighteen of the SSOH cases (48.6%) were only the definite type, 14 cases
167 (37.8%) were only the suspect type, and 5 cases (13.5%) had both types in their two eyes.
168 Twenty-three cases (62.2%) had definite type in at least one eye. Although the subjects were
169 from a large-scale eye disease screening study, and the participant's age was limited to those
170 >40 years [6], the proportion of definite SSOH type is comparable to our findings.
171
172 Comparisons of the RNFL thicknesses measured by OCT between eyes with SSOH and
173 normal controls showed a thinning of the superior RNFL sectors, and this thinning may be
174 useful in differentiating cases with SSOH from normal controls [11-13,16,17]. Unoki et al.
175 [11] reported that the RNFL thickness in 7 eyes with SSOH was reduced significantly in only
176 the 12 and 1 o'clock sectors compared to 13 normal eyes as determined by analyzing the TD-
177 OCT images. The RNFL thinning, however was reported to expand into wider areas in SSOH
178 eyes by other subsequent studies using both TD- and SD-OCT instruments. Lee et al. [12]
179 reported a decrease in the RNFL thickness in all segments except the 8-9 o'clock sector in

eyes with SSOH compared to normal subjects using TD-OCT. Fuse et al. [13] reported that the thinning of the RNFL in eyes with SSOH was present in all sectors except at the 7 to 10 o'clock segments, i.e., the inferotemporal to temporal segments using TD-OCT. Hayashi et al. [17] reported that the RNFL in eyes with SSOH was significantly thinner than that of normal subjects in the superotemporal to nasal region, 41 to 230 degrees, using SD-OCT. Recently, Han et al. [18] compared the RNFL thickness in 31 SSOH eyes, 33 NTG eyes, and 49 normal eyes using SD-OCT. They also found thinner RNFL in a wider area, e.g., all except at 6 to 9 o'clock segment, in SSOH eyes compared to normal eyes. We showed that not only the superior sectors, i.e., 11-12-1-2 o'clock, but also the 3, 5, and 6 o'clock sectors were thinner. This is in agreement with the results from previous studies.[11-13, 17,18] However, the slight differences among reports might result from the difference in the OCT device used and the SSOH patients studied. Frisen et al. [19] reported that the degree of optic nerve hypoplasia varied considerably ranging from severe to a minimal hypoplasia.

There are limitations in this study including the relatively small sample size, a hospital-based cohort, and a cross-sectional study. Because our diagnosis was based on the ocular finding at the initial visit, a future development of glaucoma cannot be ruled out. The incidence of

197 SSOH eyes accompanied by open angle glaucoma was 10.6% (6/59). Lee et al. [20] reported
198 that it was 19.7%. The estimated incidence of SSOH eyes coexisting in eyes with OAG was
199 nearly 2 to 5 times higher than that the prevalence of OAG observed in the Tajimi Health
200 Care Project [9] although our study and that of Lee et al [20] were not epidemiologic studies.
201
202 In conclusion, SD-OCT examinations showed that the RNFL in eyes with SSOH is
203 significantly thinner than that of normal controls except in the temporal segment. Evaluation
204 of the RNFL thicknesses especially the 11, 12, and 1 o'clock segments was useful for
205 differentiating normal from SSOH eyes. Although the hypoplasia in SSOH eyes is generally
206 thought to be non-progressive [21,22], care should be taken not to overlook coexisting
207 glaucoma and the future development of NTG [23]. Further large-scaled population-based
208 investigations will be required to address this issue because of the variations in the degree of
209 RNFL thickness in SSOH eyes.

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267 Table 1. Demographics and Clinical Findings of SSOH Patients

All patients	106 eyes of 59 cases			
Type of SSOH (number of cases)	Definite type (Def.)	42	Def. – Def.	14
			Def. – Susp.	20
			Def. – (-)	8
	Suspect type (Sups.)	17	Susp. – Susp.	13
			Susp. – (-)	4
Sex (men/women)	27/32			
Age (years)	35.7 ± 15.7 (7 to 71)			
IOP (mmHg)	14.9 ± 3.4 (7 to 26)			
Refractive error (diopters)	-3.63 ± 3.38 (-13.38 to +1.25).			
Mean deviation (decibels)	-2.51 ± 4.00 (-22.24 to +3.14)			

268 SSOH, superior segmental optic hypoplasia; IOP, intraocular pressure; Def, definite type;

269 Susp, suspect type.

270 Values are mean ± standard deviation (range).

271 Table 2. Comparisons of Demographics Data of SSOH Eyes to that of Normal Controls

	SSOH eyes (n=35)	Control (n=35)	P value
Age (years)	45.8±15.3 (19 to 71)	43.5±11.6 (26 to 64)	0.476
Sex (men/women)	14/21	15/20	0.808
Refractive error (diopters)	-2.11 ± 2.20 (-5.88 to +2.25)	-1.60 ± 1.25 (-5.25 to +1.85)	0.290
IOP (mmHg)	14.3 ± 3.3 (7 to 21)	13.5 ± 2.0 (10-17)	0.242

272 SSOH, superior segmental optic hypoplasia; IOP, intraocular pressure.

273 Values are the means ± standard deviations (range).

274

275 Table 3. Comparison of the Retinal Nerve Fiber Layer Thickness Measured by OCT among

276 Subjects with SSOH and Normal Controls

OCT Parameters		SSOH eyes		Control		P value
Total average		70.3	± 11.3	94.7	± 7.1	< 0.001
Quadrant	Superior	65.8	± 15.7	120.7	± 13.1	< 0.001
	Nasal	57.4	± 11.3	69.9	± 12.0	< 0.001
	Inferior	99.2	± 25.7	119.3	± 14.6	< 0.001
	Temporal	58.6	± 13.9	68.7	± 10.7	< 0.001
Clock-hour	1	53.0	± 14.3	107.3	± 19.4	< 0.001
	2	53.9	± 15.7	80.7	± 15.8	< 0.001
	3	46.9	± 11.0	56.9	± 7.8	< 0.001
	4	53.7	± 9.3	60.2	± 10.3	0.014
	5	71.4	± 21.2	92.2	± 24.5	0.001
	6	99.3	± 30.9	123.6	± 22.3	0.001
	7	127.6	± 39.5	141.2	± 19.7	0.137
	8	75.7	± 19.2	78.7	± 17.4	0.496
	9	51.5	± 7.8	55.3	± 8.2	0.076

10	66.6	± 18.7	84.0	± 16.1	< 0.001
11	83.6	± 24.9	136.8	± 19.5	< 0.001
12	60.5	± 20.1	118.0	± 21.9	< 0.001

OCT: Optical coherence tomography; SSOH: superior segmental optic hypoplasia

Values are mean ± standard deviation (range).

Quadrant sectors: Mann-Whitney U test and Bonferroni correction $P < 0.0125$, Clock-hour sectors: Mann-Whitney U test and Bonferroni correction $P < 0.0042$