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Morphological features of macular telangiectasia type 2 in Japanese patients

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Key messages

- In Caucasian patients with MacTel-2, visual function and macular ellipsoid zone (EZ) loss generally deteriorate with time.
- In Japanese patients with MacTel-2, a certain proportion of eyes showed improvement in the following parameters: BCVA in 13%, macular funduscopic findings in 29%, central macular thickness in 21%, and macular EZ loss in 43%.
- Japanese patients with MacTel-2 may have milder clinical features than Caucasian patients.

Abstract

Purpose This study aimed to demonstrate the clinical course of Japanese patients with macular telangiectasia type 2 (MacTel-2).

Methods This retrospective observational case series included 16 eyes of 8 Japanese patients (3 men and 5 women) with MacTel-2. The mean age and follow-up duration was 66.9 years and 42.8 months, respectively. Differences in best-corrected visual acuity (BCVA), funduscopic macular findings, central macular thickness (CMT), and the length of macular ellipsoid zone (EZ) loss were compared between the initial/baseline and final visits. Optical coherence tomographic changes in CMT by ≥20% and in EZ loss by ≥20% or ≥100 μm were defined as improved or worsened.

Results Numerical changes in BCVA and EZ loss during follow-up were not statistically significant. However, the mean CMT at baseline, which was lower than that of healthy control eyes ($P < 0.001$), significantly increased during follow-up ($P = 0.041$). A certain proportion of eyes showed improvement in several parameters: funduscopic findings (both parafoveal retinal graying and foveal retinal pigment epithelium depigmentation) in 29% of eyes, CMT in 21% of eyes, and EZ loss in 43% of eyes.

Conclusions The non-negligible proportion of eyes with improved parameters, marked especially by macular EZ loss, suggests that Japanese patients with MacTel-2 have milder clinical features than Caucasian patients reported in the literature.

Keywords central macular thickness・ellipsoid zone・foveal retinal pigment epithelium depigmentation・Japanese patients・macular telangiectasia type 2

Introduction

Macular telangiectasia type 2 (MacTel-2) is a bilateral macular disease characterized by a predilection for elderly women, parafoveal gray-colored reduced retinal transparency (retinal graying), retinal telangiectasia with late leakage on fluorescein angiography (FA), and neurosensory atrophy[1-4]. Progression of subretinal neovascularization and/or macular atrophy during follow-up results in loss of visual acuity [5]. Histopathologic studies revealed depletion of perifoveal Müller cells [6], as depicted by inner lamellar cavity on optical coherence tomography (OCT); however, mechanisms causing damage to Müller cells still remain controversial.

In Caucasian patients with MacTel-2, best-corrected visual acuity (BCVA) sequentially decreased at the mean rate of approximately 1 letter per year, and the 5-year probability of 10 or more letter loss was 27% of eyes [7], suggesting that patients with MacTel-2 have slowly progressive visual deterioration. In the early stage of MacTel-2, OCT demonstrated impairment in the macular ellipsoid zone (EZ) before the appearance of inner lamellar cavity [8]. The area of macular EZ loss gradually enlarged to form outer lamellar cavity, showing an association between the area of EZ loss and retinal sensitivity on perimetry [9]. These observations may indicate that deterioration in visual functions in MacTel-2 depends on the extent of photoreceptor damage. Studies using fundus autofluorescence (FAF) showed impairment in the retinal pigment epithelium (RPE) before any changes detected with FA and time-domain OCT [10]. These results suggest that RPE cells, as well as photoreceptors, are impaired at the initial stage of MacTel-2.

To date, >500 Caucasian patients with MacTel-2 have been reported [7]. However, to the best of our knowledge, only 12 Japanese patients with MacTel-2 have been reported, suggesting the rarity of MacTel-2 in Japanese population [11, 12]. Previous studies on Japanese patients with MacTel-2 showed a predilection for women at the age of around 60 years and typically good BCVA at initial presentation[11, 12]. However, longitudinal studies examining functional and anatomical changes have not been previously reported. Here we evaluated sequential changes in various

parameters including funduscopic and OCT findings together with BCVA, so as to demonstrate the clinical course of MacTel-2 in Japanese patients.

Patients and methods

Patients

This retrospective observational case series included 16 eyes of 8 patients with MacTel-2 who visited our clinics from September 2011 to October 2017. All MacTel-2 patients were followed up for ≥12 months, and their medical records were retrospectively reviewed. The inclusion criteria for MacTel-2 diagnosis followed the Gass classification [1]. The exclusion criteria were a history of other retinal diseases such as radiation retinopathy, diabetic retinopathy, and branch retinal vein occlusion, together with a history of taking oral anti-estrogen drugs [13]. For comparison of central macular thickness (CMT), 36 eyes of 19 healthy subjects who had no abnormal ocular findings except incipient cataract were included as controls.

The present study adhered to the guidelines of the Declaration of Helsinki and was approved by the institutional review board and ethics committee at Hokkaido University Hospital (#018-0207). Informed consent was obtained from all subjects after the nature and possible consequences of the study were explained.

Ophthalmologic examinations

At the initial visit, patients underwent thorough ophthalmic examinations including the decimal BCVA assessment with a Japanese standard Landolt visual acuity chart, fundus photography, FA, FAF, and OCT (RS-3000 or RS-3000 Advance, Nidek, Gamagori, Japan), all of which were thereafter repeated during follow-up. Funduscopic changes in macular lesions were independently evaluated by two of the authors (A.S. and W.S.) in 14 eyes of 7 patients who underwent fundus photography at both the initial and final visits (except Case 5).

Macular morphometric assessments

Using horizontal B-scan images through the fovea on enhanced depth imaging OCT, two of the authors (A.S. and Y.H.) manually measured CMT and the length of macular EZ loss, and the average values of the two examiners were processed for statistical analyses. These parameters were compared between baseline and final visits in 14 eyes of 7 patients with MacTel-2 who could undergo OCT with its follow-up function (except Case 5), which allows each follow-up measurement to be repeated automatically at the identical site. Sequential changes in inner and outer lamellar cavities were assessed in all the 16 study eyes.

Statistical analyses

All results are expressed as mean ± standard deviation. Decimal BCVA results were converted to the logMAR scale for statistical analyses. The Mann-Whitney U test or Fisher's exact test was used to compare baseline parameters between MacTel-2 patients and control subjects. The Wilcoxon signed-rank test was used to compare initial and final values of logMAR BCVA, CMT, and the length of macular EZ loss in patients with MacTel-2. OCT data were collected at the initial visit in most patients except Cases 2, 5, 6, and 7 who initially underwent OCT measurements at 11, 7, 5, and 0.25 months (defined as baseline) after the initial visit, respectively. Changes of ≥0.2 in BCVA, ≥20% in CMT, and ≥20% or ≥100 μm in EZ loss were defined as improved or worsened. Spearman's correlation coefficient was used to examine correlations between any two of BCVA, CMT, and the length of EZ loss. Differences were considered statistically significant at *P*-values <0.05.

Results

Patient demographics

The clinical characteristics of the patients are shown in Table 1. All the patients were Japanese consisting of 3 men and 5 women. The mean age at the first visit was 66.9 ± 7.3 years (range, 57–75

years). The follow-up duration ranged from 12 to 76 months (mean, 42.8 ± 26.3 months).

Medical and family history

Systemic diseases were noted in the medical history of 7 patients (Table 1). Case 4 had intestinal Behçet disease with no history of uveitis. Case 7 had a history of surgeries for lung adenocarcinoma and colon carcinoma without receiving adjuvant chemotherapy. None of the patients had a family history of any form of retinopathies.

Subjective symptoms

Patients' subjective symptoms included chronic central vision loss in 11 eyes (68.8%) of 7 patients, distorted vision in 7 eyes (43.8%) of 5 patients, and no symptom in 4 eyes (25.0%) of 4 patients.

Visual outcomes

The initial BCVA was ≤0.0 in 5 eyes (31.3%), >0.0 to <0.35 in 6 eyes (37.5%), and ≥0.35 to <1.0 in 5 eyes (31.3%), while the final BCVA was ≤0.0 in 6 eyes (37.5%), >0.0 to <0.35 in 5 eyes (31.3%), and ≥0.35 to <1.0 in 5 eyes (31.3%) (Table 1). Compared with the initial data, the final values improved in 2 eyes (12.5%) and worsened in no eyes, with the remaining 14 eyes (87.5%) maintaining stable vision. There was no significant difference between the initial and final values (N = 16, 0.23 ± 0.31 vs. 0.21 ± 0.27; P = 0.922).

Ophthalmologic findings

Of 6 patients, except 2 patients with a history of cataract surgery (Cases 7, 8), 7, 1, and 4 eyes were hyperopic, emmetropic, and myopic, respectively. The mean spherical equivalent was +0.61 ± 1.26 diopters. Slit-lamp examination indicated no abnormal findings in the anterior segment of any eyes but incipient cataract in 12 eyes.

Funduscopic findings

Changes in fundus photographic findings are shown in Table 2. At the initial visit, funduscopic examination showed parafoveal retinal graying (Stage 2) in 11 eyes (68.8%) of 7 patients, foveal RPE depigmentation in 14 eyes (87.5%) of 8 patients, right-angle venules (Stage 3) in 4 eyes (25.0%) of 3 patients, and punctate crystalline deposits in 1 eye (6.3%), and intraretinal pigmentation (Stage 4) in 1 eye (6.3%) (Fig. 1A, B, 4A). Subretinal neovascularization (Stage 5) was not present in any eyes.

Of 14 eyes of 7 eligible patients (except Case 5), macular lesions (retinal graying and RPE depigmentation) improved in 4 eyes (28.6%) of 2 patients (Cases 2, 4) and remained unchanged in 10 eyes (71.4%) of 5 patients (Figures 2A, B, 4B, C). In 2 of these 4 eyes showing improvement of macular lesions, intraretinal pigmentation developed (*i.e.*, progression of Stage 3 to 4) together with crystalline deposits (Case 2; Fig. 4B, C).

FA findings

Early-phase FA showed retinal telangiectasia at the macular area in all the 16 eyes. In the late phase, vascular leakage was observed around the temporal side of the macula in 14 eyes (87.5%) of 8 patients (Figures 1C, D, 4D). Of 6 eyes that could be followed with FA, the extent of vascular leakage remained unchanged in 1 eye (16.7%) of 1 patient (Case 3), decreased in 3 eyes (50.0%) of 2 patients (Cases 3, 4; Fig. 2C, D), and increased in 2 eyes (33.3%) of 1 patient (Case 2).

Disease Stages

All the study eyes were diagnosed at the initial visit with Stage 1 in 2 eyes of 2 patients, Stage 2 in 10 eyes of 6 patients, Stage 3 in 3 eyes of 2 patients, and Stage 4 in 1 eye of 1 patient (Table 2) [1]. During follow-up, 14 eligible eyes but both eyes of Case 2 (Fig. 4) showed no progression of disease stages.

FAF findings

Of 5 patients examined (Cases 2-4, 7, 8), FAF demonstrated hyper-autofluorescence in 6 eyes of 3 patients (Cases 2, 4, 8) and no abnormal findings in 4 eyes of 2 patients (Cases 3, 7), corresponding to the site of parafoveal retinal graying (Fig. 1E, F). As concerns foveal RPE depigmentation, hyper-autofluorescence was also detected in 6 eyes of 4 patients (Cases 2, 4, 7, 8; Figure 1F) and no abnormal findings in 4 eyes of 3 patients (Cases 3, 4, 8). In contrast, intraretinal pigmentation showed hypo-autofluorescence in 3 eyes of 2 patients (Cases 2, 8; Fig. 4E). During follow-up, hyper-autofluorescence decreased in all the 6 eyes at the site of parafoveal retinal graying (Fig. 2E, F, 4F) and in 3 eyes of 2 patients (Cases 2, 4) at the site of foveal RPE depigmentation, but unchanged in the remaining 3 eyes of 2 patients (Cases 7, 8) together with persisting foveal RPE depigmentation.

CMT

Regarding control subjects (6 men and 13 women), the mean age was 65.9 ± 2.7 years, and the mean refraction was +0.36 ± 1.62 diopters. There were no significant differences in age, sex, or refraction between MacTel-2 patients and control subjects (P = 0.705, 1.000, and 0.877, respectively). The mean CMT at baseline was significantly lower in eyes with MacTel-2 (N = 16, 175.2 ± 32.9 μm) than in control eyes (N = 36, 218.2 ± 16.1 μm, P < 0.001).

Changes in macular morphological findings are shown in Table 3. In patients with MacTel-2 (N = 14), CMT remained unchanged in 11 eyes (78.6%) of 7 patients, increased in 3 eyes (21.4%) of 3 patients, and decreased in no eyes at the final visit, compared with baseline values. The mean CMT was 172.6 ± 34.6 μm at baseline and 182.2 ± 32.6 μm at the final visit, showing a significant difference between the values (P = 0.041). There was no correlation in baseline values between BCVA and CMT (P = 0.757, *rho* = -0.08).

Macular EZ loss

OCT indicated loss or discontinuity of macular EZ in 14 eyes (87.5%) of 8 patients at the initial visit, while the number of eyes with macular EZ impairment was reduced to 10 eyes (71.4%) of 6 patients at the final visit (Table 3). Compared with baseline values (N = 14), macular EZ loss remained unchanged in 4 eyes (28.6%) of 4 patients, shortened in 6 eyes (42.9%) of 5 patients, and lengthened in 4 eyes (28.6%) of 3 patients at the final visit. The mean length of macular EZ loss (N = 14) was 616.6 ± 531.8 μm at baseline and 594.6 ± 511.0 μm at the final visit, showing an estimated tendency to improve by 6.3 μm per year despite no statistically significant difference between the values (P = 0.791). In Case 4, macular EZ loss almost completely disappeared in both eyes with no treatment (Fig. 3). No correlation was detected in baseline values between BCVA and the length of macular EZ loss (P = 0.354, rho = 0.248) or between CMT and the length of macular EZ loss (P = 0.132, rho = -0.394).

Macular morphological findings

At the initial visit, OCT indicated inner lamellar cavity in 7 eyes (43.8%) of 5 patients, outer lamellar cavity in 6 eyes (37.5%) of 4 patients, protrusion of the inner retinal layer to the outer layer in 4 eyes (25.0%) of 3 patients, and punctate intraretinal hyper-reflectivity in 4 eyes (25.0%) of 3 patients. At the final visit, the number of eyes with inner and outer lamellar cavities was reduced to 6 eyes (37.5%) of 5 patients and 4 eyes (25.0%) of 3 patients, respectively (Table 3), while the number of eyes with retinal inner to outer protrusion and punctate hyper-reflectivity was unaltered.

Discussion

The present longitudinal study demonstrated the following important data in Japanese patients with MacTel-2: (1) the length of macular EZ loss improved in 43% of eyes with an estimated tendency to shorten by approximately 6 μm per year; (2) CMT, which was significantly reduced compared to that of normal eyes, increased in 21% of eyes and decreased in no eyes; (3) BCVA improved in 13% of eyes and worsened in no eyes; and (4) parafoveal retinal graying and foveal RPE depigmentation

improved in 29% of eyes and worsened in no eyes.

Macular EZ loss was shown to be a sensitive anatomical surrogate marker that gradually progressed over time in association with deteriorated visual function in patients with MacTel-2 [9, 14]. Generally, improvement in photoreceptor morphology would be quite rare in Caucasian patients with MacTel-2, because only one of 56 eyes showed its recovery during follow-up [14]. In the present study, however, EZ loss actually improved in almost half of the eyes that frequently coincided with reduction of inner and outer lamellar cavities, indicating the favorable trend of structural recovery in Japanese patients compared with Caucasian patients.

A genome-wide association study revealed genetic background associated with serine metabolism in patients with MacTel-2 [15]. In relation with this, the accumulation of cytotoxic deoxysphingolipids was detected in photoreceptor and RPE cells of mice with serine-free diet, which recapitulated human MacTel-2 in terms of low serine and high deoxysphingolipid levels in the systemic circulation [16]. Cytotoxic deoxysphingolipids were shown to elevate in plasma of patients with the metabolic syndrome [17], a known risk factor of MacTel-2 [18]. In addition to these genetic and environmental factors, the currently stated difference in clinical prognosis between Japanese and Caucasian patients may also be attributable to a racial difference in the metabolic capacity of RPE cells [19], as often suggested in other retinal diseases such as age-related macular degeneration [20], acute zonal occult outer retinopathy [21], and anti-enolase autoimmune retinopathy [22].

In addition to macular EZ loss, central retinal thinning is another known anatomical abnormality [23, 24], suggesting the progressive nature of atrophic volume loss, although no longitudinal studies have been done so far. Indeed, our comparison with normal controls demonstrated the significantly reduced CMT in MacTel-2 eyes. Interestingly, in our case series often accompanied by EZ restoration over time, one-fifth of eyes exhibited sequential CMT improvement (*i.e.*, ≥20% thickening) during follow-up. Moreover, the significant increase in the mean CMT was achieved at the final visit. These results suggested a substantial contribution of EZ

loss regression to the macular whole-thickness recovery. This speculation was actually true of the natural course of anatomical restoration in Case 4, showing eventual CMT improvement after spontaneous regression of macular EZ loss (Fig. 3). CMT would therefore be a potential biomarker to readily monitor the disease activity of MacTel-2, at least in a certain proportion of Japanese patients.

Visual prognosis in MacTel-2 also appeared to be better in our patients than in Caucasian patients, whose BCVA was shown to decrease in separate studies by 1.1 letters [7] and 2.2 letters [9] per year. In contrast, changes in BCVA in this case series were calculated to be an ‘increase’ by 0.3 letters per year during the mean follow-up period of 3.5 years (4.2 years [7] and 4.5 years [9] in the aforementioned reports), suggesting the possibility of visual preservation in Japanese patients with MacTel-2. The current results on visual function would reasonably agree with favorable anatomical changes in EZ loss and CMT.

In the present study, foveal RPE depigmentation was observed at the initial visit in all the eyes with Stage 2 or more (14 of 16 eyes). To the best of our knowledge, this particular finding has not been previously documented, possibly due to a difference in background coloration affected by the number of pigmented melanocytes in the choroid between Caucasian and Japanese populations. Therefore, this newly described RPE change may be funduscopically more prominent in Japanese patients than in Caucasian patients.

This study has some limitations including its retrospective design with a relatively small number of patients, possibly due to the rarity of Japanese patients with MacTel-2. The length, but not the area, of macular EZ loss was used as the indicator of macular photoreceptor morphology; however, our use of the length may not have affected the current results because of a tight correlation reported between the length and area of EZ loss in eyes with MacTel-2 [14]. Similarly, CMT changes were measured with the line scan through the fovea, but not with the 3-dimensional analysis capable of evaluating the entire macular region, which would theoretically be more suitable to monitor MacTel-2 lesion changes. We defined changes of ≥0.2 in log MAR BCVA, ≥20% in

CMT, and ≥20% or ≥100 μm in EZ loss as improved or worsened, because no criteria have yet been established to monitor sequential changes in MacTel-2. The newly set criteria in this study may possibly be modified or revised in the future. Finally, 3 patients (Cases 6-8) with the relatively short follow-up of 12-15 months may have given bias to our current estimation of clinical parameters, at least some of which would actually be changeable for a longer period of time in MacTel-2 patients.

In conclusion, the non-negligible proportion of eyes with MacTel-2 showed substantial improvements of both anatomical and functional parameters in our case series. These results suggest that Japanese patients with MacTel-2 have milder clinical features than Caucasian patients reported in the literature. Further studies are warranted to verify our current data.

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Declarations

Funding: No funding was received for this research.

Conflict of interest/Competing interests: The authors declare that they have no conflict of interest or competing interests.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The current study was approved by the ethics committee of Hokkaido University Hospital (#018-0207).

Consent to participate: Informed consent was obtained from all individual participants included in the study.

Consent for publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

All data generated or analyzed during this study are included in this published article.

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Figure legends

Fig. 1 Images of the right (**A, C, E**) and left (**B, D, F**) eyes of a 57-year-old woman (Case 4) with macular telangiectasia type 2 (MacTel-2), later showing spontaneous regression. (**A, B)** Fundus photographs showing foveal depigmentation at the level of the retinal pigment epithelium (RPE) and surrounding retinal graying in both eyes at the initial visit. (**C, D)** Late-phase fluorescein angiography (FA) showing dye leakage at the temporal side of the fovea in both eyes at the initial visit. (**E, F)** Fundus autofluorescence (FAF) showing hyper-autofluorescence, corresponding to the sites of retinal graying in both eyes and RPE depigmentation in the left eye after 32 months.

Fig. 2 Images of the right (**A, C, E**) and left (**B, D, F**) eyes of the same patient with Figure 1 (Case 4) 47 months after the initial visit. (**A, B)** Foveal RPE depigmentation and parafoveal retinal graying subsided in both eyes compared with those at the initial visit. (**C, D)** On late-phase FA, dye leakage weakened in both eyes. (**E, F)** On FAF, hyper-autofluorescence decreased in both eyes.

Fig. 3 Changes in horizontal images through the fovea on optical coherence tomography (OCT) in the right (**A, C, E**) and left (**B, D, F**) eyes of the same patient with Figures 1 and 2 (Case 4). (**A, B**) At the initial visit, loss of the macular ellipsoid zone (EZ) were observed with outer lamellar cavity (OLC) in both eyes and inner lamellar cavity (ILC) in the left eye. The length of EZ loss (double-headed arrows) was 315 and 316 μm in the right and left eyes, respectively. (**C, D**) Twenty-four months after the initial visit, EZ loss and OLC disappeared in the right eye and markedly improved in the left eye (arrow). (**E, F**) Forty-seven months after the initial visit, EZ recovered in both eyes.

Fig. 4 Images of the left eye of a 61-year-old woman with MacTel-2 (Case 2) showing functional and anatomical improvements despite stage progression. (**A–C**) Fundus photographs. At the initial visit, foveal RPE depigmentation, parafoveal retinal graying, crystalline deposits, and right-angle venules were observed at the macular region (**A**). Best-corrected visual acuity (BCVA) was 0.6.

After 20 months, RPE depigmentation and retinal graying faded with improvement of BCVA to 1.0, although intraretinal pigmentation developed at the temporal side of the fovea, indicative of progression of disease stage (**B**). Seventy-six months after the initial visit, RPE depigmentation and retinal graying almost disappeared with stably maintained vision of 1.0 despite concurrent increases in intraretinal pigmentation and crystalline deposits (**C**). (**D**) Late-phase FA showing dye leakage at the temporal side of the fovea at the initial visit. (**E, F**) Images of FAF. Hypo- and hyper-autofluorescent areas were observed at the temporal fovea 36 months after the initial visit (**E**). Seventy-six months after the initial visit, the extent of hyper-autofluorescence weakened (**F**). (**G, H**) Horizontal images through the fovea on OCT. Eleven months after the initial visit (at baseline for comparison), EZ loss or discontinuity was seen at 1542 μm (double-headed arrow) together with ILC and intraretinal hyper-reflective spots around the temporal fovea (**G**). Seventy-six months after the initial visit, EZ loss or discontinuity shortened to 1295 μm (double-headed arrow) with resolution of ILC. Intraretinal hyper-reflective spots increased (**H**), corresponding to the formation of pigment plaques (**C**).

Table 1. Clinical characteristics and changes in visual acuity in patients with macular telangiectasia type 2 (MacTel-2)

Case	Age (years)	Sex	Follow-up (months)	Systemic medical history	BCVA (logMAR)						Changes in BCVA (RE/LE)
					Initial		Baseline		Final		
					RE	LE	RE	LE	RE	LE	
1	73	F	57	Varicose veins	0.40	0.52	0.40	0.52	0.52	0.70	→/→
2	61	F	76	Hashimoto disease, DL	0.22	0.22	0.15	0.10	0.15	0.00	→/↑
3	75	M	67	DL	0.10	0.00	0.10	0.00	0.22	-0.08	→/→
4	57	F	60	Intestinal Behçet's disease, DM	-0.08	-0.08	-0.08	-0.08	-0.08	-0.08	→/→
5	69	M	43	Aortic valve stenosis, Cerebral infarction, DL, HT, DM	0.00	0.22	-0.08	0.15	-0.08	0.30	→/→
6	59	M	12	None	-0.08	0.05	0.00	0.22	-0.08	0.15	→/→
7	66	F	15	Lung adenocarcinoma, Polyposis coli syndrome, Osteoporosis, DL	0.70	1.00	0.52	1.00	0.52	0.52	→/↑
8	75	F	12	Atrial fibrillation, HT	0.10	0.40	0.10	0.40	0.10	0.52	→/→
	66.9±7.3	3:5 (M:F)	42.8±26.3		0.23±0.31		0.21±0.29		0.21±0.27		↑: 2 eyes →: 14 eyes ↓: 0 eyes

RE, right eye; LE, left eye; BE, both eyes; M, male; F, female; BCVA, best-corrected visual acuity; DL, dyslipidemia; HT, hypertension;

DM, diabetes mellitus ; PSL, prednisolone; IVTA, intravitreal injection of triamcinolone acetonide;

STTA, posterior sub-Tenon injection of triamcinolone acetonide; ↑, improved; →, unchanged; ↓, worsened.

Table 2. Changes in fundus photographic findings in patients with MacTel-2

Case	Macular retinal graying (Initial/Final)		Macular RPE depigmentation (Initial/Final)		Changes in macular lesions (Initial/Final)	RAV (Initial/Final)		Intraretinal pigmentation (Initial/Final)		Crystalline deposits (Initial/Final)		Changes in disease stages (Initial/Final)	
	RE	LE	RE	LE	(RE/LE)	RE	LE	RE	LE	RE	LE	RE	LE
1	+/+	+/+	+/+	+/+	→/→	-/-	-/-	-/-	-/-	-/-	-/-	2/2	2/2
2	+/-	+/-	+/-	+/-	↑ / ↑	+/+	+/+	-/+	-/+	-/+	+/+	3/4	3/4
3	+/+	-/-	+/+	-/-	→/→	-/-	-/-	-/-	-/-	-/-	-/-	2/2	1/1
4	+/-	+/-	+/-	+/-	↑ / ↑	-/-	-/-	-/-	-/-	-/-	-/-	2/2	2/2
5	+/NE	+/NE	+/NE	+/NE	NA/NA	-/NE	-/NE	-/NE	-/NE	-/NE	-/NE	2/NA	2/NA
6	-/-	+/+	-/-	+/-	→/→	-/-	+/+	-/-	-/-	-/-	-/-	1/1	3/3
7	-/-	-/-	+/+	+/+	→/→	-/-	-/-	-/-	-/-	-/-	-/-	2/2	2/2
8	+/+	-/-	+/+	+/+	→/→	+/+	-/-	+/+	-/-	-/-	-/-	4/4	2/2
	Initial: 11 eyes Final: 5 eyes		Initial: 14 eyes Final: 7 eyes		↑ : 4 eyes →: 10 eyes ↓ : 0 eyes	Initial: 4 eyes Final: 4 eyes		Initial: 1 eye Final: 3 eyes		Initial: 1 eye Final: 2 eyes		↑ : 0 eyes →: 12 eyes ↓ : 2 eyes	

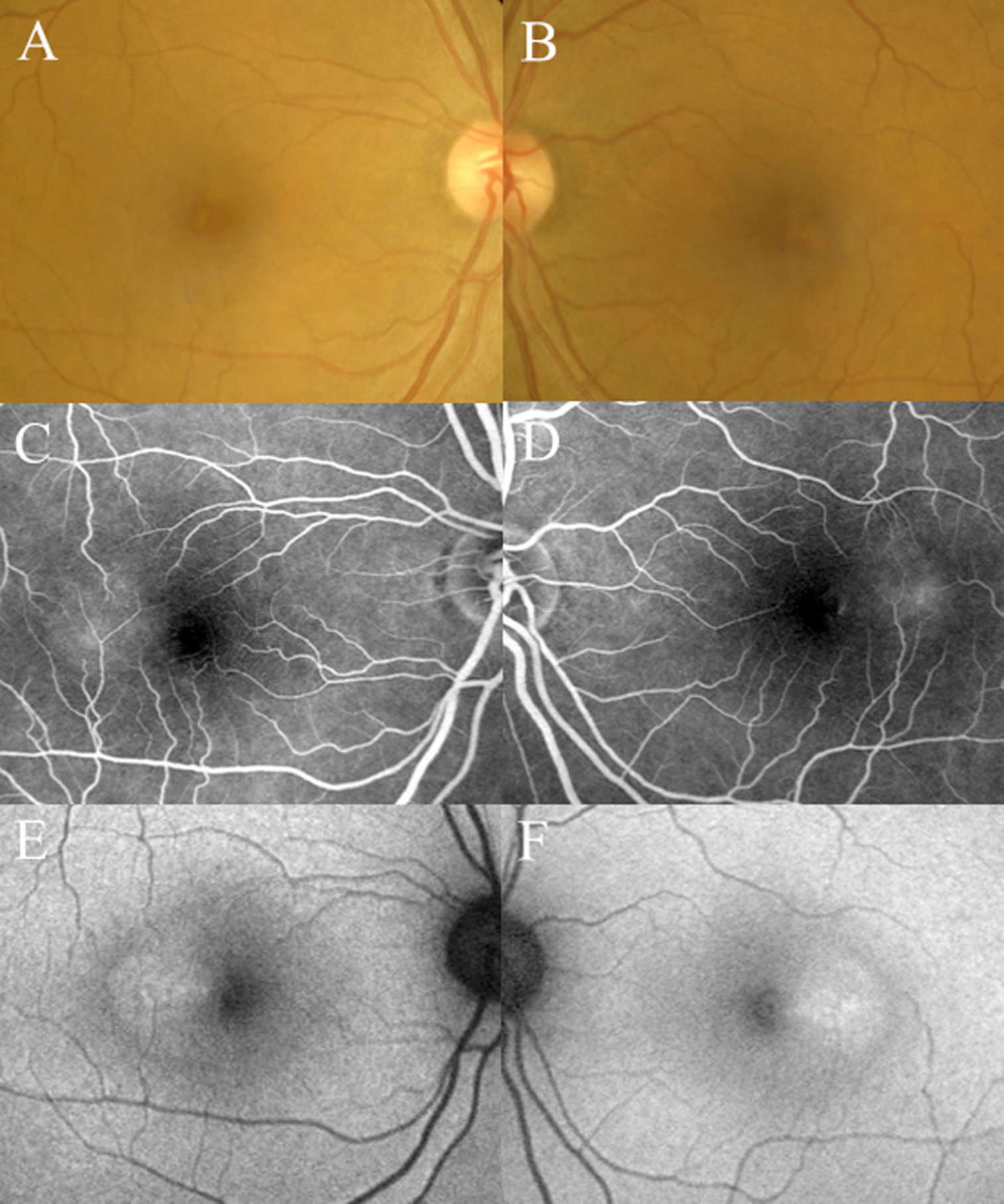
RE, right eye; LE, left eye; RPE, retinal pigment epithelium; RAV, right-angle venules; NE, not evaluated; NA, not applicable;
↑, improved; →, unchanged; ↓, worsened.

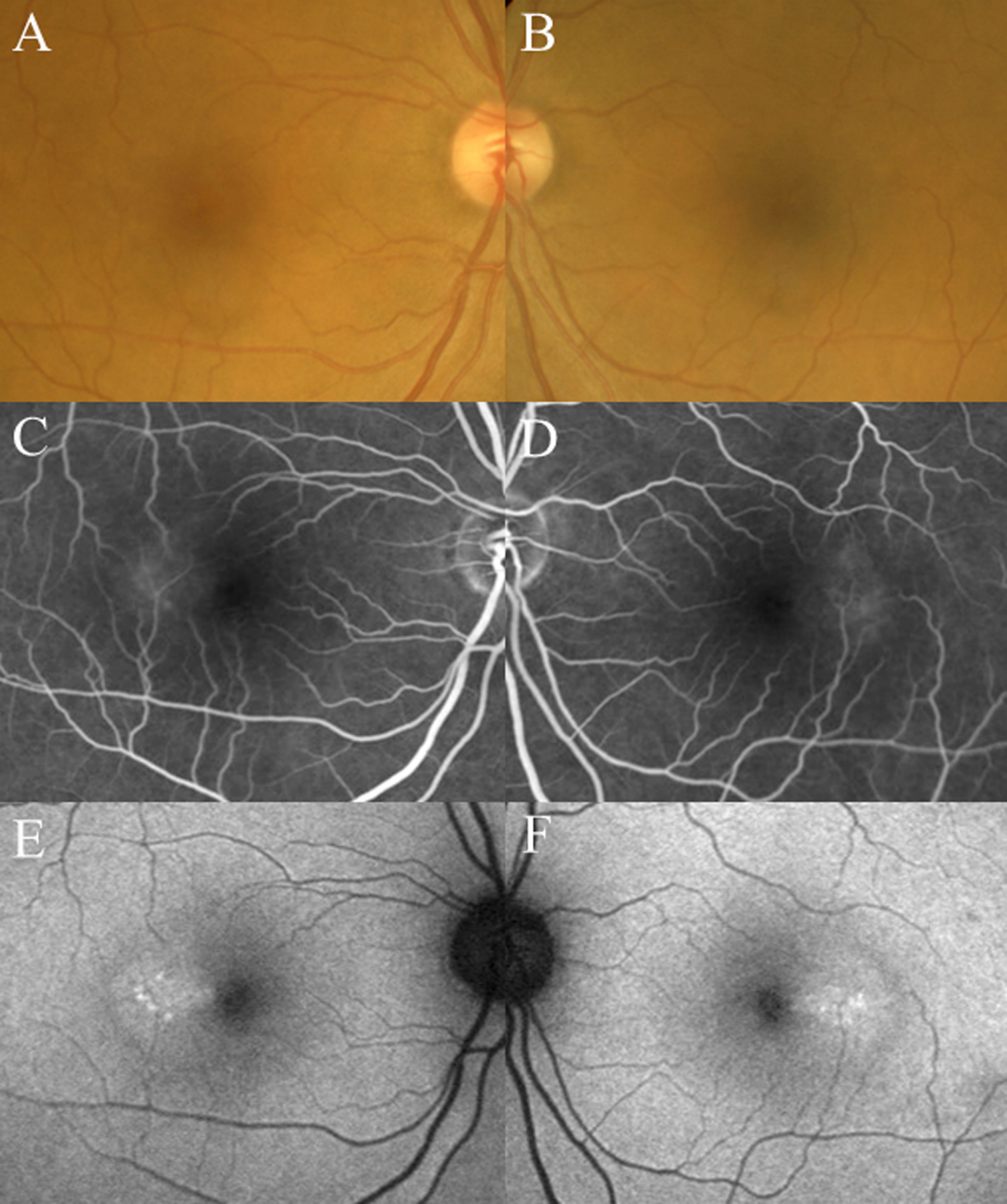
Table 3. Changes in macular morphological findings in patients with MacTel-2

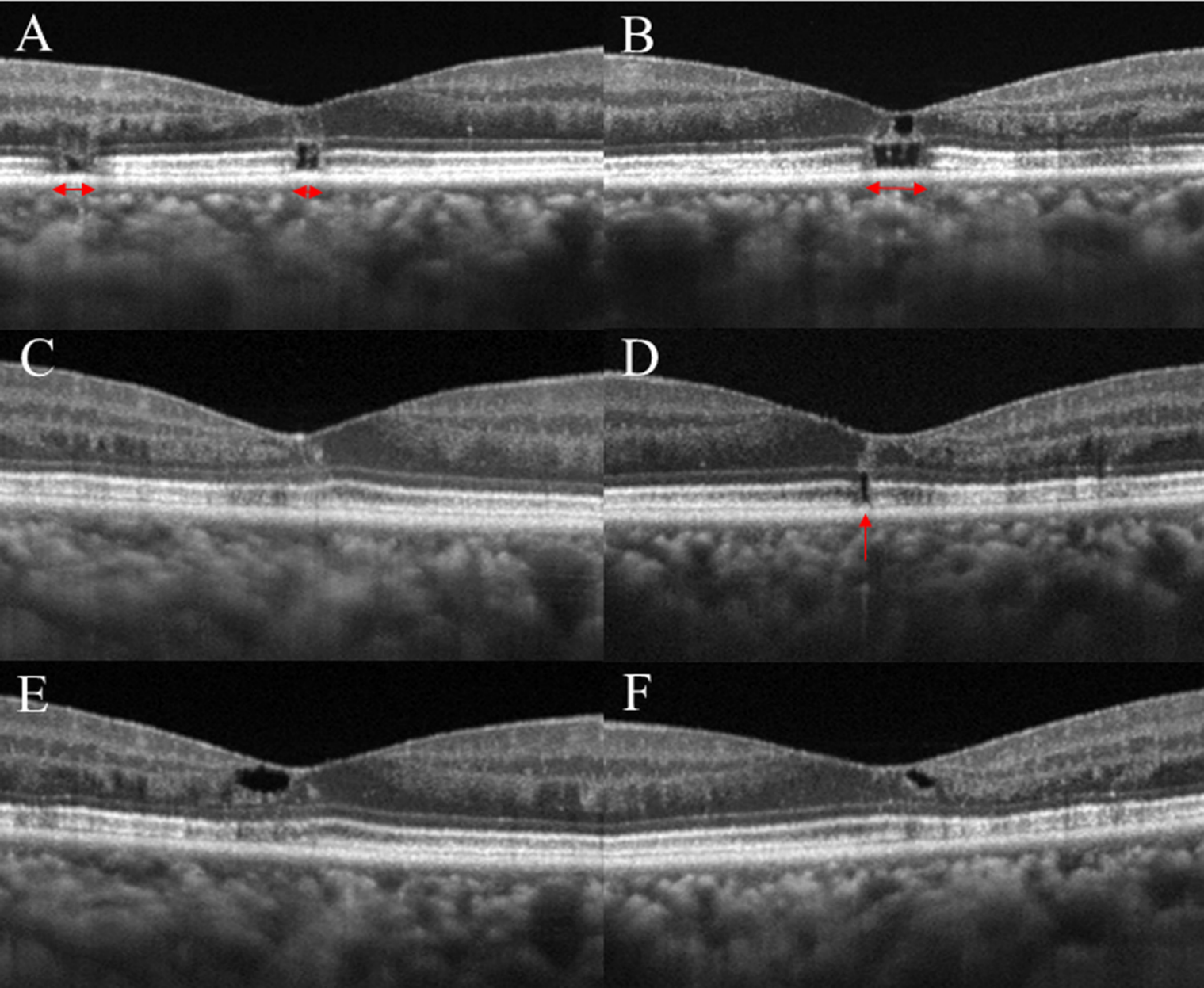
Case	CMT (μm)				Changes in CMT (RE/LE)	Length of EZ loss (μm)				Changes in EZ (RE/LE)	ILC (Baseline/Final)		Changes in ILC (RE/LE)	OLC (Baseline/Final)		Changes in OLC (RE/LE)
	Baseline		Final			Baseline		Final								
	RE	LE	RE	LE		RE	LE	RE	LE		RE	LE		RE	LE	
1	138	140	142	158	→/→	215	838	147	920	↑/→	-/-	-/+	→/↓	-/-	-/+	→/↓
2	127	132	154	136	↑/→	1182	1542	1356	1295	↓/↑	+/+	+/-	→/↑	-/-	-/-	→/→
3	216	235	202	235	→/→	154	0	346	0	↓/→	-/-	-/-	→/→	-/-	-/-	→/→
4	183	154	200	191	→/↑	315	316	0	0	↑/↑	-/-	+/-	→/↑	+/-	+/-	↑/↑
5	192	194	NE	NE	NA/NA	647	853	NE	NE	NA/NA	+/+	+/-	→/↑	+/+	+/+	→/→
6	177	140	175	140	→/→	0	935	0	786	→/↑	-/-	-/-	→/→	-/-	+/+	→/→
7	191	193	231	200	↑/→	369	316	708	627	↓/↓	-/+	+/+	↓/→	-/-	+/-	→/↑
8	181	210	181	206	→/→	1488	967	1213	926	↑/→	-/-	+/+	→/→	-/-	-/-	→/→
	175.2±32.9		182.2±32.6		↑: 3 eyes →: 11 eyes ↓: 0 eyes	633.6±498.6		594.6±511.1		↑: 6 eyes →: 4 eyes ↓: 4 eyes	Baseline: 7 eyes Final: 6 eyes		↑: 3 eyes →: 11 eyes ↓: 2 eyes	Baseline: 6 eyes Final: 4 eyes		↑: 3 eyes →: 12 eyes ↓: 1 eyes

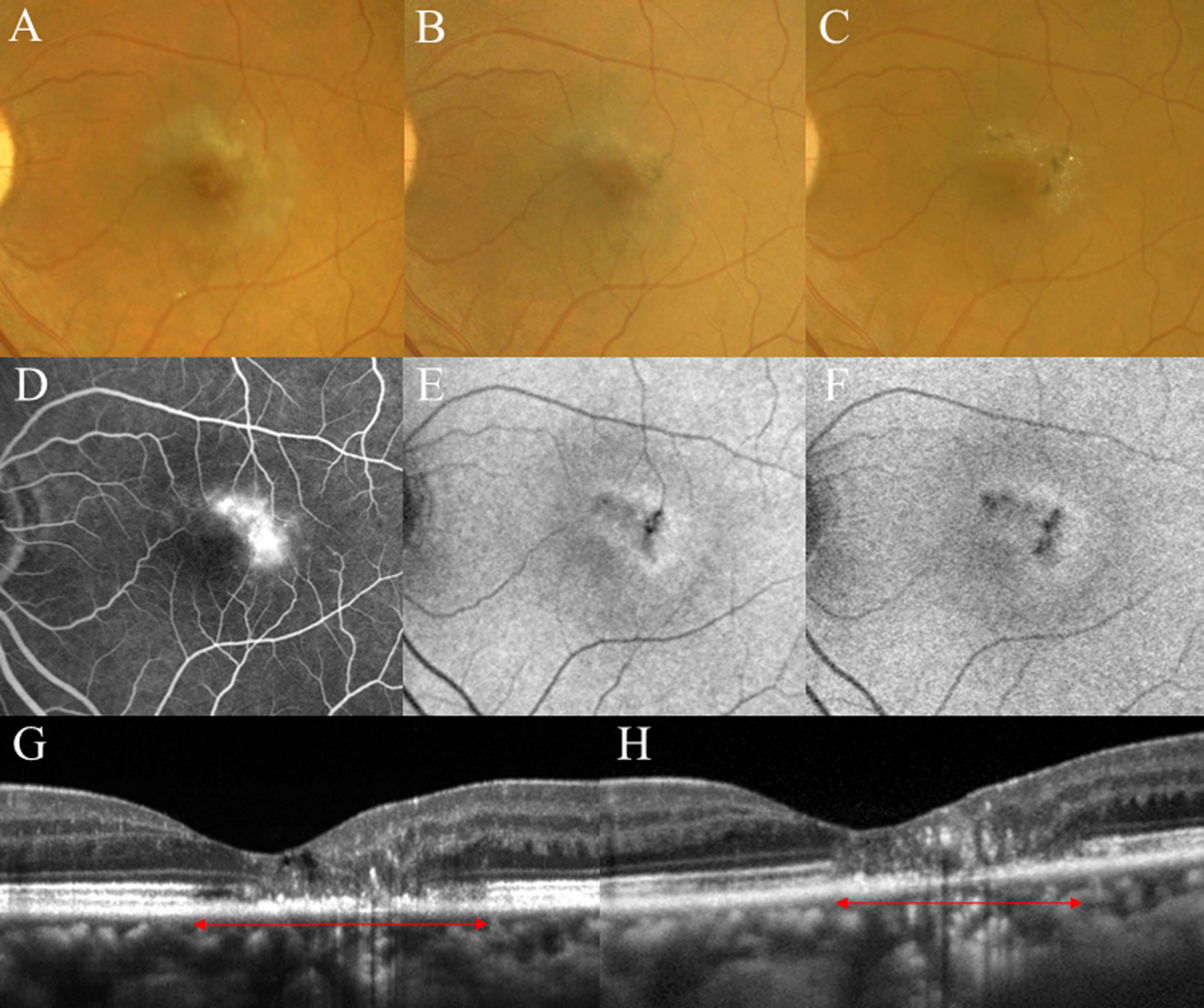
ILC, inner lamellar cavity; OLC, outer lamellar cavity; CMT, central macular thickness; EZ, ellipsoid zone;

RE, right eye; LE, left eye; NE, not evaluated; NA, not applicable; ↑, improved; →, unchanged; ↓, worsened.


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