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Retinal pigment epithelial changes in chronic Vogt-Koyanagi-Harada disease: fundus autofluorescence and spectral domain optical coherence tomography findings

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Abstract

Purpose—To determine whether fundus autofluorescence (FAF) and spectral-domain optical coherence tomography (SD-OCT) imaging allows better assessment of RPE and outer retina (OR) in subjects with chronic VKH compared to examination and angiography alone.

Methods—Cross-sectional analysis of a series of seven consecutive patients with chronic VKH undergoing FAF and SD-OCT. Chronic VKH was defined as during >3 months. Color fundus photographs were correlated to FAF and SD-OCT images. The images were later correlated to fluorescein angiography (FA) and indocyanine green angiography (ICG-A).

Results—All patients had sunset glow fundus, which resulted in no apparent corresponding abnormality on FAF or SD-OCT. Lesions with decreased autofluorescence signal were observed in 11 eyes (85%), being associated with loss of the RPE and involvement of OR on SD-OCT. In 5 eyes (38%) some of these lesions were very subtle on clinical examination but easily detected by FAF. Lesions with increased autofluorescence signal were seen in 8 eyes (61.5%), showing variable involvement of the OR on SD-OCT and corresponding clinically to areas of RPE proliferation and cystoid macular edema.

Conclusion—Combined use of FAF and SD-OCT imaging allowed noninvasive delineation of RPE/OR changes in patients with chronic VKH, which were consistent with previous histopathological reports. Some of these changes were not apparent on clinical examination.

Keywords

fundus autofluorescence; retinal pigment epithelium; spectral domain optical coherence tomography; Vogt-Koyanagi-Harada disease; uveitis

Vogt-Koyanagi-Harada disease (VKH) is a bilateral granulomatous panuveitis associated with autoimmunity against the melanocytes.^{1, 2} The acute uveitic stage of VKH is characterized by

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bilateral anterior and/or posterior segment involvement with exudative retinal detachment.^{1, 3, 4} Patients adequately treated with high-dose systemic corticosteroids undergo resolution of this acute stage. However, some may enter a chronic stage, particularly those who receive either delayed or inadequate treatment with systemic immunosuppressive agents.^{3, 5} In this chronic stage, progressive choroidal depigmentation ensues, leading to a change classically described as sunset glow fundus. During this stage, vitiligo and polyosis may also occur,^{1, 3} and some patients develop vision-threatening retinal complications, including choroidal neovascularization, subretinal fibrosis, severe chorioretinal atrophy, and glaucoma.⁶⁻⁸ These retinal complications are preceded by alterations in the retinal pigment epithelium (RPE) in the form of granular pigmentary changes, hypo- or hyperplasia, or focal loss of the RPE cells.¹ Proper evaluation of the RPE during chronic or chronic recurrent VKH may help prevent these retinal complications by guiding the modulation of anti-inflammatory therapy.

Fundus autofluorescence imaging (FAF) and spectral domain optical coherence tomography (SD-OCT) have emerged as valuable tools for noninvasive in vivo imaging of the RPE and outer retina.^{9, 10} The FAF signal is correlated with the presence or accumulation of lipofuscin and other fluorophores in the RPE and outer retina, providing functional assessment of the RPE layer and possibly additional information not obtained with conventional imaging techniques, such as fundus photography, fluorescein angiography (FA) and optical coherence tomography.^{9, 11, 12} Fundus autofluorescence imaging has been shown to allow better delineation of areas of retinal atrophy, as well as improved visualization of subclinical areas of adjacent RPE injury, which could possibly precede the occurrence of visible lesions.¹³

Commercial SD-OCT instruments feature improvements in sensitivity and resolution that enhance visualization of retinal layer detail compared with the latest generation time-domain OCT instruments.^{10, 14} In patients with acute VKH, disruption of the outer retina, especially the inner/outer segment (IS/OS) junction, and irregularities of the RPE layer have been observed by SD-OCT;¹⁵ but it is unknown whether these changes would persist or correlate with abnormalities manifested later in the chronic or chronic recurrent stages of the disease.

A combination of FAF and SD-OCT has not been reported for the evaluation of patients with chronic VKH. This approach may be advantageous, allowing precise noninvasive these patients, without the risks of angiographic tests. The goal of the present study was to report the use of concomitant FAF and OCT imaging to characterize the status of the RPE and outer retina in a series of patients with chronic VKH and to correlate those changes with the current knowledge on histopathology of VKH.

METHODS

The study protocol was approved by the Institutional Review Board of the University of Southern California and conformed to the Declaration of Helsinki. We conducted a retrospective chart review of all consecutive patients with chronic VKH undergoing FAF and SD-OCT imaging at the Doheny Eye Institute/University of Southern California from January 2007 to December 2008. From 16 patients with chronic VKH seen during the above period, 7 had undergone such testing and could be included in this study. The remaining 9 were excluded because FAF/SD-OCT test was not performed (8 patients) or because of uncertain diagnosis (1 patient).

In all patients the diagnosis of VKH had been established according to reported diagnostic criteria.³ For this study, chronic VKH was defined as duration of intraocular inflammation greater than three months.

Demographic and clinical data, including age, sex, ethnicity, past medical and ocular history, visual acuity, and results of slit-lamp biomicroscopy and ophthalmoscopy, were collected from medical charts and anonymously tabulated in an electronic database.

All FAF and SD-OCT images had been acquired using the Spectralis HRA+OCT (Heidelberg Engineering, Vista, CA). Autofluorescence signal of each lesion was classified as increased, decreased or similar to the background. The FAF and SD-OCT findings were initially correlated to each other, as well as to color fundus photographs. Subsequently, results of other imaging modalities such as fluorescein angiography (FA), and indocyanine green angiography (ICG-A) were also analyzed and compared to FAF, SD-OCT and color fundus photographs.

RESULTS

Of 7 patients with chronic VKH who underwent FAF/SD-OCT testing, 5 were female (71.4%) and 4 (57.1%) were Hispanic. Their ages varied from 29 to 46 years (mean: 37.3 ± 7 years; median: 41 years). Three patients had active intraocular inflammation at the time of FAF and SD-OCT testing, and six were on immunosuppressive drugs and/or oral prednisone. All seven patients had been treated with high-dose oral steroids during the acute uveitic stage of VKH, 4 months to 10 years before FAF/SD-OCT imaging (mean: 46.2 months; median: 43 months). Relevant demographic and clinical data are summarized in Table 1.

All 13 eyes of the 7 patients exhibited various degrees of sunset glow fundus (one eye was blind due to neovascular glaucoma, allowing no view of the fundus). None of the eyes showed abnormal autofluorescence signal in correspondence to the sunset glow fundus seen on clinical examination (Figures 1, 2 and 3). Moreover SD-OCT revealed intact retinal architecture at these sites. Most of the eyes (11 eyes of 6 patients) showed additional fundus changes, including lesions with decreased and/or increased autofluorescence signal (Table 2).

Fundus lesions with decreased autofluorescence signal were detected in all patients except one and manifested in different patterns (Table 2). Eleven eyes (85%) in 6 patients demonstrated a peripapillary halo of decreased autofluorescence signal, corresponding clinically to peripapillary atrophy. This halo correlated with thinning of the RPE/Bruch's membrane (BM) layer on SD-OCT (RPE atrophy), as well as with loss of outer retinal layers (IS/OS junction, external limiting membrane, and the outer nuclear layer). At these sites FA and ICG-A respectively depicted hyperfluorescence (window defects) and hypofluorescence (nonperfusion of the choriocapillaris) (Figure 3). Multiple nummular and/or irregular foci of decreased autofluorescence signal were seen in 9 eyes (69.2%) of 5 patients (71.4%). On SD-OCT, these foci correlated with thinning of the RPE/BM layer (RPE atrophy) and variable involvement of the outer retina. This involvement ranged from sparing of the IS/OS junction, external limiting membrane and outer nuclear layer to selective loss of one or more of these layers. Fluorescein angiogram and ICG-A revealed a pattern of hyperfluorescence (window defect) and hypofluorescence (choriocapillaris nonperfusion), respectively (Figures 1, 2 and 3). When present in areas of sunset glow fundus, these hypopigmented lesions were sometimes subtle on regular fundus examination but were easily detected by FAF (Figure 1). Some of the atrophic scars showed a pigmented component in 4 eyes (3 patients), also with decreased autofluorescence signal. On SD-OCT, a thickening of the RPE/BM layer (RPE hyperplasia or hypertrophy) and variable involvement of the outer retina could be appreciated. The hyperpigmented component of these lesions invariably revealed blockage of fluorescence on FA and ICG-A (Figure 2).

Fundus lesions with increased autofluorescence signal were detected in 8 eyes (61.5%) of 5 patients (71.4%) and were associated with a wide range of RPE and outer retinal abnormalities. Proliferation of RPE, manifesting as pigmented patches, irregular tracks, or bands (subretinal

fibrosis) was associated with increased autofluorescence signal relative to adjacent areas. In these cases, SD-OCT revealed a thickening of RPE/BM layer (RPE hyperplasia), usually with an intact outer retina. Fluorescein angiography disclosed corresponding hypofluorescence (blockage) (Figure 4). Increased autofluorescence signal was also observed in a granular pattern that correlated with a loss of the IS/OS junction in one patient and irregularities on the top of RPE/BM layer in another one. One patient with cystoid macular edema also exhibited increased autofluorescence signal of the intraretinal foveal cystoid spaces.

The last observed pattern was that of fundus lesions displaying autofluorescence signal similar to the background of normal adjacent areas. As mentioned above, the sunset glow fundus displayed this normal autofluorescence signal (Figures 1, 2 and 3). A similar autofluorescence signal was also seen in one patient, in correspondence to a large area of sectoral atrophy of the neural retina, RPE, and choroid, with visualization of the underlying sclera. Fluorescein angiography and ICG-A showed hypofluorescence of that atrophic area, denoting atrophy of choriocapillaris/choroid. In addition, one patient with a disciform scar from previously treated choroidal neovascularization exhibited autofluorescence signal of the subretinal gliotic tissue which was similar to the normal background. At this site, the overlying outer retina was relatively preserved. However the lesion was surrounded by an area of decreased autofluorescence signal (RPE atrophy). Fluorescein angiography and ICG-A revealed mixed hypo- and hyperfluorescence.

When comparing FAF, SD-OCT, FA and ICG-A, the first three were concordant in the detection of fundus lesions, although the interpretation of the lesions differed upon the imaging modality (Figures 1-4). Regarding ICG-A, it often revealed less lesions than FAF, SD-OCT and FA, unless there was damage to the choriocapillaris, which led to foci of hypofluorescence (Figures 1-4).

DISCUSSION

We looked at the combination of FAF and SD-OCT to assess the status of the RPE and outer retina in a series of patients with chronic VKH. In addition to choroidal depigmentation and atrophic nummular lesions involving the RPE that are seen in the chronic stage of VKH, there is a persistent diffuse chronic granulomatous inflammation of the uvea, associated with RPE proliferation.^{7, 8} This combination of RPE changes and retinal atrophy has been associated with decreased vision in chronic VKH patients either directly^{6, 16, 17} or indirectly, as a forerunner or epiphenomenon of severe vision-threatening complications, such as choroidal neovascularization and subretinal fibrosis.^{6, 18, 19} Our study analyzed RPE / outer retinal changes in light of FAF / SD-OCT, but was not designed to verify whether these changes were specifically correlated to a worse prognosis.

All patients included in the present study were in the chronic stage of VKH. Most were taking prednisone and/or immunosuppressive drugs. Imaging studies had been performed long after the acute phase in most patients (mean: 46.2 months later) (Table 1).

All eyes in this study exhibited sunset glow fundus unassociated with any FAF abnormality. This finding is in line with histopathologic studies showing that sunset glow fundus in VKH is due to postinflammatory depigmentation or loss of choroidal melanocytes rather than to RPE involvement.^{8, 20} Comparison of color fundus photography to FAF imaging facilitated the delineation of areas with actual RPE loss (RPE atrophy) from areas with mere choroidal depigmentation (sunset glow fundus) (Figure 1). Moreover, especially in areas with a background of sunset glow fundus, foci of RPE atrophy are less apparent and may be overlooked on fundus examination (and color fundus photography), but are easily demonstrated by FAF (Figure 1).

Fundus autofluorescence imaging in our patients revealed various patterns of abnormal autofluorescence signal (Table 2 and Figures 1, 2, 3 and 4). In general, lesions with decreased autofluorescence signal were associated with RPE loss and often accompanied by involvement of the outer retinal layers on SD-OCT (Figures 1, 2 and 3). These findings are consistent with the histopathology of the round depigmented atrophic lesions in the sunset glow fundi of chronic VKH patients.⁷ In the past these lesions were clinically confused with Dalén-Fuchs nodules; but the latter are significantly smaller, occur mostly in the acute uveitic phase, and represent elevated mounds of RPE cells with infiltration of inflammatory cells overlying Bruch's membrane.⁷ Loss of the RPE and disruption of the outer retina in the former may result from the inflammatory insult in the acute stage or from recurrent inflammation in the chronic-recurrent stage of VKH.⁷ Even when those atrophic scars had a pigmented component, decreased autofluorescence signal was the invariable finding (Figure 2), as hyperplastic RPE in these areas of disrupted outer retina may lack fluorophores, as it does not have access to the outer segments of the photoreceptors to phagocytose them.

Increased hyperautofluorescence signal was observed in the fundi of some patients and may be due to various pathogenetic mechanisms (Table 2). Proliferation of the RPE, observed in the form of pigmented plaques or tracks, manifested increased autofluorescence signal and corresponded to areas of focal thickening of the RPE/BM layer on SD-OCT, with variable involvement of the outer retina (Figure 4). We hypothesize that the abnormally higher hyperautofluorescence of these areas of RPE proliferation might be due either to the presence of fluorophores within the RPE cells or to their accumulation in the outer segments of photoreceptors. Another observed pattern of increased autofluorescence was that of areas of a granular signal, which might also reflect some abnormality at the level of the RPE and/or outer retina. Whether RPE in these areas will remain unchanged or will evolve to hyperplasia, fibrous metaplasia, or atrophy remains to be seen. In age-related macular degeneration, increased autofluorescence signal surrounding areas of geographic atrophy has been observed to evolve to atrophy as disease progresses.¹¹ Increased autofluorescence was also observed in the fovea of a patient with CME, probably due to displacement of the luteal pigment in areas of cystoid spaces (disrupting the physiologic foveal hypoautofluorescence).¹²

Finally the finding of autofluorescence signal similar to the background in the large area of chorioretinal atrophy in one patient is likely due to the autofluorescent properties of scleral fibers, as previously described in the setting of lacunae in lesions of congenital hypertrophy of the RPE.²¹ In the eye with a disciform scar, the autofluorescence signal is possibly associated with some preservation of the outer retina. However there was decreased autofluorescence signal adjacent to the subretinal tissue, indicating RPE atrophy associated with disruption of the outer retina. These changes were confirmed by SD-OCT. Similar RPE and outer retinal changes have been described in choroidal neovascularization caused by AMD and are more pronounced in late-stage cases.²²

The combined approach of FAF / SD-OCT offers advantages over FA and ICG-A. First, both FAF and SD-OCT are noninvasive tests that may be repeated frequently to closely monitor the status of the RPE and outer retina, in contrast to angiographic tests. In addition, FAF is probably a better indicator of the functional status of the RPE than FA and ICG-A, which only show the indirect consequences of RPE damage on the kinetics of the dye (either fluorescein or indocyanine green). SD-OCT, in turn, provides anatomic information with details close to histopathological sections. Though FAF did not show any additional lesion when compared to FA (as observed in Figures 1-4), interpretation and follow-up of the fundus changes may be enhanced with FAF. It is known that ICG-A may be highly useful in the assessment of inflammatory choroidal involvement in chronic VKH,²³ but it was not as good as FAF or FA in the evaluation of RPE changes, unless there is involvement of the choriocapillaris (Figures 1-4).

The present study has some limitations, most notably the retrospective cross-sectional design and the small and heterogeneous sample, which did not allow correlation of FAF / SDOCT changes with visual acuity and clinical complications. Moreover, more peripheral lesions could not be evaluated by FAF imaging or by SD-OCT. However, the clinical appearance of these peripheral lesions was similar to that of more posteriorly located ones that were studied by FAF and SD-OCT. In addition, vision threatening retinal complications in chronic VKH, such as choroidal neovascularization and subretinal fibrosis, occur primarily in the posterior pole,^{1, 6} which could be appropriately studied by the combination of these two imaging techniques.

This combined approach of FAF and SD-OCT offers valuable information on the status of the RPE and outer retina in patients with chronic VKH. Such information may provide insights into the pathophysiology of RPE alterations in this disease and may allow an accurate observation of the extent and severity of RPE/outer retinal changes, some of which may be subclinical. These FAF/SD-OCT findings are consistent with observations in previous histopathologic reports. Further prospective studies are warranted to assess the prognostic significance of these findings.

Brief statement

Combined FAF and SD-OCT allowed noninvasive evaluation of RPE and outer retinal changes in a series of patients with chronic VKH, easily disclosing the extent of RPE damage and occasionally detecting subclinical lesions. These imaging techniques could prove useful in the close follow-up of patients with chronic VKH with RPE alterations.

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Fig. 1.

Right eye of a 42-year-old female with chronic Vogt-Koyanagi-Harada disease (Case 1). **A.** Color fundus photograph shows sunset glow fundus, a peripapillary halo and subtle hypopigmented lesions inferiorly. **B.** Fundus autofluorescence imaging reveals decreased autofluorescence signal of these lesions and of the peripapillary halo. Autofluorescence of the areas of sunset glow fundus is similar to that of normal areas. **C.** Infrared imaging of the fundus, with corresponding spectral domain optical coherence tomography (SD-OCT) image. The red arrow points to a hypopigmented lesion and the red box marks the area shown in higher magnification below. **D.** Intermediate-phase fluorescein angiography, revealing hyperfluorescence (window defect) of the peripapillary halo and hypopigmented lesions. **E.** Late-phase indocyanine green angiography revealing hypofluorescence (choriocapillaris nonperfusion) of the peripapillary halo and hypopigmented lesions. **F.** Magnified view of red box indicated in C. The red arrow corresponds to the hypopigmented lesion in C. Thinning of retinal pigment epithelium/Bruch's membrane layer (RPE atrophy) is demonstrated between the black arrows. The remaining retina is preserved.

Fig. 2.

Right eye of a 41-year-old female with chronic Vogt-Koyanagi-Harada disease (Case 2). **A.** Color fundus photograph shows sunset glow fundus inferior to the optic disc. In addition, a subtle peripapillary halo and focal lesions with variable pigmentation are seen. **B.** Fundus autofluorescence imaging demonstrates decreased autofluorescence of both pigmented and atrophic scars. Note normal autofluorescence in area of sunset glow fundus. **C.** Infra-red imaging of the fundus, with corresponding spectral domain optical coherence tomography (SD-OCT) image. The red arrows point to hyperpigmented lesions and the black arrow indicates an atrophic focus. The red box marks the area shown in higher magnification below. **D.** Intermediate-phase fluorescein angiography, revealing hyperfluorescence (window defect) of the peripapillary halo and hypopigmented lesions. The hyperpigmented lesions block fluorescence. **E.** Mid-phase indocyanine green angiography revealing hypofluorescence of atrophic lesions, peripapillary atrophic halo, and of pigmented lesions. **F.** Magnified view of the red box delineated in C. The red arrows indicate pigmented scars, with thickening of retinal pigment epithelium/Bruch's membrane (RPE/BM) layer (RPE hyperplasia/hypertrophy) and disruption of outer retinal layers. The hypopigmented focus shows thinning of RPE/BM layer (RPE atrophy) and disruption of outer retinal layers.

Fig. 3.

Left eye of a 41-year-old female with chronic Vogt-Koyanagi-Harada disease (Case 2). **A.** Color fundus photograph discloses sunset glow fundus, peripapillary halo, multiple nummular atrophic lesions and few pigmented lesions. **B.** Fundus autofluorescence imaging reveals decreased autofluorescence of atrophic nummular scars, pigmented scars, and peripapillary halo. Area of sunset glow fundus has normal autofluorescence. **C.** Infrared imaging of the fundus, with corresponding spectral domain optical coherence tomography (SD-OCT) image. The red arrows delineate the area of peripapillary atrophy shown in the SD-OCT image, while the black arrows delineate the nummular atrophic scar. The red box marks the area shown in higher magnification below. **D.** Intermediate-phase fluorescein angiography, revealing hyperfluorescence (window defect) of the peripapillary halo and hypopigmented lesions. Areas with hyperpigmentation block fluorescence. **E.** Mid-phase indocyanine green angiography revealing hypofluorescence of atrophic lesions, peripapillary atrophic halo, and pigmented lesions. **F.** Magnified view of the red box in C. The red arrows delineate the peripapillary atrophy whereas the black arrows encompass a nummular atrophic scar. Note the corresponding thinning of retinal pigment epithelium/Bruch's membrane layer (RPE atrophy), as well as disruption of the outer retina.

Fig. 4. Left eye of a 30-year-old female with chronic Vogt-Koyanagi-Harada disease (Case 5). **A.** Color fundus photograph shows extensive areas of hyperpigmentation. **B.** Fundus autofluorescence imaging discloses mostly increased autofluorescence signal of the pigmented areas. **C.** Infrared imaging of the fundus, with corresponding spectral domain optical coherence tomography (SD-OCT) image. The red arrows delineate the hyperpigmented plaque shown in the SD-OCT image. **D.** Intermediate-phase fluorescein angiography, revealing hypofluorescence of the hyperpigmented areas. **E.** Magnified view of the area indicated by the red box in C. The area between the red arrows consists of the hyperpigmented plaque, which shows thickening of retinal pigment epithelium/Bruch's membrane layer (RPE hyperplasia) with sparing of the outer retina.

Table 1

Features of seven patients with chronic* Vogt-Koyanagi-Harada disease[†] at the time of FAF/SD-OCT testing

Nº	Sex	Age	Ethnicity	Disease duration	Uveitis status	Current treatment	BCVA OD OS	Fundus changes [‡]
1	F	42	Hispanic	127 months	Inactive	Prednisone, MFM	20/20 20/40	SGF (2), PPA (2), Focal RPE atrophy (2), Disciform scar (1)
2	F	41	Hispanic	74 months	Inactive	Prednisone, MFM	20/25 20/25	SGF (2), PPA (2), Focal RPE atrophy (2)
3	F	42	Filipino	4 months	Active	Prednisone, MFM	20/80 20/25	SGF (2), PPA (2), CME (2)
4	F	31	Hispanic	23 months	Active	No**	20/20 20/20	SGF (2)
5	F	30	African-American	4 months	Active	Prednisone	20/40 20/50	SGF (2), PPA (2), Focal RPE atrophy (2), RPE proliferation (1),
6	M	29	Hispanic	43 months	Inactive	Prednisone, MFM, FI	20/20 20/60	SGF (2), PPA (2), Focal RPE atrophy (2), subretinal fibrosis (2), CR atrophy (2) CME (1),
7	M	46	Asian	49 months	Inactive	Prednisone	20/60 NLP	SGF (1), PPA (1), Focal RPE atrophy (1), CR atrophy (1)

* defined as duration [int] 3 months

[†] according to criteria in reference ³, N^o, case number

[‡] number in parenthesis indicate the number of eye(s) with each finding

** presented with mild anterior segment recurrence and was started on topical steroid; FAF, fundus autofluorescence; SD-OCT, spectral domain-optical coherence tomography; BCVA, best-corrected visual acuity; F, female; M, male; MFM, mycophenolate mofetil; SGF, sunset glow fundus; PPA, peripapillary atrophy; RPE, retinal pigment epithelium; CME, cystoid macular edema; FI, intravitreal fluocinolone implant; CR, chorioretinal; NLP, no light perception, with no view of the fundus.

Table 2

Interpretation of fundus autofluorescence and spectral domain OCT findings in fundi of patients with chronic* Vogt-Koyanagi-Harada disease

FUNDUS APPEARANCE	FAF PATTERN	SD-OCT FINDINGS	INTERPRETATION
Peripapillary atrophy		Thinning of RPE/BM layer and loss of outer retinal layers	Atrophy of the RPE and outer retina
Multiple nummular and/or irregular atrophic scars	Decreased autofluorescence signal	Thinning of RPE/BM layer $\pm$ loss of outer retinal layers	Atrophy of the RPE and variable involvement of the outer retina
Pigmented scars		Thickening of RPE/BM layer and loss of outer retinal layers	RPE hyperplasia/hypertrophy and outer retina atrophy
Patches, strands or irregular areas of pigmentation		Thickening of RPE/BM layer $\pm$ loss of outer retinal layers	RPE hyperplasia $\pm$ fibrous metaplasia with variable atrophy of the outer retina
Cystoid macular edema	Increased autofluorescence signal	Intraretinal cystoid spaces	Intraretinal cystoid spaces
Normal retina		Mild irregularities on top of RPE/BM layer or involvement of the outer retina	Subclinical involvement of RPE and outer retina
Sunset glow fundus		No corresponding RPE abnormality	Choroidal depigmentation
Disciform scar	Autofluorescence signal similar to background of normal areas	Subretinal tissue surrounded by area of thinning of RPE/BM layer	Subretinal gliotic tissue with viable overlying RPE/outer retina, but surrounded by area of RPE/outer retinal atrophy [†] .
Sectoral chorioretinal atrophy		Marked atrophy of neural retina, RPE and choroid	Marked chorioretinal atrophy allowing observation of autofluorescence of scleral tissue.

* defined as with duration > 3 months; FAF, fundus autofluorescence; SD-OCT, spectral domain-optical coherence tomography; RPE, retinal pigment epithelium; BM, Bruch's membrane;

[†] The area of RPE atrophy revealed decreased autofluorescence signal.