



Fundus autofluorescence imaging in acute posterior multifocal placoid pigment epitheliopathy

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ABSTRACT

Purpose: Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a disease characterized by multiple yellowish-white placoid lesions. Although most lesions resolve spontaneously, some turn into scars and lead to permanent visual dysfunction. In this report, we found suggestive findings in fundus autofluorescence (FAF) that may be useful for distinguishing severe lesions requiring treatment in APMPPE.

Observation: Case 1: A 29-year-old woman was referred to our hospital with multiple yellowish-white placoid lesions on the fundi of both eyes (OU). FAF showed hyperautofluorescence in some of these placoid lesions. Based on the findings of fluorescein angiography, a diagnosis of APMPPE was established, and oral prednisolone (PSL) was initiated, given that some lesions were located in the macula. One week later, exacerbation occurred with the newly developed hyperautofluorescent lesions. Some lesions in the right eye (OD) that were hyperautofluorescent at the first visit became hypoautofluorescent. Afterward, although all hypoautofluorescent lesions persisted, most of the hyperautofluorescent lesions disappeared, so oral PSL could be stopped. Two months later, however, the recurrence occurred along with multiple new placoid lesions. Some lesions located at the macula were hyperautofluorescent on FAF OU, indicating the possibility of becoming scar lesions with hypoautofluorescence. Accordingly, oral PSL was given again.

Case 2: A 47-year-old woman noticed decreased vision OD, and she was referred to us. Multiple yellowish-white placoid lesions were seen in the fundi OU. FAF showed hyperautofluorescence both with and without corresponding hypoautofluorescence in the placoid lesions OU. A diagnosis of APMPPE was established, and oral PSL was initiated. Four months later, some lesions that were hyperautofluorescent at the first visit had turned isoautofluorescent, and some lesions OU became hypoautofluorescent. However, all hypoautofluorescent lesions remained hypoautofluorescent OU. Only some hyperautofluorescent lesions recovered to isoautofluorescence without scars.

Conclusions and Importance: In APMPPE, lesions showing hyperautofluorescence on FAF may change into hypoautofluorescence indicating scar formation. Therefore, the presence of hyperautofluorescent lesions in the macula may be a good indicator of the need for intensive corticosteroid treatments to avoid leaving hypoautofluorescent scars that are related to irreversible visual dysfunction.

1. Introduction

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is an acute-onset and bilateral disease characterized by

multiple yellowish-white placoid lesions from the posterior pole to the mid-periphery, and the inflammatory impairment of choroidal circulation is considered to be a pathological condition of it.¹⁻³ While most lesions resolve spontaneously, some lesions turn into scarred lesions

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that, if present in the macula, can lead to permanent visual dysfunction.^{1,4} Therefore, it is important to detect and treat such potentially vision-threatening lesions as soon as possible at the time of onset or recurrence.

Fundus autofluorescence (FAF) is a non-invasive examination that shows the luminance of fluorescence emitted by lipofuscin that is derived from the photoreceptor's outer segment when it is damaged by light stimulation, phagocytosed and digested by the retinal pigment epithelium (RPE) cells. In the case of RPE cell dysfunction, lipofuscin accumulates more in RPE cells, and FAF shows hyperautofluorescence; in the case of RPE cell loss, FAF shows hypoautofluorescence.⁵ We report 2 cases of APMPPE in which FAF seemed to be useful in detecting highly severe lesions as hyperautofluorescence involving the macula, which may be a good indicator of the need for intensive treatments.

2. Findings

Case 1: A 29-year-old woman experienced anorthopia and visual field defects in her both eyes (OU) for 3 days and visited an ophthalmology clinic. At the clinic, multiple yellow-white lesions were seen on

the fundi OU, and she was referred to our hospital. She had no particular medical or family history except for diabetic retinopathy experienced by her father.

At the first visit, her best-corrected visual activity (BCVA) was 20/20 in her right eye (OD) and 20/16 in her left eye (OS) with no refractive error OU; her intraocular pressure was within the normal range OU. No inflammation in the anterior chamber or the vitreous cavity was found OU. Fundus examination revealed multiple yellowish-white placoid lesions in the posterior poles without any vitreous haze OU (Fig. 1-A, B). Optic discs were normal OU. Enhanced depth imaging optical coherence tomography (EDI-OCT) showed the choroidal thickening and blurring of the ellipsoid zone (EZ) and interdigitation zone (IZ) at the sites corresponding to the placoid lesions OU (Fig. 1-C, D, arrowheads). Serous retinal detachment (SRD) was also seen in the macula OD. Fluorescein angiography (FA) showed hypofluorescence at the early phase and hyperfluorescence at the late phase corresponding to the placoid lesions (Fig. 1-E, F, G, H). Indocyanine green angiography (ICGA) showed hypofluorescence from the early to late phases (Fig. 2-A, B). FAF showed hyperautofluorescence in some, but not all, hypofluorescent lesions on ICGA OU (Fig. 2-C, D).

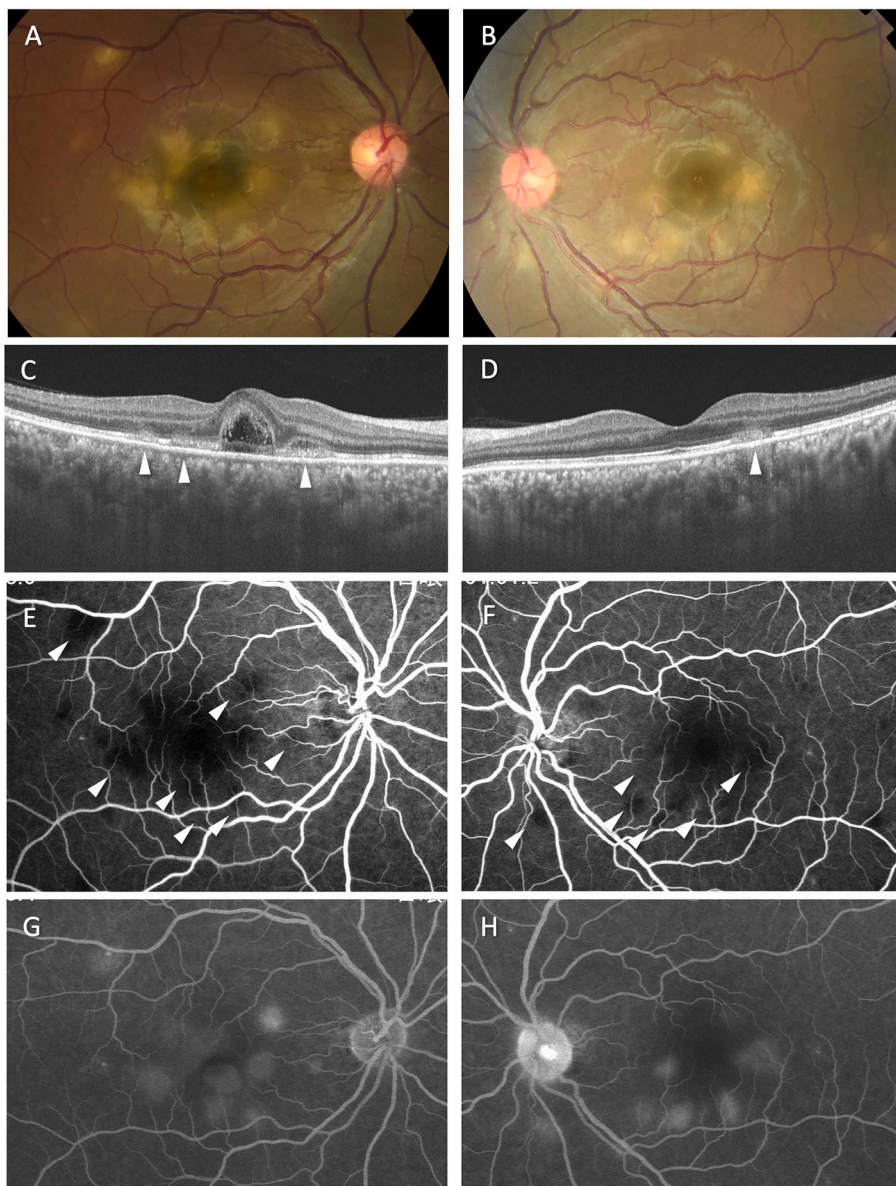


Fig. 1. Fundus photographs and FA findings OU at the initial visit in Case 1. Multiple yellowish-white placoid lesions were observed in the posterior poles of the fundi OU (A, OD; B, OS). EDI-OCT showed the choroidal thickening and the blurring of EZ and IZ at the sites corresponding to the placoid lesions OU (C, OD; D, OS; arrowheads). FA showed hypofluorescence corresponding to the placoid lesions (arrowheads) in the early phase (E, OD; F, OS). In the late phase, FA showed hyperfluorescence corresponding to the hyperfluorescent lesions in the early phase (G, OD; H, OS).

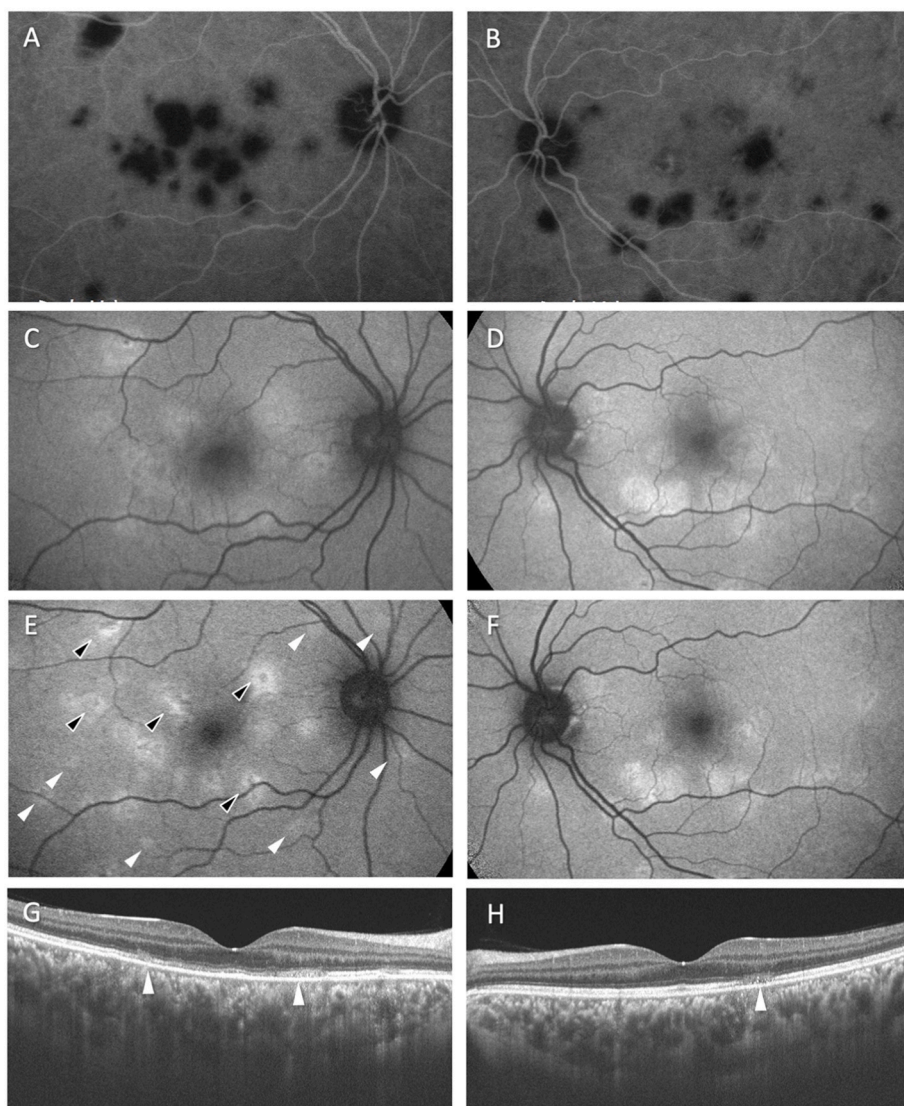


Fig. 2. ICGA and FAF findings in Case 1. ICGA showed hypofluorescence from the early to late phases at the first visit (A, OD; B, OS). FAF showed hyperautofluorescent lesions corresponding to the placoid lesions at the first visit (C, OD; D, OS). Upon exacerbation, FAF showed new hyperautofluorescent lesions OD (white arrowheads) (E, OD). Most old hyperautofluorescent lesions became brighter (white arrowheads), and new hypofluorescent lesions were detected at the center of the hyperautofluorescent lesions (black arrowheads) OD; few changes were observed OS (F, OS). On EDI-OCT, choroidal thickening did not change OU and the blurring of EZ and IZ was also seen (arrowheads), whereas SRD disappeared OD (G, OD; H, OS).

A lumbar puncture did not detect any cells in the cerebrospinal fluid, indicating the absence of pleocytosis. Routine blood tests including T-SPOT, TB, syphilis serological tests, urinalysis and chest X-ray showed no abnormal findings. Based on the results of the ocular findings and the laboratory tests outlined above, the diagnosis of APMPPE was established. Oral prednisolone (PSL) at 20 mg/day (0.4mg/kg) was initiated because the placoid lesions that were revealed to be hyperautofluorescent on FAF were located in the macula.

One week later, the patient still presented with anorthopia OU. Fundus examination revealed the development of additional placoid lesions OD. FAF detected new lesions with hyperautofluorescence OD (Fig. 2-E, white arrowheads). In the lesions that had been hyperautofluorescent during the patient's first visit, increased autofluorescent intensity was noted; moreover, the centers of the lesions changed to hypofluorescence OD (Fig. 2-E, black arrowheads). No changes were observed OS (Fig. 2-F). On EDI-OCT, choroidal thickening did not change OU and the blurring of EZ and IZ was also seen (arrowheads), whereas SRD disappeared OD (Fig. 2-G, H). To treat the exacerbated lesions, sub-Tenon injection of triamcinolone acetonide (STTA) (40 mg) was performed OD, and oral PSL was continued. With the tapering of PSL doses, most of the placoid lesions disappeared within 2 months. Choroidal thickness had recovered to the normal range OU. On FAF, almost all lesions became isoautofluorescent, although some

hypofluorescent lesions persisted. Therefore, oral administration of PSL could be stopped.

However, 2 months later, i.e., 4 months after the initiation of PSL therapy, the patient became aware of floaters OS and visited us again. New yellowish-white placoid lesions developed again OS. FA revealed the presence of hyperfluorescence in a few lesions among scattered window defects in the posterior pole. ICGA detected new multiple hypofluorescent lesions that were seen throughout the early to late phases OU (Fig. 3-A, B). FAF showed a few new hyperautofluorescent lesions and some hypofluorescent lesions that had been hyperautofluorescent during the first visit OU (Fig. 3-C, D). On EDI-OCT, although the burring of EZ and IZ had recovered OD (Fig. 3-E), the blurring of the EZ and IZ corresponding to the new lesion was seen OS (Fig. 3-F). Because hyperautofluorescent lesions with the potential to change into scarred lesions were located in the macula, oral PSL of 30 mg/day (0.6mg/kg) was restarted.

Case 2: A 47-year-old woman noticed decreased vision OD and visited an ophthalmology clinic a week later. At the clinic, her BCVA was 20/100 OD; however, no abnormality was found at that time. Within a few months, her BCVA recovered to 20/28 OD. However, 2 months later, her BCVA decreased to 20/60 OD, and she was referred to us. She had no particular medical or family history.

At the initial visit, her BCVA was 20/100 OD and 20/16 OS with

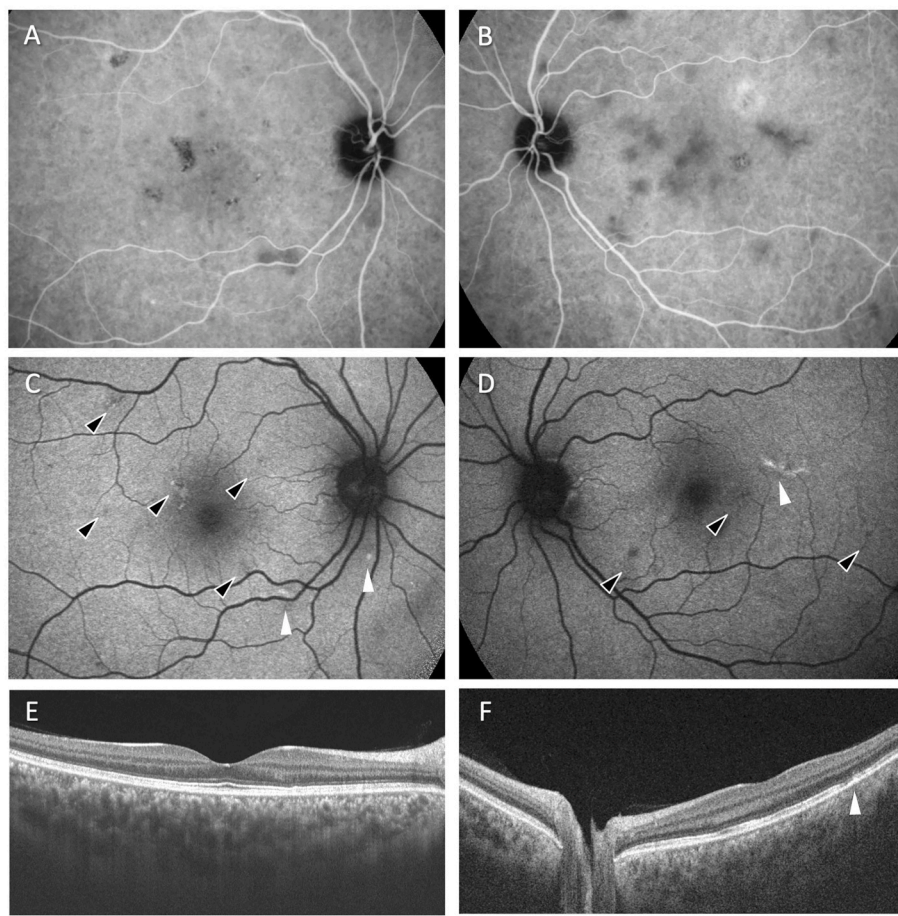


Fig. 3. ICGA and FAF findings at recurrence in Case 1. ICGA showed multiple new hypofluorescent lesions from early to late phases OU (A, OD; B, OS). FAF showed some new hyperautofluorescent lesions were seen OU (white arrowheads). Some lesions that were hyperautofluorescent at the first visit turned hypofluorescent (black arrowheads) OU (C, OD; D, OS). On EDI-OCT, although the blurring of EZ and IZ had recovered OD (E), the blurring of the EZ and IZ corresponding to the new lesion was seen OS (F, arrowhead).

myopia of -6.0 D, and intraocular pressure was within the normal range OU. There were no inflammatory findings in the anterior chamber, whereas anterior vitreous cells were observed OU. A fundus examination showed multiple yellowish-white placoid lesions in the posterior pole OU. EDI-OCT detected the blurring of the EZ and IZ at the sites corresponding to the placoid lesions, as well as mild choroidal thickening without SRD OU (Fig. 4-A, B).

FA revealed staining only among placoid lesions around the optic disc in addition to window defects in other lesions OD and staining in all placoid lesions OS. Some lesions showed hypofluorescence at the early phase and hyperfluorescence at the late phase, corresponding to some of the placoid lesions.

ICGA showed hypofluorescence from the early to late phases, corresponding to the placoid lesions (Fig. 4-C, D).

On FAF, most lesions showed hyperautofluorescence, and some lesions near the optic disc showed hypofluorescence OD. Lesions displaying hyperautofluorescence and hypofluorescence coexisted OS (Fig. 4-E, F).

Routine blood tests including T-SPOT. TB, syphilis serological tests, urinalysis and chest X-ray showed no abnormal findings.

Based on the results of the ocular imaging examinations and laboratory tests, a diagnosis of APMPPE was established. Oral PSL at 30 mg/day (0.5mg/kg) was initiated because hyperautofluorescent lesions were detected in the macula OU. The dose of PSL was tapered, and 3 months later, it was discontinued.

Four months after that, the patient's BCVA was 20/200 OD and 20/24 OS; some yellowish-white placoid lesions disappeared while others turned into scarred lesions OU.

FAF revealed that many hyperautofluorescent lesions at the first visit turned into isoautofluorescent lesions, some remained

hyperautofluorescent, and others changed into hypofluorescent lesions. All the lesions that were hypofluorescent at the first visit remained hypofluorescent OU (Fig. 4-G, H).

3. Discussion

During the acute inflammatory phase of APMPPE, yellowish-white placoid lesions appear. Although Gass originally suspected that inflammation occurred in RPE and the outer segment of photoreceptors,¹ Deutman et al. hypothesized that acute inflammation of the choriocapillaris might be the initial insult, while the RPE impairment might occur secondarily.² Spaide et al. noted that FAF findings appeared later than the appearance of FA and ICGA findings.⁶ These results support the hypothesis of Deutman et al.

Scheufele et al. showed that moderately backscattered lesions were observed in the outer nuclear layer of the retina with optical coherence tomography (OCT) at the sites corresponding to the yellowish-white lesions; they also reported that RPE atrophy was demonstrated after the lesions had healed. These findings suggested that if the choroidal inflammation was severe enough, it resulted in the damage to the outer layer of the retina and in RPE atrophy. Furthermore, Scheufele et al. described that structural RPE changes were not visible until the lesions began to heal or had healed; it is possible that RPE dysfunction, which is not detectable by OCT, occurred in the acute setting.⁷

In the first case in this paper, the onset of APMPPE appeared at the first visit, while the second case appeared to show recurrence. In both cases, large number of hypofluorescent lesions were observed on ICGA, whereas on FAF, some lesions were hyperautofluorescent indicating RPE dysfunction; other lesions were hypofluorescent, indicating the loss of RPE cells (Fig. 2-C, D; Fig. 4-C, D). In both cases, when FAF indicated

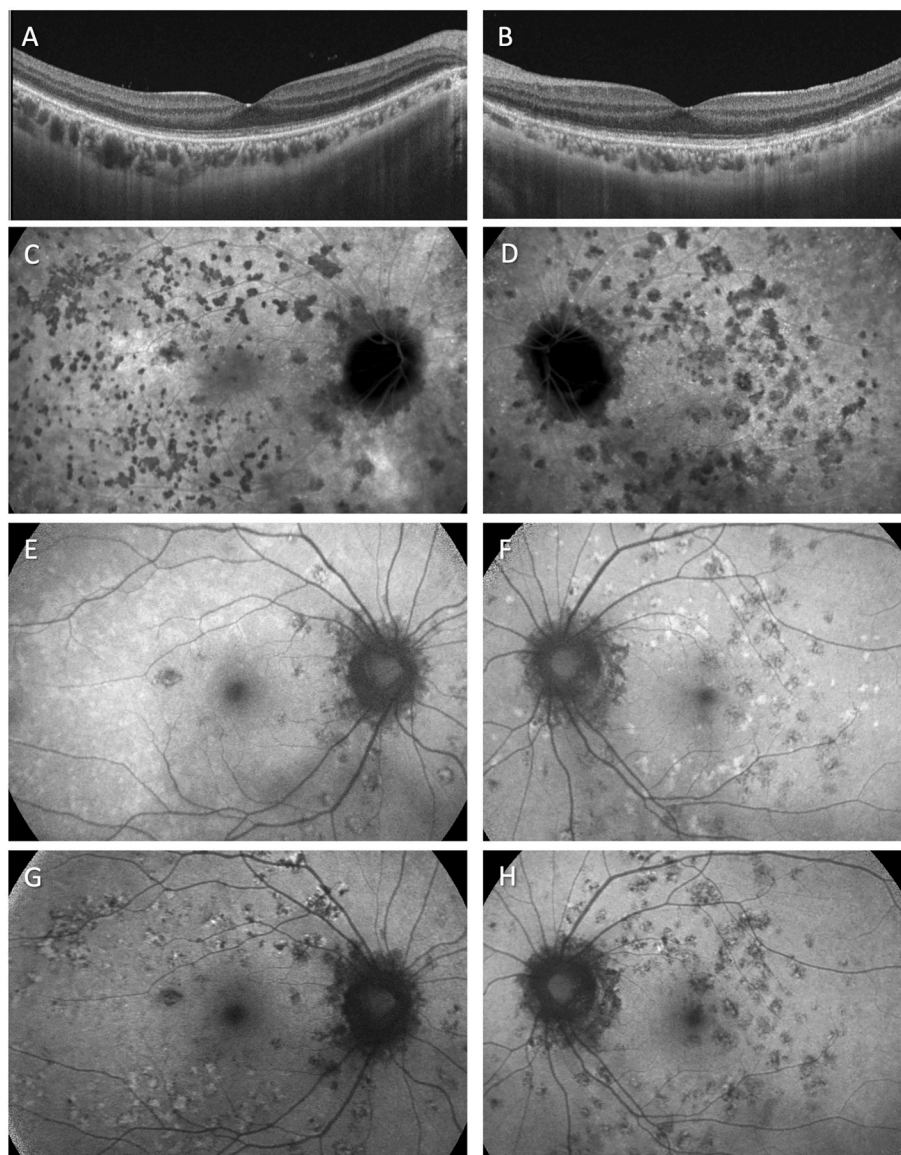


Fig. 4. EDI-OCT detected the blurring of the EZ and IZ at the sites corresponding to the placoid lesions, as well as mild choroidal thickening without SRD OU (A, OD; B, OS). ICGA and FAF findings in Case 2. ICGA showed hypofluorescence from the early to late phases (C, OD; D, OS). On FAF, most lesions were hyperautofluorescent, and some near the optic disc were hypoautofluorescent OD (E), whereas lesions with hyperautofluorescence and hypoautofluorescence coexisted OS (F). Four months later, many lesions that were hyperautofluorescent at the first visit turned isoautofluorescent; some lesions remained hyperautofluorescent, and others changed to hypoautofluorescent. All hypoautofluorescent lesions at the first visit remained hypoautofluorescent (G, OD; H, OS).

the presence of hyperautofluorescent lesions in the macula, intensive treatments were given. Many lesions recovered to isoautofluorescence and healed without leaving scars, while some changed into hypoautofluorescence and did not recover, indicating permanent RPE damage (loss of RPE cells) (Fig. 3-C, D; Fig. 4-E, F). The interventions provided are thought to have prevented many lesions from scarring. Therefore, in APMPE cases when macular lesions are hyperautofluorescent at the onset or recurrence, intensive treatments, (e.g., oral PSL and/or STTA) may be considered.

In APMPE, most lesions disappear spontaneously. However, some may develop into scars, leading to severe visual impairment if these scars are located in the macula. Therefore, it is important to detect such severe lesions early and to provide intensive treatments to ensure as little scarring as possible. In the 2 cases presented in this report, to detect severe lesions with dysfunctional RPE cells, FAF was a more useful than OCT and ICGA. ICGA was useful in visualizing lesions, as hypofluorescence can indicate impairment of choroidal circulation. However, such hypofluorescent lesions included both inactive scarred lesions and newly active lesions, and distinguishing between them was difficult. In contrast, FAF could distinguish between these types of lesions: new lesions, especially severe lesions, as hyperautofluorescent, mild lesions as isoautofluorescent (invisible), and inactive scarred lesions as

hypoautofluorescent. Therefore, FAF is considered to offer important information to visualize severe lesions in which RPE is dysfunctional and may die soon. That information may contribute to determining the subsequent treatment.

OCT is also useful tool to detect lesions in APMPE showing the impairment of outer retinal layer characterized by the blurring or the disappearance of the EZ and/or IZ. However, it is difficult to clearly distinguish between new and old lesions. In addition, OCT basically shows only cross-sections but not the entire posterior pole. Therefore, FAF appears to be more useful in detecting new lesions in APMPE than OCT.

In addition, subjective symptoms may not always accompany recurrence, as happened in Case 1. Therefore, periodic examinations are considered to be mandatory for patients with APMPE, even after recovery. FAF is a short, non-invasive examination and would therefore be suitable for such periodic examinations to detect active and severe lesions requiring treatment. Framme et al. reported that placoid lesions appeared hyperautofluorescent in the acute phase of APMPE. Later, the intensity of autofluorescence decreased, and some of the hyperautofluorescence turned into hypoautofluorescence. They hypothesized that acute inflammation of the RPE leads to characteristic long-term damage, even after months or years, and finally to localized RPE

atrophy.⁸ Their hypothesis is consistent with our findings that FAF hyperautofluorescence in the macula at the onset or recurrence of APMPE may turn either isoautofluorescent or hypoautofluorescent. Therefore, the presence of hyperautofluorescent lesions in the macula may be a good indicator of the need for intensive corticosteroid treatments to avoid leaving hypoautofluorescent scars that are related to irreversible visual dysfunction.

The utilities of FAF in other chorioretinal diseases have been reported. Lesions were hyperautofluorescence in acute zonal occult outer retinopathy,⁹ and also in multiple evanescent white dot syndrome.¹⁰ However, in both diseases, although FAF findings were helpful for the diagnosis, they are not useful indicators of the need for treatments.

4. Conclusions

From the findings in our two cases of APMPE, we propose the usefulness of FAF in detecting severe lesions that require intensive treatments during the acute phase of APMPE. This report warrants further case-control studies to confirm our FAF-based management of APMPE.

Patient consent

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

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Authorship

All authors attest that they meet the current ICMJE criteria for

Authorship.

Declaration of competing interest

The authors declare that they have no competing interests.

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