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Case Report

White Dot Syndromes: Report of Three Cases

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Keywords
White dot syndromes · Multiple evanescent white dot syndrome · Punctate inner choroidopathy · Acute posterior multifocal placoid pigment epitheliopathy · Fundus autofluorescence

Abstract
Introduction: The term white dot syndromes has been used to refer conditions that differ in their morphology and prognosis. We report three cases of different pathologies encompassed within the white dot syndromes. ***Case Presentations:*** Case 1: A 26-year-old female presented with scotoma in her right eye. Fundus examination revealed multiple white dots that demonstrated early hyperfluorescence with late staining on FA. OCT showed discontinuities in inner segment-outer segment junction associated with columnar-shaped outer retinal hyperreflective bands. AF revealed multiple hyperautofluorescent dots around the posterior pole, compatible with multiple evanescent white dot syndrome. The symptoms improved without treatment. Case 2: A 16-year-old male presented with retinal lesions compatible with punctate inner choroidopathy in his right eye. OCT showed lesion in the outer retinal layer. FAF revealed parafoveal hypoautofluorescent dots with early hyperfluorescence and late staining on FFA. After oral corticotherapy, they progress to atrophic scars. Case 3: A 65-year-old male presented with scotoma and decreased vision in his right eye. OCT showed hyperreflectivity in the outer layer that progresses to a large atrophic plaque with foveal affectation. FAF demonstrated hyperautofluorescent placoid lesion occupying macular area, compatible with acute posterior multifocal placoid pigment epitheliopathy. Retinal lesions improved with systemic corticosteroids. ***Conclusion:*** The FAF pattern helps know the distribution of the lesions. It represents a noninvasive method that has been shown to be useful in the diagnosis and monitoring of white dot syndromes.

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Introduction

White dot syndromes are a group of inflammatory chorioretinopathies of unknown etiology that share the presence of yellowish-white lesions affecting multiple layers of the retina, retinal pigment epithelium (RPE), choriocapillaris, and the choroid. In this group are included multiple evanescent white dot syndrome (MEWDS), acute posterior multifocal placoid pigment epitheliopathy (APMPPE), birdshot chorioretinopathy, punctate inner choroidopathy (PIC), serpiginous choroidopathy, multifocal choroiditis and panuveitis (MCP), and subretinal fibrosis and uveitis syndrome [1, 2].

Although they share some features, white dot syndromes can be differentiated by the morphology and evolution of the lesions, their natural history, and their appearance on imaging tests [2]. The aims of this study were to present three cases diagnosed with different pathologies encompassed within the white dot syndromes and to show the morphological difference of the lesions by fundus autofluorescence (FAF), fundus fluorescein angiography (FFA), and optical coherence tomography (OCT). The CAse REport (CARE) Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000536336).

Case Presentations

Case 1

A healthy 26-year-old woman presented to our emergency department with complaints of scotoma in her right eye, without being preceded by a pseudogrippal-like condition. Best-corrected visual acuity (BCVA) in the right eye was 10/10 with no inflammation in anterior chamber. Fundus examination revealed multiple white dots in the peripapillary and perimacular areas extending to the periphery with subtle posterior vitritis (Fig. 1).

In the presence of discrete, multiple, well-defined, yellow-white lesions in the fundus of the eye, the initial diagnostic suspicion was an inflammatory chorioretinopathy. However, a complete medical history was taken, and a blood test was requested to perform a differential diagnosis with systemic and ocular infectious entities such as syphilis, diffuse unilateral subacute neuroretinitis, and ocular histoplasmosis syndrome, as well as noninfectious entities such as sarcoidosis, sympathetic ophthalmia, Vogt-Koyanagi-Harada syndrome, and intraocular lymphoma, that were ruled out.

FFA demonstrated early hyperfluorescence with late staining of the retinal lesions (Fig. 2). OCT showed discontinuities in inner segment-outer segment junction associated with columnar-shaped outer retinal hyperreflective bands (Fig. 3). FAF revealed multiple hyperautofluorescent dots around the posterior pole following the distribution of the arcades (Fig. 4). The symptoms improved without treatment after 2 months. The lesions on FAF showed resolution. Taking into account the characteristics of the imaging tests and the self-resolution of the lesions, the case was compatible with MEWDS.

Case 2

A 16-year-old male was being followed for anisometric amblyopia due to hypermetropia. In one of the revisions, funduscopy of the right eye evidenced multiple, small, round, yellow-white lesions in the posterior pole without vitritis (Fig. 5). BCVA in the right eye was 8/10 with no inflammation in anterior chamber. OCT showed the presence of focal elevations of the RPE with underlying hyporeflective space, without choroidal neovascular (CNV) membranes (Fig. 6). FAF revealed the presence of parafoveal hypoautofluorescent dots (Fig. 7) with early hyperfluorescence and late staining on FFA (Fig. 8).

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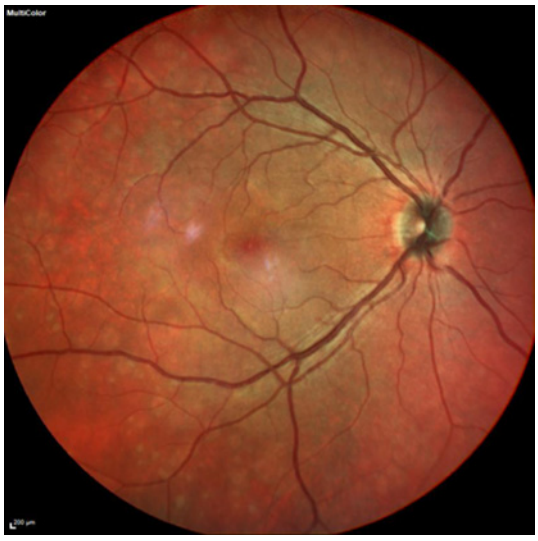

Fig. 1. Fundus photograph. Image reveals multiple white dots in the peripapillary and peri-macular areas extending to the periphery.

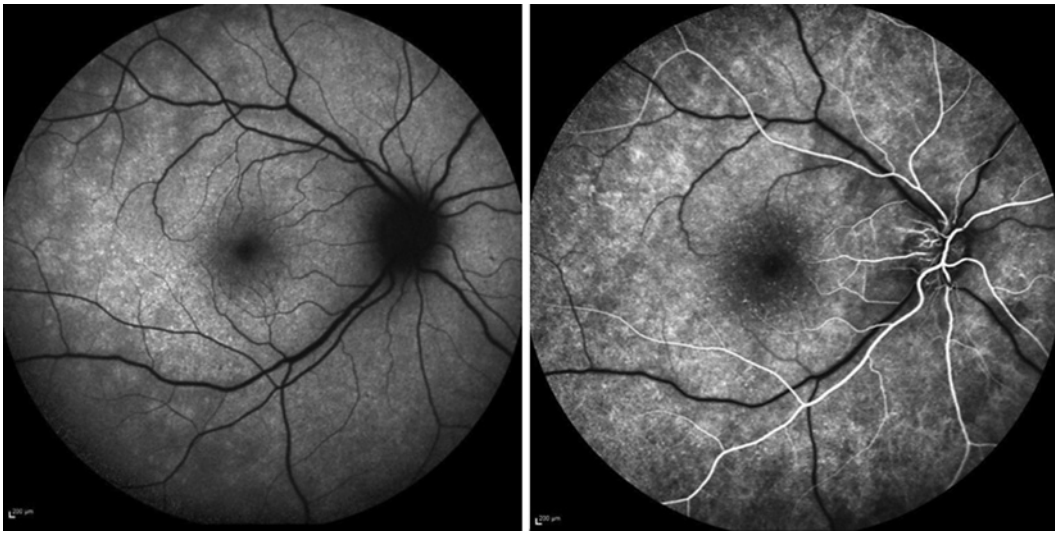

Fig. 2. FFA. The left image demonstrates early punctate hyperfluorescence in a wreath-like pattern, and the right image shows late staining in areas corresponding to the white dots.

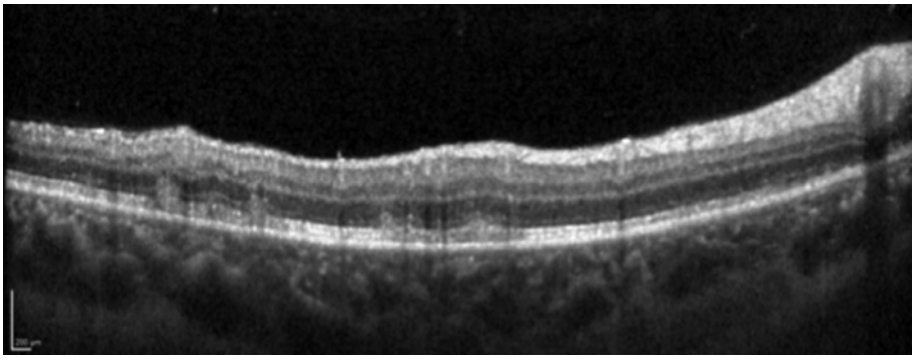

Fig. 3. OCT. Picture reveals discontinuities in inner segment-outer segment junction associated with columnar-shaped outer retinal hyperreflective bands.

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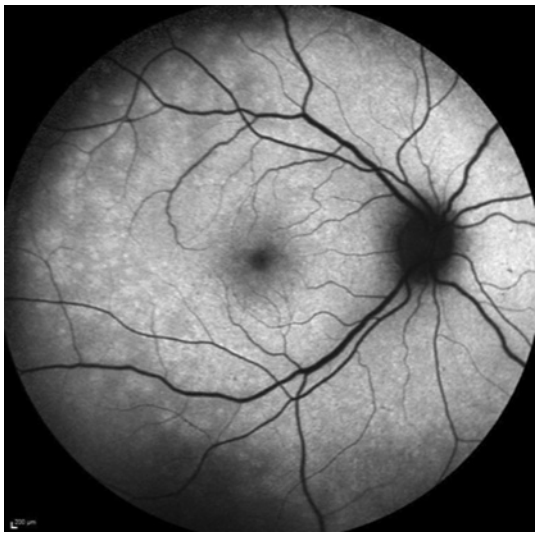

Fig. 4. FAF. Image shows multiple hyperautofluorescent dots around the posterior pole following the distribution of the arcades.

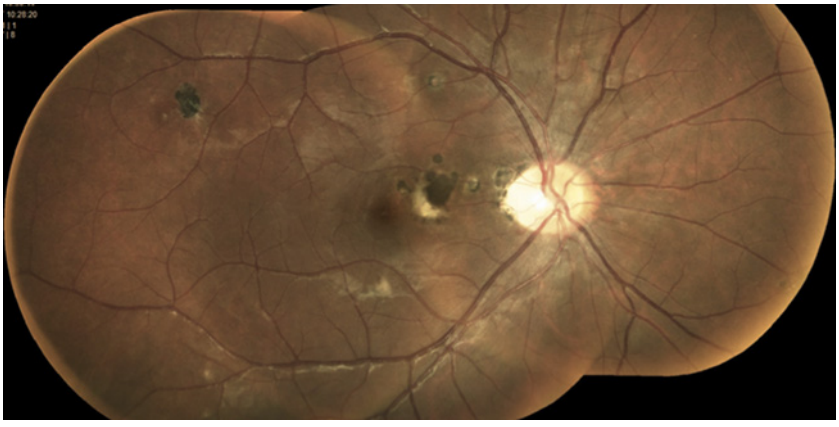

Fig. 5. Fundus photograph. Image evidences multiple, small, round, and yellow-white lesions in the posterior pole.

Infectious etiology was ruled out through blood analysis. To make a differential diagnosis among white dot syndromes, emphasis was placed on the morphology of the lesions observed in imaging tests. Using OCT, FAF, and FFA, the focus was directed toward MCP and PIC. The diagnosis was refined due to the size (smaller than in MCP), localization (without extension to the midperiphery) of the lesions, and the absence of vitritis that was compatible with PIC.

Afterward, oral corticosteroid therapy was started, showing partial remission of the lesions. Seven years later, atrophic scars were seen on OCT. The atrophic PIC lesions appeared to be hypoautofluorescent spots on FAF (Fig. 9). In the follow-up, no new lesions are observed in the additional tests.

Case 3

A 65-year-old male with history of plaque maculopathy in the right eye presented with vision loss and scotoma in his right eye. He does not report previous viral symptoms. BCVA in the right eye was counting fingers at 50 cm, previously 20/20 with no inflammation in anterior chamber. Fundus examination showed multiple, yellow-white placoid lesions at the posterior pole without vitritis (Fig. 10). On OCT, the placoid lesions appeared as disruption of

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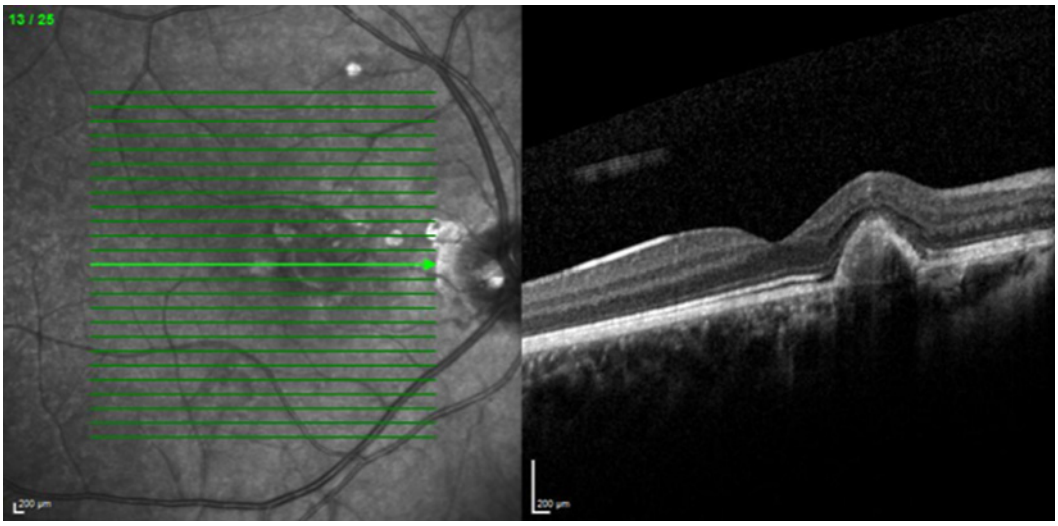

Fig. 6. OCT. Picture shows the presence of focal elevations of the RPE with underlying hyporeflective space, without CNV.

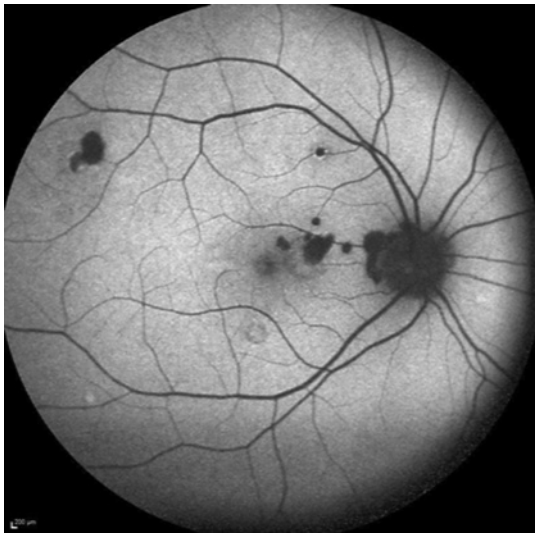

Fig. 7. FAF. Image evidences the presence of parafoveal hypoautofluorescent dots.

the outer retinal and ellipsoid zone, with the presence of hyperreflectivity in the outer retinal layers (Fig. 11). FAF demonstrated hyperautofluorescent placoid lesion occupying macular area (Fig. 12). FFA showed early hypofluorescent lesions corresponding to those apparent on funduscopy and late hyperfluorescent staining. One month later, a large atrophy plaque with foveal involvement was observed. The lesions evolved into areas of hypoautofluorescence on FAF (Fig. 13). The same findings were also observed 4 years later. During this period, no new lesions were observed in imaging tests including FAF.

Differential diagnostic consideration was performed with serpiginous choroiditis, choroidal metastasis, viral retinitis, sarcoidosis, Vogt-Koyanagi-Harada syndrome, and pneumocystis choroiditis. Taking into account that an infectious cause was ruled out in blood analysis, the characteristics of the lesion and APMPPE is an acute, usually nonrecurring disease, whereas serpiginous choroiditis is insidious and progressive, it was compatible with APMPPE with aggressive clinical course.

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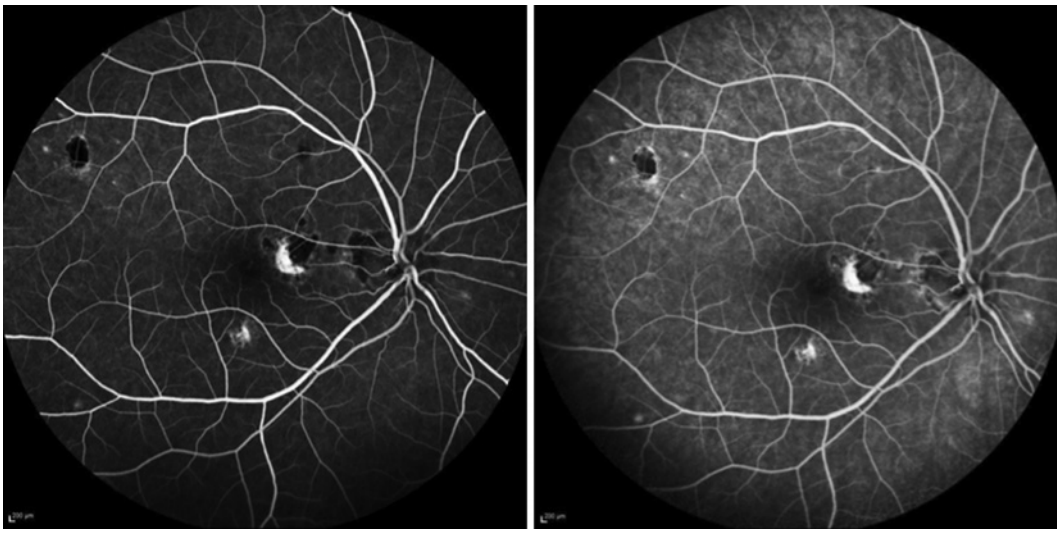

Fig. 8. FFA. The left picture shows early hyperfluorescence, and the right picture demonstrates late staining of the lesions.

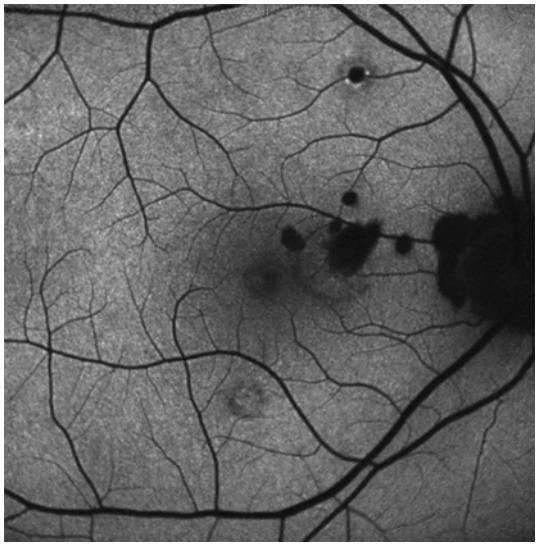

Fig. 9. FAF. Image reveals hypoautofluorescent spots corresponding to the atrophic PIC lesions, without new lesions.

He started with the same symptoms in his left eye after 1 year. The ocular examinations were similar to those presented in the right eye. Consequently, intravenous corticosteroid treatment was started. Subsequent examinations showed a good response with improvement of the outer retinal and ellipsoid layer lesion with less residual atrophy compared to the contralateral eye.

Discussion

The term white dot syndromes has been used to refer conditions that differ in their morphology and prognosis. Complementary tests are necessary to make a correct diagnosis, after a complete anamnesis and examination with slit-lamp biomicroscopy. FAF is an

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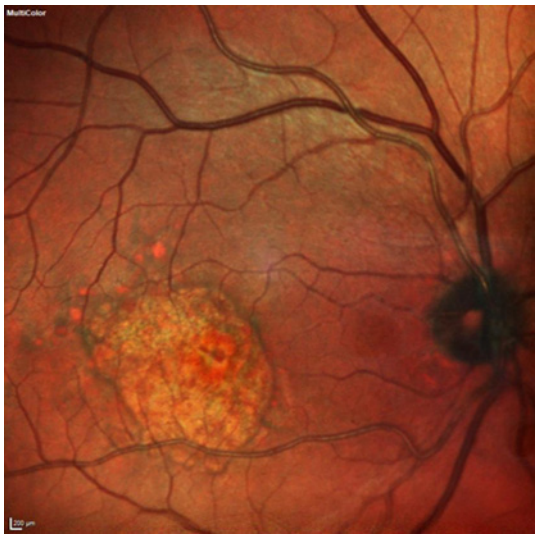

Fig. 10. Fundus photograph. Image evidences multiple, yellow-white placoid lesions at the posterior pole.

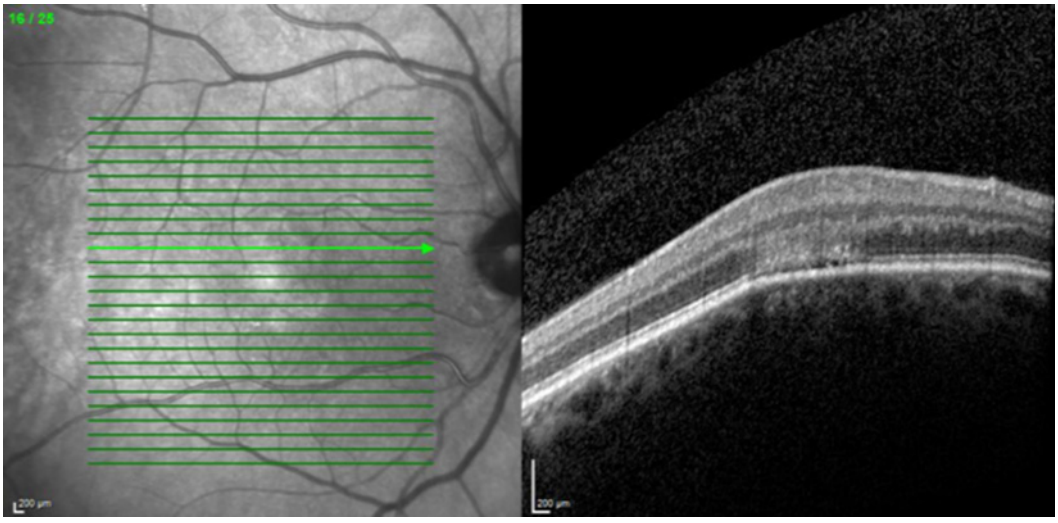

Fig. 11. OCT. The placoid lesions appeared as disruption of the outer retinal and ellipsoid zone, with the presence of hyperreflectivity in the outer retinal layers.

important tool in the diagnosis of white dot syndromes, since it uses fluorescence properties of intrinsic fluorophores to evaluate RPE metabolism and photoreceptor layers, which are involved in the pathogenesis of these diseases. The FAF pattern helps know the distribution of the lesions. It is also relevant for the evaluation of the prognosis and progression of the lesions.

FAF findings in MEWDS consist of hyperautofluorescent lesions distributed around the papilla and sometimes reaching the macular area. Even in the absence of white dots in the fundoscopy, FAF may show characteristic hyperautofluorescent lesions. MEWDS is usually a self-limiting condition with complete visual recovery after 2–6 weeks, although subsequent retinal sequela could be possible [3, 4].

PIC is characterized by single hypoautofluorescent punctate lesions localized in the macula. These inflammatory lesions progress to scarring that may lead to the formation of CNV that is treated with anti-VEGF. Corticosteroids and immunosuppressants may be useful in the control of CNV recurrence. Central vision may be affected because of foveal injury or CNV [5].

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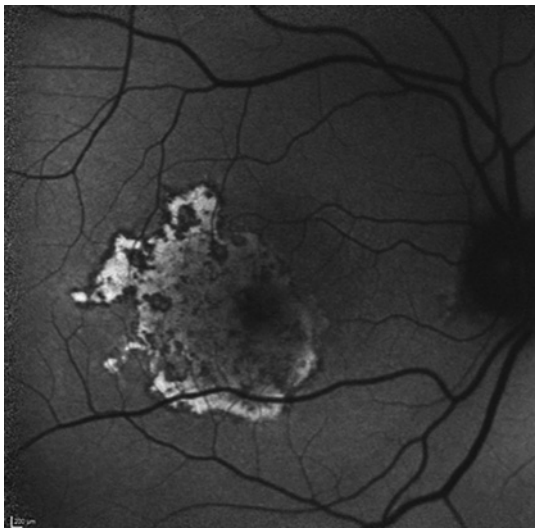

Fig. 12. FAF. Image demonstrates hyperautofluorescent placoid lesion occupying macular area.

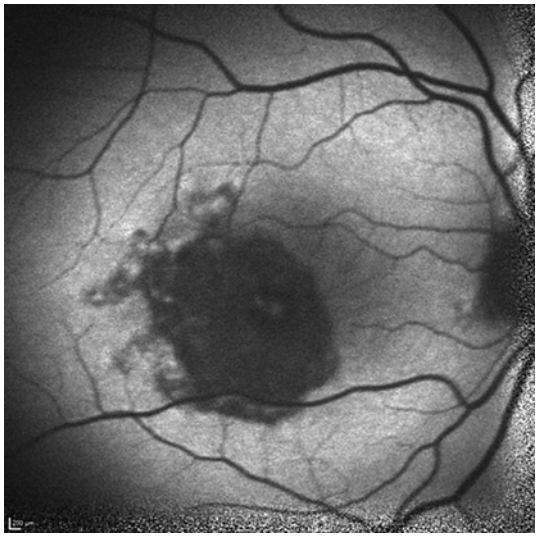

Fig. 13. FAF. Image demonstrates hypoautofluorescent placoid lesion occupying macular area.

The characteristic clinical finding in APMPPE is the presence of multiple placoid lesions in the posterior pole. FAF shows hyperautofluorescence corresponding to the more recent lesions and hypoautofluorescence matching the healed lesions. The active lesions are replaced by RPE atrophy and hyperpigmentation within a few days after the onset of the symptoms. The prognosis is good in most cases. However, new active lesions may appear and patients could experience prolonged recovery associated with persistent scotomas and more uncommonly even severe vision loss as a result of the RPE and foveal photoreceptor lesion. Therefore, corticosteroids should be considered in patients with macular affectation [6].

Wintergerst et al. [7] and Yeh et al. [4] emphasized the utility of FAF in the ocular examination of white dot syndromes. It is a rapid and noninvasive tool to monitor lesions, guide treatment, detect recurrences, and evaluate patient's response to the treatment.

Yeh et al. [4] indicated that conventional FAF imaging is particularly beneficial for monitoring posterior uveitis. In comparison with conventional color fundus photography, FAF allows for the identification of a greater number of chorioretinal lesions, reveals a more extensive extent of RPE damage, and aids in distinguishing between active and inactive regions of inflammatory lesions [4].

While traditional ophthalmic assessments, fundus photography, and FFA played crucial roles in white dot syndrome evaluation, FAF imaging emerged as a valuable tool for emphasizing areas of disease activity and facilitating distinctions between different conditions. Wintergerst et al. noted that foveal hypoautofluorescence seemed to serve as an indicator for moderate to severe visual impairment [7].

Wintergerst et al. [7] introduced the green emission fluorescent component/red emission fluorescent component ratio as a novel imaging biomarker for inflammatory chorioretinopathies using spectrally resolved FAF. It provides means for differentiation of posterior uveitis entities, which can be difficult to distinguish otherwise [7]. Besides, Yeh et al. [4] observed the correlation between vision loss and foveal hypoautofluorescence.

Conclusion

In conclusion, FAF has been shown to be useful in the diagnosis and monitoring of white dot syndromes. This represents a noninvasive method to detect RPE changes reflecting choroidal and retinal alterations and highlighting areas of disease activity. Future studies are warranted to evaluate the use of FAF in the inflammatory chorioretinopathies.

Acknowledgments

We thank the patients for their support in our study.

Statement of Ethics

The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from the patients (case 3 and case 1) and parent/legal guardian (case 2) for publication of this report of three cases and any accompanying images. This retrospective review of patient data did not require ethical approval in accordance with local/national guidelines.

Conflict of Interest Statement

The authors declare that they have no competing interest.

Funding Sources

This study received no specific financial support.

Author Contributions

Leire Olazaran conceived the research idea, designed the study protocol, analyzed and interpreted data, and drafted and revised the manuscript. Ana Jiménez contributed to the study design and protocol development, collected, analyzed, and interpreted data, and provided critical revisions to the manuscript. Pablo González de los Mártires assisted in the conceptualization and design of the research, conducted data analysis and interpretation, and participated in the manuscript writing and revision. Gonzalo Guerrero and Irene Reyzabal played a key role in the study design, contributed to data collection, analysis, and interpretation, and provided substantial input during manuscript preparation. Nerea Gangoitia, Santiago López, Henar Heras and Esther Compains contributed to the study design and data collection, analyzed and interpreted data, and participated in the drafting and revision of the manuscript. Iñigo Salmeron assisted in the development of the research protocol, conducted data analysis and interpretation, and provided critical feedback and revisions to the manuscript. Ane Galarza contributed to the conception and design of the study, participated in data collection and analysis, and revised and approved the final version of the manuscript. Ana Sofía Argüelles contributed to the study design and protocol development, analyzed and interpreted data, and provided substantial input during manuscript writing and revision. Beatriz Elso assisted in the conceptualization and design of the research, conducted data analysis and interpretation, and participated in manuscript writing and revision. All authors have read and approved the final version of the manuscript and have agreed to be accountable for all aspects of the work.

Data Availability Statement

Data were collected from patients' medical records on clinical findings and retinal imaging including fundus autofluorescence (FAF), fundus fluorescein angiography (FFA), and optical coherence tomography (OCT). Further inquiries can be directed to the corresponding author. The data that support the findings of this study are not publicly available due to privacy reasons but are available from the corresponding author upon reasonable request.

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