Fundus Autofluorescence Imaging of the White Dot Syndromes

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Objective: To characterize the fundus autofluorescence (FAF) findings in patients with white dot syndromes (WDSs).

Methods: Patients with WDSs underwent ophthalmic examination, fundus photography, fluorescein angiography, and FAF imaging. Patients were categorized as having no, minimal, or predominant foveal hypoautofluorescence. The severity of visual impairment was then correlated with the degree of foveal hypoautofluorescence.

Results: Fifty-five eyes of 28 patients with WDSs were evaluated. Visual acuities ranged from 20/12.5 to hand motions. Diagnoses included serpiginous choroidopathy (5 patients), birdshot retinochoroidopathy (10), multifocal choroiditis (8), relentless placoid chorioretinitis (1), presumed tuberculosis-associated serpiginouslike choroidopathy (1), acute posterior multifocal placoid pigment epitheliopathy (1), and acute zonal occult outer retinopathy (2). In active serpiginous choroidopathy, notable hyperautofluorescence in active disease distinguished it from the variegated FAF features of tuberculosis-associated serpiginouslike choroidopathy. The percentage of patients with visual acuity impairment of less than 20/40 differed among eyes with no, minimal, and predominant foveal hypoautofluorescence \((P < .001)\). Patients with predominant foveal hypoautofluorescence demonstrated worse visual acuity than those with minimal or no foveal hypoautofluorescence \((P < .001)\).

Conclusions: Fundus autofluorescence imaging is useful in the evaluation of the WDS. Visual acuity impairment is correlated with foveal hypoautofluorescence. Further studies are needed to evaluate the precise role of FAF imaging in the WDSs.


The White Dot Syndromes (WDSs) comprise a heterogeneous group of posterior uveitic syndromes characterized by multiple lesions of the posterior pole due to inflammation of the choroid, retinal pigment epithelium (RPE), and retina. The WDSs classically include acute posterior multifocal placoid pigment epitheliopathy (APMPPE), serpiginous choroidopathy (SPC), birdshot retinochoroidopathy (BRC), multiple evanescent white dot syndrome (MEWDS), and multifocal choroiditis (MFC). Other conditions sometimes included in this category of diseases include relentless placoid chorioretinitis (RPC), presumed tuberculosis-associated serpiginouslike choroidopathy (TB-SPLC), acute zonal occult outer retinopathy (AZOOR), persistent placoid maculopathy, and amipigous choroiditis.

Classification of a WDS typically requires an assessment of the patient age, history of a viral prodrome, laterality of the disease process, lesion size, fluorescein angiographic characteristics, and the clinical course. For instance, APMPPE and SPC are associated with early blockage and late hyperfluorescence on fluorescein angiography; SPC, however, is associated with a relapsing disease course requiring immunosuppressive medications. Although these disease features have helped us to classify the various disease entities, our understanding of the pathogenic mechanisms of inflammation that underlie these disease processes is limited.

Fundus autofluorescence (FAF) has been used for the evaluation of the RPE in degenerative, inflammatory, and neoplastic disease conditions. The FAF signal is derived primarily from lipofuscin accumulation within the RPE and may be...
indicative of altered structure and function.\textsuperscript{11,12} The ocular tissues involved in the WDSs include the RPE, choroid, and outer retinal layers. However, whether the RPE is primarily involved in disease pathogenesis or secondarily affected by adjacent chorioretinal inflammation (eg, choroidal vasculitis with secondary RPE perturbation in APMPPE) remains unclear.

Alterations in the FAF signal have been observed in case series and several case reports of patients with BRC,\textsuperscript{13} MFC,\textsuperscript{14} APMPPE,\textsuperscript{15,16} MEWDS,\textsuperscript{17,18} and SPC.\textsuperscript{19} One important question that remains is whether FAF patterns may be used to distinguish these disease entities. Another question is whether FAF changes may help in the detection and localization of ongoing inflammatory disease activity. We reviewed our experience with FAF imaging in a large series of patients with WDSs during periods of disease activity and quiescence. We describe herein the FAF characteristics from a spectrum of patients with various WDSs and correlate visual impairment with pathologic foveal hypoautofluorescence.

Patients underwent evaluation using an institutional review board–approved protocol in the uveitis and ocular immunology clinic at the National Eye Institute from February 1, 2007, through June 30, 2008. All patients with posterior uveitis classified as a WDS who had an available FAF image of adequate quality for analysis (Topcon Medical Systems, Paramus, New Jersey) (excitation filter, 585 nm; barrier filter, 690 nm) were included for review. Data collected included patient age, laterality of disease activity (unilateral or bilateral), visual acuity, dilated funduscopy examination findings, fundus photography (TRC-50EX, Topcon Medical Systems), fluorescein angiography, spectral-domain optical coherence tomography (Carl Zeiss Meditec, Dublin, California), and history of therapy with immunosuppressive agents. Serial examinations and FAF images were available for some patients, but data for only the initial visit were available for other patients owing to the nature of our tertiary referral setting.

Patients were categorized into 3 groups on the basis of the presence and location of hypoautofluorescence in the anatomic fovea on FAF imaging. Patients with a normal FAF signal in the fovea (ie, central 1500 µm surrounding the foveola) were assigned to the category of no hypoautofluorescence (none). Patients with hypoautofluorescent areas affecting less than 50% of the anatomic fovea were assigned to the minimal hypoautofluorescence category. Patients with at least 50% of their anatomic fovea affected were assigned to the predominant hypoautofluorescence category (Figure 1). Two independent graders (S.Y. and F.F.) performed the classification, and a third independent grader adjudicated discordances (L.J.F.). We used χ² analysis to determine whether the groups differed in the proportion of eyes with moderate or severe impairment of visual acuity (ie, visual acuity of <20/40). We performed a Kruskal-Wallis analysis with the Dunn posttest to determine whether the mean logMAR visual acuity differed among these 3 groups. Statistical significance was determined at an α value of .05.

RESULTS

We included 55 eyes of 28 patients who were diagnosed as having a WDS for analysis in this series. The mean age of patients was 47 (range, 24-74) years. The diagnoses and baseline characteristics of patients undergoing evaluation are summarized in Table 1. A number of WDSs were evaluated and included BRC, MFC, AZOOR, SPC, presumed TB-SPLC, APMPPE, and RPC. Nineteen of the patients (68%) were receiving immunosuppressive medications at the time of the ophthalmic evaluation. All cases were bilateral with the exception of 1 patient who un-
derwent an enucleation procedure after a traumatic injury in childhood. Fourteen of the 28 patients (50%) had undergone serial examinations and imaging studies, with a mean follow-up time of 9.1 (range, 4-13) months; the remainder of patients were seen at only 1 visit.

The proportion of eyes with at least moderate visual impairment (defined as visual acuity of <20/40) was statistically different among eyes classified as having no, minimal, and predominant foveal hypoautofluorescence (P < .001). Also, the mean logMAR visual acuity was significantly worse in eyes in the predominant category compared with those in the none (P < .001) or minimal (P < .001) category (Figure 2). The percentages of eyes with at least moderate visual impairment and mean visual acuities of eyes in each category are summarized in Table 2. The FAF findings and clinical features of all patients are summarized in Table 3.

SERPIGINOUS CHOROIDOPATHY

Ten eyes of 5 patients with SPC underwent evaluation. Four patients underwent serial FAF imaging, with a mean follow-up of 9 (range, 4-13) months. In all 10 eyes, hypoautofluorescence corresponded closely with areas of chorioretinal atrophy from areas of prior disease activity.

In 3 eyes of 2 patients, new areas of hyperautofluorescence appeared at the border of a hypoautofluorescent area during disease exacerbations. Results of the ophthalmic examination also disclosed subtle pigmentary changes at the level of the RPE in the region of active inflammation, which was distinct from the areas of preexisting chorioretinal atrophy. Findings on fluorescein angiography confirmed active disease in the region of activity. In both patients, these changes on FAF imaging were featured more prominently than those appreciated on fundus photography or angiography (Figure 3). Both patients were treated with a dose escalation of their immunosuppressive regimens with subsequent stabilization of their disease. In another patient with macular SPC, hyperautofluorescence heralded the development of choroidal neovascularization (CNV) detected by optical coherence tomography and fluorescein angiography.

PRESUMED TB-SPLC

Patient 6 was referred to our service for possible SPC. This patient was monocular owing to an enucleation procedure of his right eye after a childhood trauma. He was a 28-year-old Pakistani man who had experienced decreased vision for several months and who developed worsening symptoms after prednisone therapy. His visual acuity was 20/20 at our initial examination, and Humphrey visual field testing 30-2 revealed dense superior and inferior visual field deficits with a mean deviation of −17.32 dB. No anterior chamber or vitreous cells were seen. Fundus examination of the left eye disclosed widespread areas of hyperpigmentary and hypopigmentary changes, which extended from the posterior pole and peripapillary region to the midperipheral retina in a pattern similar to that found in SPC. However, FAF

![Figure 2](http://archopht.jamanetwork.com/pdfaccess.ashx?url=/data/journals/ophth/6924/)

**Figure 2.** Proportions of patients with moderate or severe visual impairment. A, After χ² analysis, differences are apparent between the groups in which the degree of foveal hypoautofluorescence is none, minimal, or predominant. B, Kruskal-Wallis analysis shows that the mean logMAR visual acuity was significantly lower in patients with predominant foveal hypoautofluorescence compared with patients with minimal or no foveal hypoautofluorescence (both P < .001).

![Table 2](http://archopht.jamanetwork.com/pdfaccess.ashx?url=/data/journals/ophth/6924/)

**Table 2.** Moderate Visual Impairment and Mean Visual Acuity Data by Foveal Hypoautofluorescence Category

<table>
<thead>
<tr>
<th>Foveal Hypoautofluorescence Category</th>
<th>Total No. of Eyes</th>
<th>Visual Acuity, No. (%) of Eyes</th>
<th>Mean logMAR (Snellen) Visual Acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>19</td>
<td>17 (89)</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Minimal</td>
<td>18</td>
<td>12 (67)</td>
<td>6 (33)</td>
</tr>
<tr>
<td>Predominant</td>
<td>18</td>
<td>2 (11)</td>
<td>16 (89)</td>
</tr>
</tbody>
</table>

a Indicates a visual acuity of less than 20/40.
Table 3. FAF Imaging and Clinical Characteristics of Patients

<table>
<thead>
<tr>
<th>Patient No./Sex/Age, y</th>
<th>Diagnosis</th>
<th>Eye</th>
<th>Visual Acuity</th>
<th>Funduscopic Examination Findings</th>
<th>FAF Findings</th>
<th>Follow-up, mo</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/31</td>
<td>SPC</td>
<td>OD</td>
<td>20/20</td>
<td>CRA extending from peripapillary area into macula</td>
<td>HOAF corresponding to CRA, HRAF in active region</td>
<td>13</td>
<td>Prednisone, azathioprine sodium, cyclosporine, POT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/16</td>
<td>CRA extending from peripapillary area nasally</td>
<td>HOAF corresponding to CRA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/M/60</td>
<td>SPC</td>
<td>OD</td>
<td>20/125</td>
<td>CRA extending from peripapillary region involving macula</td>
<td>HOAF corresponding to CRA, HRAF in active region</td>
<td>4</td>
<td>Prednisone, azathioprine, cyclosporine, POT</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/80</td>
<td>CRA extending from peripapillary region involving macula, nasal retina</td>
<td>HOAF corresponding to CRA, HRAF in active region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3/F/41</td>
<td>SPC</td>
<td>OD</td>
<td>20/125</td>
<td>CRA</td>
<td>Diffuse HOAF</td>
<td>11</td>
<td>Prednisone, azathioprine, cyclosporine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/25</td>
<td>Peripheral CRA and mottling</td>
<td>Focal HOAF in area of CRA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/F/42</td>
<td>SPC</td>
<td>OD</td>
<td>1/200E</td>
<td>Macular RPE scarring and CRA</td>
<td>Diffuse HOAF</td>
<td>8</td>
<td>Sirolimus, POT, bevacizumab</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/20</td>
<td>Macular RPE scarring, RPE hyperplasia, and CRA</td>
<td>Mottled HOAF, HRAF in region of CNV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5/M/58</td>
<td>SPC</td>
<td>OD</td>
<td>20/50</td>
<td>CRA involving macula and midperipheral retina</td>
<td>HOAF corresponding to CRA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/63</td>
<td>CRA involving macula and midperipheral retina</td>
<td>HOAF corresponding to CRA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/M/28</td>
<td>Presumed</td>
<td>OS</td>
<td>20/20</td>
<td>Widespread RPE hyperpigmentation and atrophy</td>
<td>Complex pattern of HOAF and HRAF within macula and midperipheral retina</td>
<td>NA</td>
<td>RIPE</td>
</tr>
<tr>
<td>TB-SPLC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7/M/68</td>
<td>MFC</td>
<td>OD</td>
<td>20/125</td>
<td>Punched-out CR lesions involving macula and periphery</td>
<td>HOAF corresponding to CR lesions</td>
<td>12</td>
<td>Mycophenolate mofetil</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/20</td>
<td>Punched-out CR lesions involving macula and periphery</td>
<td>HOAF corresponding to CR lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8/M/44</td>
<td>MFC</td>
<td>OD</td>
<td>20/50</td>
<td>PPA and multiple punched-out peripheral CR lesions</td>
<td>Perivascular HOAF involving macula and periphery, some corresponding to CR lesions</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/63</td>
<td>PPA and multiple punched-out peripheral CR lesions</td>
<td>Perivascular HOAF involving macula and periphery, some corresponding to CR lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9/F/43</td>
<td>MFC</td>
<td>OD</td>
<td>HM</td>
<td>PPA and multiple peripheral CR lesions</td>
<td>Diffuse HOAF spots, greater than visualized with fundus photography</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/80</td>
<td>PPA and multiple peripheral CR lesions</td>
<td>Diffuse HOAF spots, greater than visualized with fundus photography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/F/24</td>
<td>MFC</td>
<td>OD</td>
<td>20/32</td>
<td>Foveal RPE hyperpigmentation, RPE mottling, and peripheral CR lesions</td>
<td>HOAF during active phase and quiescence</td>
<td>11</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/25</td>
<td>Foveal RPE hyperpigmentation, RPE mottling, and peripheral CR lesions</td>
<td>HRAF during active phase, HOAF during quiescence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11/F/44</td>
<td>MFC/PIC</td>
<td>OD a</td>
<td>20/200</td>
<td>Macular scarring and RPE hyperplasia</td>
<td>Macular HOAF</td>
<td>12</td>
<td>Sirolimus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS a</td>
<td>20/160</td>
<td>Macular scarring and RPE hyperplasia</td>
<td>Macular HOAF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12/F/35</td>
<td>MFC/PIC</td>
<td>OD a</td>
<td>20/125</td>
<td>Graying of RPE in region of CNVM, few areas of CRA</td>
<td>HRAF in area of CNVM activity, some HOAF spots</td>
<td>NA</td>
<td>Sirolimus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS a</td>
<td>20/80</td>
<td>CRA and RPE hyperplasia</td>
<td>HOAF corresponding to scarring, mild persistent perifoveal HRAF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>13/M/74</td>
<td>MFC</td>
<td>OD</td>
<td>20/32</td>
<td>CRA involving macula and peripheral retina</td>
<td>HOAF corresponding to CRA in macula, peripheral retina</td>
<td>12</td>
<td>Methotrexate sodium</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/40</td>
<td>CRA involving macula and peripheral retina</td>
<td>HOAF corresponding to CRA in macula, peripheral retina</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14/F/28</td>
<td>MFC</td>
<td>OD</td>
<td>20/20</td>
<td>Multifocal, peripheral hyperpigmented spots</td>
<td>HOAF corresponding to lesions with granular HRAF within each lesion (active)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/20</td>
<td>Multifocal, peripheral hyperpigmented spots</td>
<td>HOAF corresponding to lesions with granular HRAF within each lesion (active)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15/F/56</td>
<td>BRC</td>
<td>OD</td>
<td>20/20</td>
<td>Multiple atrophic CR lesions within macula</td>
<td>Multiple HOAF dots within macula</td>
<td>13</td>
<td>Cyclosporine, mycophenolate mofetil</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/20</td>
<td>Multiple atrophic CR lesions within macula</td>
<td>Multiple HOAF dots within macula</td>
<td></td>
<td></td>
</tr>
<tr>
<td>16/M/35</td>
<td>BRC</td>
<td>OD</td>
<td>20/25</td>
<td>Multiple atrophic CR lesions involving periphery, few macular lesions</td>
<td>Diffuse HOAF involving macula and peripapillary area</td>
<td>NA</td>
<td>Cyclosporine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>OS</td>
<td>20/20</td>
<td>Multiple atrophic CR lesions involving periphery, few macular lesions</td>
<td>HOAF of nasal peripapillary region</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
imaging demonstrated a variegated pattern of hypoauf-
fluorescent and hyperautofluorescent signals that also
included areas of stippled hyperautofluorescence in the
macula (Figure 4). The FAF findings of the affected
areas in this case differed from the pattern of contiguous
hypoaufi uorescence seen for SPC (Figure 3) and sug-
gested a separate diagnosis. Further testing revealed that
the patient had a positive purified protein derivative test,
and a pericardial effusion was seen on computed tomography. The diagnosis of TB-SPLC was made, and 4-drug antituberculosis therapy consisting of rifampin, isoniazid, pyrimethamine, and ethambutol hydrochloride was initiated after consultation with an infectious disease specialist. Long-term follow-up for this patient was unavailable.

MULTIFOCAL CHOROIDITIS

Sixteen eyes of 8 patients with MFC underwent assessment with FAF imaging. Four patients were followed up for a mean of 12 (range, 11-12) months. In 12 of the 16 eyes (75%), punctate hypoautofluorescent spots corresponding to multiple areas of chorioretinal atrophy were the predominant finding, consistent with the findings described in a previous series of patients with MFC. In both eyes of a patient with active MFC, macular hyperautofluorescence was observed in the area of active chorioretinitis. Institution of immunosuppressive therapy led to a resolution of clinical signs of disease activity, which also correlated with the complete disappearance of the hyperautofluorescent signal (Figure 5).

BIRDSHOT RETINOCHOROIDOPATHY

In 20 eyes of 10 patients with BRC, the predominant FAF findings in most cases were scattered hypoautofluorescent areas corresponding to areas of chorioretinal atrophy. However, in eyes with widespread lesions, the correlation between hypoautofluorescence and choroidal atrophy was less evident. In some cases, despite the appearance of multiple choroidal lesions appreciated on funduscopy, the FAF signal in these areas appeared normal. It is possible that, in the patients in whom the outer choroid was predominantly involved, the overlying RPE may not have undergone significant injury. In patients with other retinal features, including vasculitis and cystoid or diffuse macular edema, the RPE accumulation of lipofuscin may be more readily appreciated. The possibility of inflammatory disease affecting the RPE and choroid independently has been suggested previously, and our findings are consistent with those observations.

ACUTE ZONAL OCCULT OUTER RETINOPATHY

Two patients with AZOOR underwent evaluation. In 3 eyes of the 2 patients with subtle RPE abnormalities on
clinical examination and fluorescein angiography, a hypoautofluorescent area corresponded to this area of RPE change. A hyperautofluorescent halo surrounded this area of hypoautofluorescence in all eyes undergoing evaluation. In one of these patients, we also observed multiple smaller hypoautofluorescent lesions with surrounding hyperautofluorescent haloes, which were not appreciable on the clinical examination findings (Figure 6). This finding is supportive of the hypothesis that AZOOR likely represents a multifocal process, although, in some situations, focal RPE atrophy is appreciated clinically. This same patient showed no evidence of change in the autofluorescent signal during her 10-month follow-up, when the patient’s disease remained clinically stable.

APMPPE AND RPC

In the patient with APMPPE who underwent evaluation in our series, ophthalmic examination disclosed placoid lesions involving the posterior pole with varying areas of RPE hyperpigmentation and atrophy. The FAF imaging showed macular hypoautofluorescence with few hyperautofluorescent spots. In another patient with RPC, which is thought to bear clinical characteristics similar to APMPPE, the FAF imaging findings were markedly different. In the second patient, we observed widespread hypoautofluorescence, which involved the posterior pole and midperipheral retina (Figure 7). The decreased autofluorescent signal may have been derived from the absence of normal fluorophores in the regions of atrophy and possibly from blockage of the autofluorescence signal in the regions of RPE hyperplasia. Although these FAF imaging features differed from those of the patient with APMPPE, further studies are needed to determine whether active APMPPE or active RPC may show differences in autofluorescence prior to the onset of diffuse RPE atrophy and scarring.

**COMMENT**

The autofluorescence features of the WDSs described herein provide insight into the structural changes of the
RPE found in each disease entity. We also evaluated the association of visual impairment with the degree of foveal hypoautofluorescence observed. The proportion of patients with at least moderate visual impairment differed between eyes classified as having predominant, minimal, and no foveal hypoautofluorescence. The mean logMAR visual acuity for patients with predominant foveal hypoautofluorescence was significantly worse than for patients with minimal or no foveal hypoautofluorescence. Placoid macular hypoautofluorescence has been correlated with visual acuity of 20/50 or less in BRC13; however, the association of a visual acuity impairment with hypoautofluorescence in other WDSs has not been established.

In this cohort of patients, a number of patients were observed longitudinally and showed FAF imaging changes that could be useful for the serial evaluation of the disease processes. In its active and inactive disease states, SPC demonstrated a characteristic FAF imaging appearance with hypoautofluorescence corresponding closely to areas of regressed disease activity and hyperautofluorescence highlighting areas of active disease. The observations of the 5 patients with SPC in this series are consistent with those of 2 patients recently described who demonstrated hyperautofluorescence during a period of disease activity, which later regressed.19 In 2 of our 5 patients, we observed that hyperautofluorescence was a sensitive indicator of a new border of activity during serial FAF imaging evaluation. This potentially represents a noninvasive method of following up patients with SPC. In another patient with macular SPC, hyperautofluorescence heralded the development of CNV. This phenomenon has been described in MFC previously14 but, to our knowledge, has not been observed in SPC. Because the inciting events in CNV asso-

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**Figure 5.** Findings in a 28-year-old woman with multifocal choroiditis (patient 10). A, Areas of retinal pigment epithelial (RPE) hyperplasia and a few punctate areas of atrophy and decreased visual acuity to 20/32 are evident. B, The initial fundus autofluorescence (FAF) image shows hyperautofluorescence in the region of the RPE hyperpigmentation with scattered areas of hypoautofluorescence that were difficult to appreciate on fundus photography. C, The corresponding optical coherence tomography (OCT) image shows RPE elevation in the region of RPE hyperpigmentation (arrow). D, Eleven months after cyclosporine therapy, visual acuity improved to 20/16, and the fundus photograph shows minimal RPE change with mottling. E, The corresponding FAF image shows scattered areas of hypoautofluorescence. F, The OCT image shows resolution of the RPE abnormalities (arrow).
CIated with MFC and SPC are likely similar (i.e., T-cell–mediated choroidal inflammation with subsequent damage to the RPE and Bruch membrane), the autofluorescence characteristics of SPC-associated CNV could resemble those of MFC-associated CNV.

In another patient with presumed TB-SPLC, the FAF characteristics during a period of disease activity differed from SPC of nontuberculous origin. There is growing evidence that, in some patients diagnosed as having SPC, the disease may be associated with immune-based inflammation targeting *Mycobacteria* antigens. It is possible that in presumed TB-SPLC the RPE is more severely disrupted as a primary event than in SPC because *Mycobacterium tuberculosis* DNA has been detected in RPE specimens of *M tuberculosis*-infected individuals. In SPC, choroidal inflammation may be the primary event, with RPE disruption seen as a secondary consequence. Further imaging studies in tuberculosis-associated uveitis are warranted to determine whether this imaging modality could be an adjunctive diagnostic method to distinguish SPC from presumed TB-SPLC.

Most of the patients with MFC in our series were receiving immunosuppressive therapy at the time of evaluation, and most of those were clinically quiescent. The hypoautofluorescent spots corresponded to areas of chorioretinal atrophy, which is consistent with previous observations. One patient with active inflammation by fluorescein angiography was notable in that the hyperautofluorescence in the region of RPE remodeling faded with minimal RPE mottling changes after immunosuppressive therapy. In other conditions, such as geographic atrophy associated with age-related macular degeneration, hyperautofluorescence at the border of a zone of geographic atrophy is thought to be a marker for future atrophy progression. In this patient, we were able to avert the development of atrophic change in the foveal region by administering immunosuppressive therapy. During follow-up, the patient also experienced a decrease in hyperautofluorescence intensity in the affected region in addition to a resolution of her clinical symptoms, an improvement in her visual acuity, and resolution of her visual field deficit. This result suggests that the disappearance of pathologic hyperautofluorescence was correlated with improved visual function.

A previous study of autofluorescence in 8 patients with BRC demonstrated RPE atrophy that did not correspond with the birdshot lesions, suggesting that the RPE and choroid could be damaged independently in BRC. We similarly observed fewer multiple hypoautofluorescence spots than would be expected given the number of birdshot lesions observed in some patients. In patients with BRC who have advanced disease with multiple areas of chorioretinal atrophy, the areas of hyperautofluorescence were better correlated with the lesions. It is possible that patients with predominantly choroidal inflammation without overlying RPE and outer retinal injury may have fewer autofluorescent findings. If the clinically observed choroidal lesions consistently precede FAF changes, consideration could be given to immunosuppressive therapy for patients with BRC before the onset of chorioretinal atrophy.

Acute zonal occult outer retinopathy is an inflammatory condition thought to involve outer-segment photoreceptor dysfunction, which is characterized by subtle clinical RPE atrophic features in association with photopias, visual field defects often involving the blind spot, and a nonprogressive clinical course. A report of FAF imaging in a patient with AZOOR showed a hyperautofluorescent border surrounding a depigmented area from a typical lesion of AZOOR. In 2 patients with AZOOR, we found a similar area of central hypoautofluorescence with surrounding areas of hyperautofluorescence. In one of these patients, multiple smaller haloes were observed on FAF imaging that were not readily apparent on fundus photography.
In a previous report of FAF imaging in APMPPE, early hypoautofluorescence was seen in the area of placoid lesions; after resolution of disease activity, hyperautofluorescence was observed. Our patient with APMPPE underwent evaluation during a period of disease quiescence and displayed placoid areas of hypoautofluorescence that corresponded to areas of previous RPE scarring from APMPPE. These differed from the autofluorescence findings in RPC, which showed large, confluent areas of hyperautofluorescence corresponding to areas of atrophic RPE and diffuse RPE hyperplasia involving the posterior pole and peripheral retina. The FAF findings remained stable after immunosuppressive therapy. Although it is possible that these 2 diagnoses represent different ends of a disease spectrum, the FAF findings derived from the scarring response in the quiescent phase of the disease suggest potentially disparate processes.

Limitations of this study include the retrospective nature of the data collection, the heterogeneity of the disease conditions, limited follow-up FAF imaging, and the possible introduction of bias in the grading of the FAF images. Because, to our knowledge, this is the first report of this FAF grading system for WDSs, the interobserver and intraobserver reliabilities of FAF grading have not been established. To reduce the likelihood of bias, the grading scheme was designed so that only a gross estimation of foveal hypoautofluorescence was required. The development of a masked, standardized grading scheme to evaluate FAF images is desirable in further studies.

In summary, we have described a range of FAF imaging findings in the WDSs. Although ophthalmic examination, fundus photography, and fluorescein angiography played a significant role in the evaluation of the WDSs, FAF imaging was valuable in highlighting areas of disease activity and may allow distinctions between diseases. In this series of patients, we also observed that foveal hypoautofluorescence appeared to be a marker for moderate to severe visual impairment. Although further studies on FAF imaging for the WDSs are needed, our findings suggest that this imaging method may be valuable for the characterization of the WDSs and, potentially, for the localization of disease activity.

Figure 7. Findings in a 36-year-old man diagnosed as having relentless placoid chorioretinitis (patient 28). A and B, Fundus photography showed central chorioretinal atrophy and widespread retinal pigment epithelial (RPE) hyperpigmentation with variable atrophy in both eyes. C and D, Fundus autofluorescence imaging highlights these changes, showing widespread hypoautofluorescence in both of the areas of chorioretinal atrophy and RPE hyperpigmentation.
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