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1 MULTIMODAL IMAGING IN ACUTE POSTERIOR MULTIFOCAL PLACOID PIGMENT
2 EPITHELIOPATHY DEMONSTRATING OBSTRUCTION OF THE CHORIOCAPILLARIS.

3

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26 **Abstract:**

27

28 Optical coherence tomography angiography (Angio-OCT) provides non-invasive in-vivo
29 vascular imaging of the retina and choriocapillaris. To highlight Angio-OCT utility we
30 align structural changes and their resolution with functional outcome. We present a case
31 of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and sequential
32 changes during transition to inactive disease. In the acute phase, altered flow and non-
33 perfusion were seen in defined islands of choriocapillaris. Over time progressive re-
34 perfusion was observed and accompanied clinical resolution and functional visual
35 restoration. The imaging features acquired described the level of non-perfusion we had
36 assumed when extrapolating findings from multiple independent imaging modalities.

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40 **Introduction**

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42 Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) was first described
43 by Gass as a condition that affects the choriocapillaris, retinal pigment epithelium (RPE),
44 and outer retinal layers.¹ However, the pathophysiology in APMPPE is not well
45 understood, with no histopathologic studies reported due to the condition's transience.²
46 Nevertheless, continued advances in ophthalmic imaging have provided additional
47 information, but still none has demonstrated a direct primary involvement of the
48 choriocapillaris, which remains inferred.³⁻⁵

49 Fluorescein (FA) and indocyanine green (ICG) angiography are well-established invasive
50 techniques for assessing, in part, retinal and choroidal flow and defining active disease
51 in APMPPE. The typical angiographic findings in APMPPE are well reported. However,
52 localisation of lesion depth can be difficult, particularly in the context of blocking and
53 staining by lesions.

54 Fundus autofluorescence (FAF) findings also have been described in this pathology and
55 overlapping entities such as macular serpiginous choroidopathy, with
56 hypoautofluorescent in the acute lesion, and subsequently hyperautofluorescence to
57 final hypoautofluorescence of the lesions due to retinal pigment epithelium (RPE)
58 damage.^{4,6}

59 These two-dimensional modalities do not provide segmental views of the retinal plexus
60 and choriocapillaris. Optical coherence tomography angiography (Angio-OCT) provides
61 a means for in-vivo direct visualization of the vascular flow and microstructure in the
62 retina and choroid.⁷ The technology allows segmentation to specific depths, including
63 deep and superficial plexus and choriocapillaris, with potential to localise and delineate

64 pathology. We present a case of acute APMPE studied with multi-modal imaging
65 including Angio-OCT and describe evolution over time.

66

67 **Case report**

68

69 A 27-year-old man presented with a three-day history of bilateral central visual loss
70 after a viral 'flu' like illness. Visual acuity was 0.3 (logMAR) in the right eye and 1.0
71 (logMAR) in the left eye with no intraocular cellular activity. Multiple cream-coloured
72 placoid lesions were present in the central macular area of both eyes. Classical features
73 were present and included: FA features of early hypofluorescent lesions with
74 hyperfluorescent borders and late staining (Figure 1); indocyanine green angiographic
75 (ICG) features of persistent hypofluorescent lesions in the late frames as well as classical
76 hypofluorescent ICGA lesions that were not initially evident on FA imaging (figure 1).

77 Angio-OCT (AngioVue; Optovue Inc., Fremont, California, USA) segmentation images
78 demonstrated normal morphology and texture of the superficial and deep capillary
79 retinal plexus. The choriocapillaris was imaged with segmentation below the retinal
80 pigment epithelium (RPE) and alterations to the capillary density and pattern were
81 evident. Features included disruption of the typical packed honeycomb structure at the
82 central fovea within lesions. The morphology and texture of the choriocapillaris angio-
83 flow was disrupted indicating reduction of vascular flow. Defined areas of non-perfusion
84 corresponded to the lesions observed on FA and ICG angiography. These patterns were
85 not observed in areas of normal retina and were clearly differentiated from artefacts.
86 En-face OCT at the level of the choriocapillaris areas revealed hyporeflectance
87 corresponding with the area of impaired choriocapillaris perfusion. Fundus
88 autofluorescence (FAF) demonstrated ill-defined hypoautofluorescence of the lesions.

89 Infrared reflectance (IRR) disclosed ill-defined areas of hyperreflectance corresponding
90 with the lesions. Spectral domain optical coherence tomography (SD-OCT) at the level of
91 the fovea revealed significant disruption, including partial disappearance of the ellipsoid
92 zone in areas corresponding to the lesions (figure 2, figure 3).

93 The clinical and imaging features were consistent with the diagnosis of APMPE.
94 Syphilis, HIV serology, and QuantiFERON Gold tests performed at presentation, were
95 negative. Oral corticosteroid was commenced (prednisolone 60mg OD) because of
96 central macular involvement with severe visual impairment at presentation. Over the
97 following three weeks, the placoid lesions progressively faded and were replaced by
98 hyperpigmentation and atrophy (figure 2, figure 3). The visual acuity improved to 0.0
99 (logMAR) in both eyes over the course of 3 weeks and oral prednisolone was tapered
100 according to clinical resolution. Sequential FAF imaging demonstrated progressive
101 development of hyperautofluorescence at the edges of the lesions (figure 2, figure 3).
102 IRR showed a progressive definition of the lesion borders and increase in the
103 hyperreflectance over time. The en face OCT showed a progressive increase in the
104 hyperreflectance of the lesions (figure 2, figure 3). SD-OCT demonstrated a restoration
105 of the inner segment ellipsoid layer but persistent disruption of the RPE within the
106 lesions (figure 2, figure 3). Repeat Angio-OCT images (at 3, 11 and 21 days after
107 presentation) demonstrated changes in choriocapillaris flow images with progressive
108 evidence of reduction in extent of the non-perfused areas and signs of vascular re-
109 perfusion (figure 2, figure 3).

110

111 **Discussion**

112

113 The nature of lesions and associated choriocapillaris non-perfusion in APMPE remains
114 elusive. Using Angio-OCT this case demonstrates isolated choriocapillaris non-perfusion
115 within 'placoid' lesions in the active disease phase. Our images support theories of
116 primary choriocapillaris pathology in this condition.⁸ During disease resolution,
117 sequential improvement in flow and reduction in size of the non-perfused area was seen
118 supporting previous inferences that vascular re-perfusion and re-modelling occurred.
119 This technology provides new imaging evidence of the site and area of choriocapillary
120 vascular pathology during the acute and later phases of the disease. These Angio-OCT
121 findings support the notion that APMPE is a primary inflammatory
122 choriocapillaropathy,⁸ where the visualisation of non-perfusion in the lesions may be
123 the consequence of occlusive vasculitis.

124 Angio-OCT is a non-invasive and quick image modality for the detection and monitoring
125 of choriocapillary involvement in APMPE patients. This new technology is a potential
126 alternative to invasive angiography. Further studies are warranted to develop our
127 understanding of Angio-OCT changes in inflammatory diseases, particularly those
128 involving the choriocapillaris.

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155 **FIGURE LEGENDS:**

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157 **Figure 1.-** Fundus fluorescein angiography (FFA) and indocyanine green angiography
158 (ICGA) at presentation. Row A shows the early frames of the angiography for the right
159 (A1) and the left eye (A2). Row B and C show later frames for the right (B-C1) and the
160 left eye (B-C2). Row D shows peripheral shots for the right (D1) and left eye (D2). The
161 FFA disclosed early hypofluorescence of the lesions with late staining and leakage, ICGA
162 showed persistent hypofluorescence during the angiogram, with evidence of multiple
163 lesions, the majority of them not apparent in the FFA.

164

165

166 **Figure 2.-** Multimodal imaging of the right eye at presentation and follow-up. Row 1
167 shows the images at presentation, row 2 shows findings 4 days later, and row 3 shows
168 findings 11 days after presentation, and row 4, 21 days. Column A represents the colour
169 pictures, column B OCT angiography findings, column C shows fundus autofluorescence,
170 column D spectral domain OCT findings.

171

172

173 **Figure 3.-** Multimodal imaging of the left eye at presentation and follow-up. Row 1
174 shows the images at presentation, row 2 shows findings 4 days later, and row 3 shows
175 findings 11 days after presentation, and row 4, 21 days. Column A represents the colour
176 pictures, column B OCT angiography findings, column C shows fundus autofluorescence,
177 column D spectral domain OCT findings.

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