Two for One! Epiphenomenon of Multiple Evanescent White Dot Syndrome: A Case Report

Dois em Um! Epifenómeno do Síndrome de Múltiplas Manchas Brancas Evanescentes: A Propósito de um Caso Clínico

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ABSTRACT

We present a case of a 24-year-old female with unilateral subacute visual loss (20/40 OD and 20/16 OS) and metamorphopsias for one week. Examination of the right eye revealed multiple white dots involving the posterior pole and mid periphery, an old chorioretinal scar in the inferior vascular arcade, and atrophic punched-out lesions in the inferior periphery. Optical coherence tomography showed choroidal neovascularization (CNV) arising from the superior border of the main scar. The patient was diagnosed with secondary multiple evanescent white dot syndrome (MEWDS) complicated by CNV, in the presence of a quiescent multifocal choroiditis (MFC). She was treated with anti-VEGF injection and corticosteroids. Two months later, vision improved to 20/20 OD, the white spots faded and CNV regressed. Secondary MEWDS seems to be an epiphenomenon that occurs by triggered inflammation of the outer retina and is associated with MFC. Multimodal imaging improves the diagnosis of the spectrum of MEWDS.

KEYWORDS: Choroidal Neovascularization; Multifocal Choroiditis; White Dot Syndromes.

RESUMO

Apresentamos o caso de uma mulher de 24 anos com diminuição subaguda e unilateral de visão (20/40 OD e 20/16 OE) e metamorfopsias com uma semana de evolução. No exame oftalmológico do olho direito (OD), observou-se múltiplas manchas pequenas esbranquiçadas no polo posterior, cicatriz corioretiniana na arcada vascular inferior e lesões "punched-out" na periferia inferior. A tomografia de coerência ótica revelou neovascularização coroideia (NVC) no bordo superior da cicatriz. A doente foi diagnosticada com síndrome de múltiplas manchas brancas evanescentes (MEWDS) secundária, complicada por NVC, na presença de coroidite multifocal (CMF) quiescente. A doente foi tratada com injeção anti-VEGF e corticoterapia. Dois meses depois, a visão OD recuperou para 20/20, as manchas brancas esvaneceram e NVC regrediu. A forma secundária de MEWDS parece ser um epifenómeno que ocorre na presença de inflamação na retina externa e está associada a CMF. A investigação multimodal ajuda no diagnóstico do espectro de MEWDS.

PALAVRAS-CHAVE: Coroidite Multifocal; Neovascularização de Coroide; Síndrome das Manchas Brancas.

INTRODUCTION

Multiple evanescent white dot syndrome (MEWDS), first described in 1984, is defined as a self-limited inflammatory chorioretinopathy. It is most often unilateral and typically affects young healthy myopic female patients.[1-5]

Clinically, MEWDS is characterized by multiple subretinal white dots and foveal granularity, which results in acute loss of visual acuity (VA) and visual field defects.[2-5] Although these clinical features are well described, the pathogenesis of MEWDS remains poorly understood.[4] Different theories implicate a host's genetic susceptibility and/or autoimmune-mediated mechanism contributing to the development of this distinct entity.[3]

Recently, a secondary form of MEWDS has been described as occurring in conjunction with other unrelated ocular diseases, such as multifocal choroiditis (MFC) or punctuate inner choroidopathy (PIC), either concurrently or over the course of follow-up.[4,5] Although overlap and spectrums exist among these diseases, multimodal imaging enhances our understanding of all forms of MEWDS and helps to differentiate it from other entities.

Herein, we present a rare case of a young woman with a possible quiescent MFC with acute onset of a secondary MEWDS and choroidal neovascularization (CNV).

CASE REPORT

A 24-year-old female presented to the Ophthalmology emergency department with unilateral subacute visual loss and metamorphopsias for one week. Past ocular history was relevant for right ocular trauma during childhood, but no visual sequelae derived from it. Medical history was remarkable for depression treated with a selective serotonin reuptake inhibitor. Otherwise, she was healthy with no history of respiratory illness or recent vaccinations.

At presentation, best-corrected visual acuity (BCVA) was 20/40 on the right eye (OD) and 20/16 on the left eye (OS), and intraocular pressure was 14 mmHg in both eyes (OU). The anterior segment evaluation was unremarkable. On dilated fundus examination, OD revealed multiple deep white dots involving the posterior pole and the mid periphery, an old chorioretinal scar in the inferior vascular arcade, and three atrophic punched-out lesions in the inferior periphery (Fig. 1A). No vitreous haze was detected. Fundus autofluorescence (FAF) revealed scattered hyperautofluorescence dots (Fig. 1B). Optical coherence tomography (OCT) confirmed several focal disruptions of the ellipsoid and interdigitation zones corresponding to the dots (Fig. 1D), and a localized CNV arising from the superior border of the mid-peripheric scar (Fig. 1C). Contralateral examination was unremarkable (Fig. 1E-G).

A laboratory work-up including a serum complete blood count, metabolic panel with C-reactive protein, venereal disease research laboratory test, and anti-tuberculosis (Quantiferon) was performed, to rule out systemic disorders such as infectious or autoimmune disorders.

Based on the clinical presentation, multimodal imaging, and negative blood work-up, the patient was diagnosed with secondary MEWDS complicated by CNV, in the presence of a probable quiescent non-previously identified MFC.

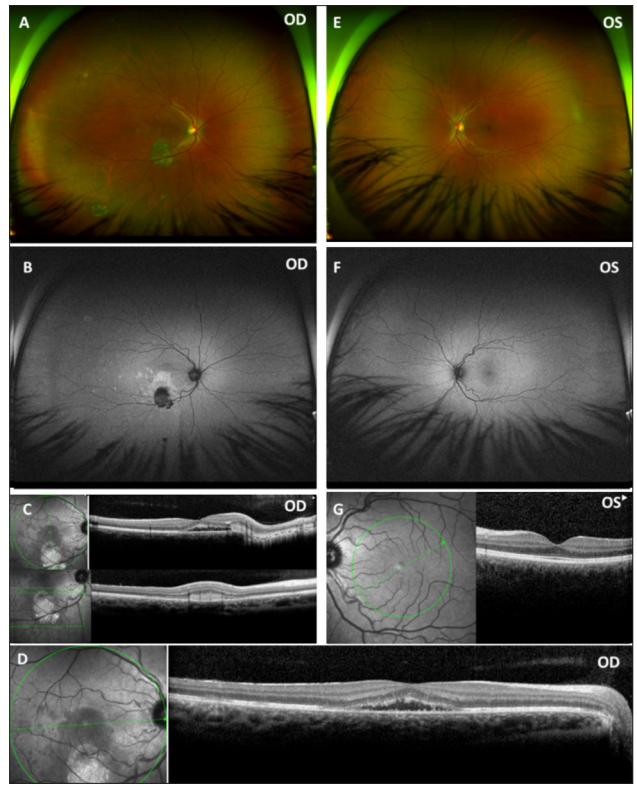

Figure 1. Wide-field pseudocolor fundus photographs, FAF and OCT images at presentation. A) Fundus photographs show deep white dots in the posterior pole and the mid periphery, an old chorioretinal scar in the inferior vascular arcade, and three atrophic punched-out lesions in the inferior periphery only on the OD; B) FAF OD revealed scattered hyperautofluorescence dots, an area of hyperautofluorescence in the superior border of the atrophic lesion in the inferior posterior pole, corresponding to the inflammatory activity, and hypoautofluorescence atrophic lesions; C) OCT OD shows disruption of the ellipsoid zone and highlights the CNV arising from the upper border of chorioretinal scar; D) OCT OD displays focal disruptions of the ellipsoid and interdigitation zones corresponding to the dots; E) Fundus photograph OS unremarkable; F) FAF OS without alterations; G) OCT OS with normal retinal and macular architecture.

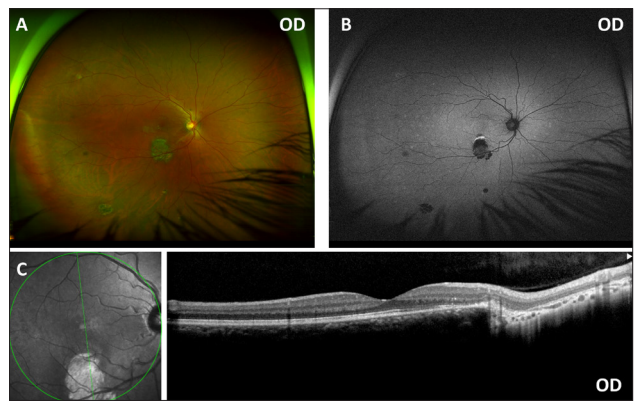

Figure 2. Wide-field pseudocolor fundus photographs, FAF and OCT images at 2 months follow-up. A) Fundus photograph OD shows previous chorioretinal scars; B) FAF OD revealed decreased hyperautofluoresence of lesions; C) OCT OD shows regression of CNV, with normal macular architecture.

Due to the presence of active CNV, the patient was treated with one intravitreal injection of aflibercept, an anti-vascular endothelial growth factor OD together with a course of oral methylprednisolone tapered over eight weeks. At two weeks follow-up, the patient reported improvement in symptoms and BCVA OD to 20/25. Two months after the initial presentation, VA OD recovered to 20/20, the white spots faded, and the previous existing scars remained unchanged (Fig. 2A). OCT revealed reorganization of the ellipsoid zone (EZ), a decrease in outer retinal hyperreflectivity, and the disappearance of CNV (Fig. 2C). Additionally, fundus autofluorescence (FAF) demonstrated a reduction in hyperautofluorescence (Fig. 2B).

DISCUSSION

In the spectrum of MEWDS, the secondary form is considered an "epiphenomenon" (EpiMEWDS) that occurs alongside a chorioretinal inflammatory pathology.[5] The main underlying pathologies reported to trigger secondary MEWDS, include MFC, PIC, CNV, acute macular neuroretinopathy, acute zonal occult outer retinopathy, Best disease, pseudoxanthoma elasticum, and other retinal insults.[2,4,5] Among those, MEWDS secondary to MFC or PIC (MFC/PIC) is the most common type.[2]

The recognition of EpiMEWDS has contributed to the long-standing controversy on whether MEWDS and MFC share the same pathogenesis.[3,5] It has been hypothesized that the disruption of the tunica *Ruyschiana* (choriocapillaris, Bruch membrane, and retinal pigment epithelium (RPE) complex) caused by MFC/PIC, may compromise the posterior retinal blood-brain barrier and lead to a subsequent loss of immune privilege of the outer retina and trigger a local inflammatory response.[2-5] Such speculation can explain the tendency for secondary MEWDS to arise in proximity to an area of chorioretinal scarring before spreading peripherally, which was what seemed to occur with our patient.[4,5] Moreover, two recent reviews compared the primary and secondary forms of MEWDS and concluded that lesions from EpiMEWDS arise from the underlying pathologies.[2,3]

Supporting evidence from a multimodal imaging study of MEWDS helped establish more distinguishing features of these two entities and provided a better understanding of the pathogenesis (Table 1).[2,6,7] Our patient presented in the acute phase with characteristics for both MEWDS and MFC. On FAF we could see discrete hyperautofluorescent dots on posterior-pole and mid-peripheral suggestive of MEWDS. In contrast, a hypoautofluorescent lesion in the posterior pole and three in the inferior periphery on FAF were related to MFC. On OCT, foveal granularity was an acute manifestation of MEWDS, while the sub-RPE lesion extending into the outer retina with choroidal hyperreflectivity appeared about MFC.

A serious complication of inflammatory chorioretinopathies is CNV.[9-11] Although it can occur secondary to MEWDS, the frequency is scarce due to the duration and the extent of inflammation being limited.[8,9] Interestingly, it has been reported a sequence in which MEWDS developed following or concomitant to CNV.[12] A few characteristics of the present patient suggested that a choroidal membrane occurred due to quiescent MFC and was followed by MEWDS. First, the arising of CNV from an old chorioretinal scar. Second, MFC did not recur after the onset of MEWDS, suggesting that the primary choriocapillaris was not involved in MEWDS. Lastly, CNV regressed with immunosuppressive therapy in addition to anti-VEGF therapy, which is more suggestive of an inflammatory cause and more frequently associated with MFC rather than MEWDS.

Secondary MEWDS seems to have a similar course to idiopathic MEWDS regarding a spontaneous resolution of the transient white dots and restoration of visual function.[4] The principal factors distinguishing primary from EpiMEWDS include bilaterality and recurrence,[2,5] which were absent in this report. However, currently, these attributes are considered largely observational. Our patient presented a complete resolution of symptoms, white dots, and a good visual outcome. Also, on short-term follow-up (3 months) the regressed CNV lesion did not recur, and the contralateral eye remained unaffected.

Table 1. Multimodal imaging findings seen in the MEWDS, MFC and PIC.

	MEWDS	MFC	PIC
OCT	Disruption of the EZ. Accumulation of hyperreflective material that rests on the RPE and extends anteriorly.	Drusen-like sub-RPE material Choroidal hyperreflectivity below the lesions. Overlying vitreous cells.	Focal elevation of the RPE with underlying hyporeflective space. Focal atrophy of the outer retina and RPE. Focal hyperreflective dots in the inner choroid and focal thinning of the choroid adjacent to lesions.
FAF	Areas of hyperautofluorescence (acute phase). Pinpoint hypoautofluorescence corresponds to foveal granularity.	Hypoautofluorescent lesions in the posterior pole and periphery.	Hypoautofluorescent spots with a hyperautofluorescent margin.
FA	Early hyperfluorescent lesions in a wreathlike configuration in the mid-retina.	Early hypofluorescence with late hyperfluorescent staining.	Early hyperfluorescence lesions, and late stain (more than seen on exams).
ICGA	Atrophic lesions appear as window defects.	Hypocyanescent spots within the choroid (quantities greater than lesions seen on exams).	Hypofluorescent spots (same number seen on FA).

OCT - optical coherence tomography; FAF – fundus autofluorescence; FA – fluorescein angiography; ICGA – indocyanine green angiography.

Adapted from Raven M, et al. Multi-modal imaging and anatomic classification of the white dot syndromes. 2017. Int J Retin Vitr. 2017;3:12.[6]

CONCLUSION

We report a case of a young woman with quiescent MFC complicated by CNV that triggered EpiMEWDS with complete restoration of VA and retinal findings. Our case supports the hypothesis that local chorioretinal damage may be pro-inflammatory and potentially trigger MEWDS and/or CNV.

A heightened awareness of these inflammatory entities and thorough use of multimodal imaging may help to improve the diagnosis of MEWDS and enhance our understanding of EpiMEWDS. Further, longitudinal studies are necessary to clarify the relationship of previous or concurrent distinct events involving damage to the outer retina in a susceptible host.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

TM: Investigação, Análise formal, Visualização, Escrita do projeto original.

CF: Investigação, Análise formal, Visualização, Recursos, Escrita - Revisão e Edição.

Todos os autores leram e aprovaram o manuscrito.

TM: Investigation, Formal analysis, Visualization, Writing Original Draft.

CF: Investigation, Formal analysis, Visualization, Resources, Writing - Review & Editing.

All authors have read and approved the manuscript.

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