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Choroidal nonperfusion on optical coherence tomography angiography in a case of unilateral posterior segment ocular sarcoidosis misdiagnosed as MEWDS

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ABSTRACT

Purpose: To report a case of presumed ocular sarcoidosis initially presenting with features of multiple evanescent white dot syndrome (MEWDS) with atypical optical coherence tomography angiography (OCTA) findings.

Observations: A 23 year-old woman presented with a unilateral central scotoma, photophobia, and decreased visual acuity after a viral illness. Examination of the right eye revealed multiple round white macular spots and stippled granularity at the fovea. Multimodal imaging with fluorescein angiography (FA), indocyanine green angiography (ICG), fundus autofluorescence (FAF), and optical coherence tomography (OCT) was consistent with a diagnosis of MEWDS. However, OCTA demonstrated choriocapillaris (CC) flow deficits, which is not typical for MEWDS. The clinical course was initially consistent with MEWDS, with spontaneous recovery of symptoms over ensuing months. The patient presented five months later with floaters and a central scotoma. Examination showed panuveitis, and systemic evaluation revealed an elevated angiotensin converting enzyme (ACE) and hilar lymphadenopathy on chest x-ray consistent with presumed sarcoidosis.

Conclusions and Importance: A case of MEWDS atypically demonstrated CC flow deficits on OCTA and subsequently presented as uveitis secondary to presumed sarcoidosis. Atypical features in MEWDS may be a sign of another disorder masquerading early on as MEWDS and ought to prompt further investigation.

1. Introduction

Multiple evanescent white dot syndrome (MEWDS) is a rare, acute retinal inflammatory disease that typically affects young to middle-aged women with a self-resolving course.[1] Patients present with unilateral sudden decrease in vision, paracentral scotoma, or photopsia. Multimodal imaging with fluorescein angiography (FA), indocyanine green angiography (ICG), and optical coherence tomography (OCT) assist in distinguishing MEWDS from other white dot syndromes.[2] OCT angiography (OCTA), a novel imaging modality, reveals intact choriocapillaris (CC) perfusion in MEWDS despite hypocyanescence on ICG, consistent with the theory of the disease's pathogenesis in the photoreceptors.[3–5] While MEWDS has been hypothesized to be a post-viral phenomenon, there are no systemic sequelae.

In contrast, sarcoidosis is a multisystem disorder characterized by the presence of non-caseating granulomas in affected organs. Ocular involvement has been reported in 30–60% of sarcoidosis patients, with uveitis representing the most common manifestation.[6] Other posterior segment findings include cystoid macular edema, segmental retinal periphlebitis with or without a characteristic peripheral "candle wax dripping" appearance, vitreous opacities, and choroidal granulomas.[7] Because ocular sarcoidosis can present with a variety of symptoms and findings, many of which are non-specific signs of uveitis, the entity can be difficult to diagnose.

This case describes a patient whose initial presentation was consistent with MEWDS, despite atypical findings on OCTA, who was subsequently diagnosed with presumed ocular sarcoidosis. MEWDS may be mimicked by other disorders and atypical imaging is a clue to consider alternate inflammatory entities.[8]

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2. Case report

A 23-year old Caucasian woman with a past medical history of irritable bowel syndrome presented with a central blind spot and photophobia after a gastrointestinal viral illness. She denied flashes, ocular redness, or pain. Her visual acuity was 20/70 in the right eye from a baseline of 20/20 and 20/20 in the left eye. Refraction testing revealed a −0.50 spherical in both eyes. Examination of the right eye showed multiple ~50 μm yellow-white round spots in the macula extending into the mid periphery and stippled orange granular pigmentary mottling in the fovea (Fig. 1A and B). The left retina had only trace stippling at the fovea. OCT of the right eye showed irregular elevation of the retinal pigment epithelium (RPE) and disruption of the overlying outer retina including the external limiting membrane (ELM), ellipsoid zone (EZ), and the interdigitation zone (Fig. 1C). Hyperreflective foci in the outer nuclear layer in linear extension with the disrupted EZ were also noted on OCT (Fig. 1C). Imaging of the left eye was unremarkable. Both eyes were otherwise white and quiet without anterior chamber or vitreous cell. The patient was given a presumptive diagnosis of MEWDS based on the history and fundus examination. She returned for follow-up one week later with a visual acuity reduction to 20/100 in the right eye. Fundus examination was unchanged. Fundus autofluorescence (FAF) showed hyperautofluorescent spots in greater number than the spots observed on color fundus photography (Fig. 1D). FA showed numerous hyperfluorescent spots beginning in early phases that corresponded to the yellow-white spots on exam, as well as hyperfluorescent, wreath-like punctate in the fovea, and late disk leakage (Fig. 1E and F). ICG showed hypocyanescent spots beginning in early phases that corresponded to the yellow-white spots on exam (Fig. 1G). Spectral-domain OCTA acquired on the RTVue XR Avanti (Optovue, Inc., Fremont, CA) showed numerous areas of nonperfusion of the CC corresponding to the hypocyanescent spots seen on ICG, as well as improving areas of EZ disruption and focal RPE impairment on OCT associated with hypertransmission on the B-scan (Fig. 2). It was determined that her outer retina was improving and she was recommended to follow up again in one month.

The patient was lost to follow up but presented five months later with two days of new floaters, reduced vision, and a spot in the central vision. She reported her vision had been subjectively better during the interval since her last visit but had declined over the last week. Visual acuity was 20/50 in the right eye and 20/20 in the left eye. Examination of the right eye showed conjunctival granulomas, anterior chamber cell and vitritis. There were 1+ vitreous cell and stippled RPE changes in the central macula with nasal retinal spots. Fundus photography revealed foveal and perifoveal RPE changes, prominent peripheral perivascular white spots, and possible periphlebitis (Fig. 3A). OCT showed outer retinal changes including EZ attenuation as well as interdigitation zone and ELM disruption (Fig. 3B). FAF showed peripheral hyperautofluorescent dots around the inflamed veins (Fig. 3C and D). FA revealed right sided disc leakage and segmental periphlebitis with stippled macular leakage (Fig. 3E). Spectral-domain OCTA acquired on the RTVue XR Avanti again revealed dark spots in the CC (Fig. 3F and G). Since these lesions on OCTA were not correlated with shadowing on the structural OCT, they were considered to be areas of choroidal hypoperfusion.

Review of systems at this time was positive for erythema nodosum, fatigue, gastrointestinal disturbance, and joint pain. Systemic workup revealed an elevated ACE level. Lysozyme, treponemal antibody titer, and QuantiFERON-GOLD were within normal limits. Chest x-ray revealed small nodular calcifications in the bilateral perihilar and infrahilar regions, consistent with granulomatous disease. She was diagnosed with presumed sarcoidosis with ocular manifestations and referred to pulmonology for further evaluation.

3. Discussion

In this case, a young low myopic female initially presented with a unilateral central scotoma and photophobia in the setting of a viral prodrome with the absence of any other apparent systemic concerns. Fundus examination and imaging at presentation were primarily consistent with the diagnosis of acute MEWDS, including white dots and foveal granularity, hyperfluorescence and hypocyanescent spots, macular wreath-like punctate, as well as EZ interruption on OCT. However, when the patient returned five months later with similar symptoms, a recurrence of MEWDS was considered unlikely given the perivascular of

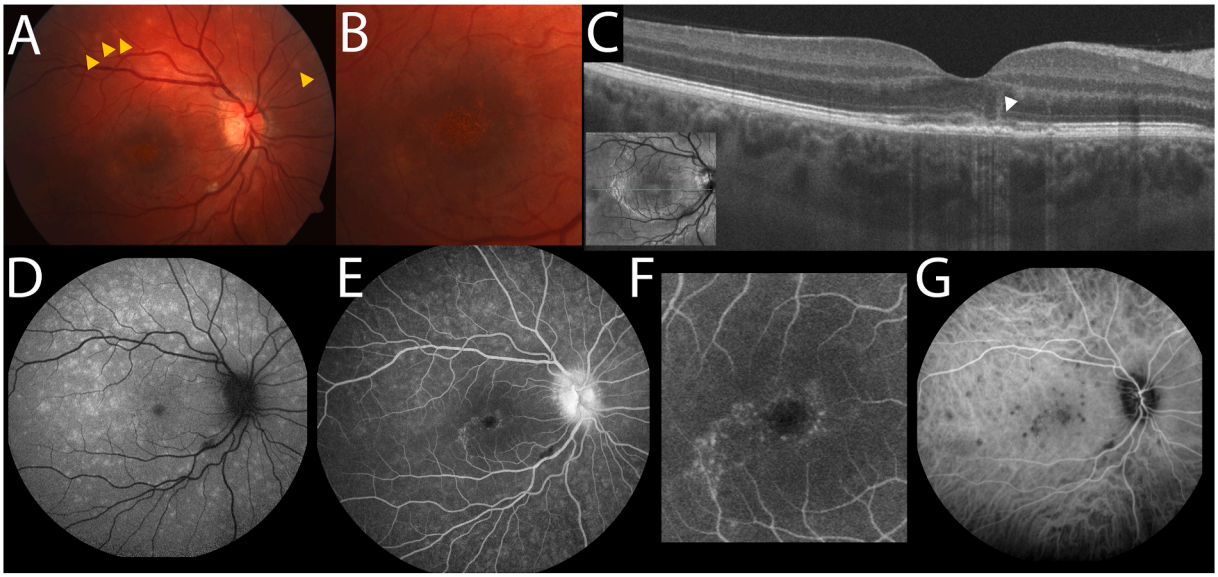

Fig. 1. Color fundus photograph of the right eye showing multiple white spots (yellow arrowheads) and orange granularity in the fovea (A). Detailed view of the orange foveal granularity (B). Optical coherence tomography B-scan revealing EZ and interdigitation zone discontinuities (white arrowhead), hyperreflective foci in the outer nuclear layer in linear extension with the disrupted EZ (adjacent to white arrowhead), and a shallow RPE elevation and irregularity (C). Inset depicts en face OCT with a turquoise line through the fovea to denote the location of the B-scan. Fundus autofluorescence revealing numerous hyperfluorescent spots (D). Fluorescein angiography revealing wreath-like macular hyperfluorescent spots and late disc leakage (E). Detailed view of the foveal stippling (F). Early indocyanine green angiography showing numerous central hypocyanescent spots (G). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

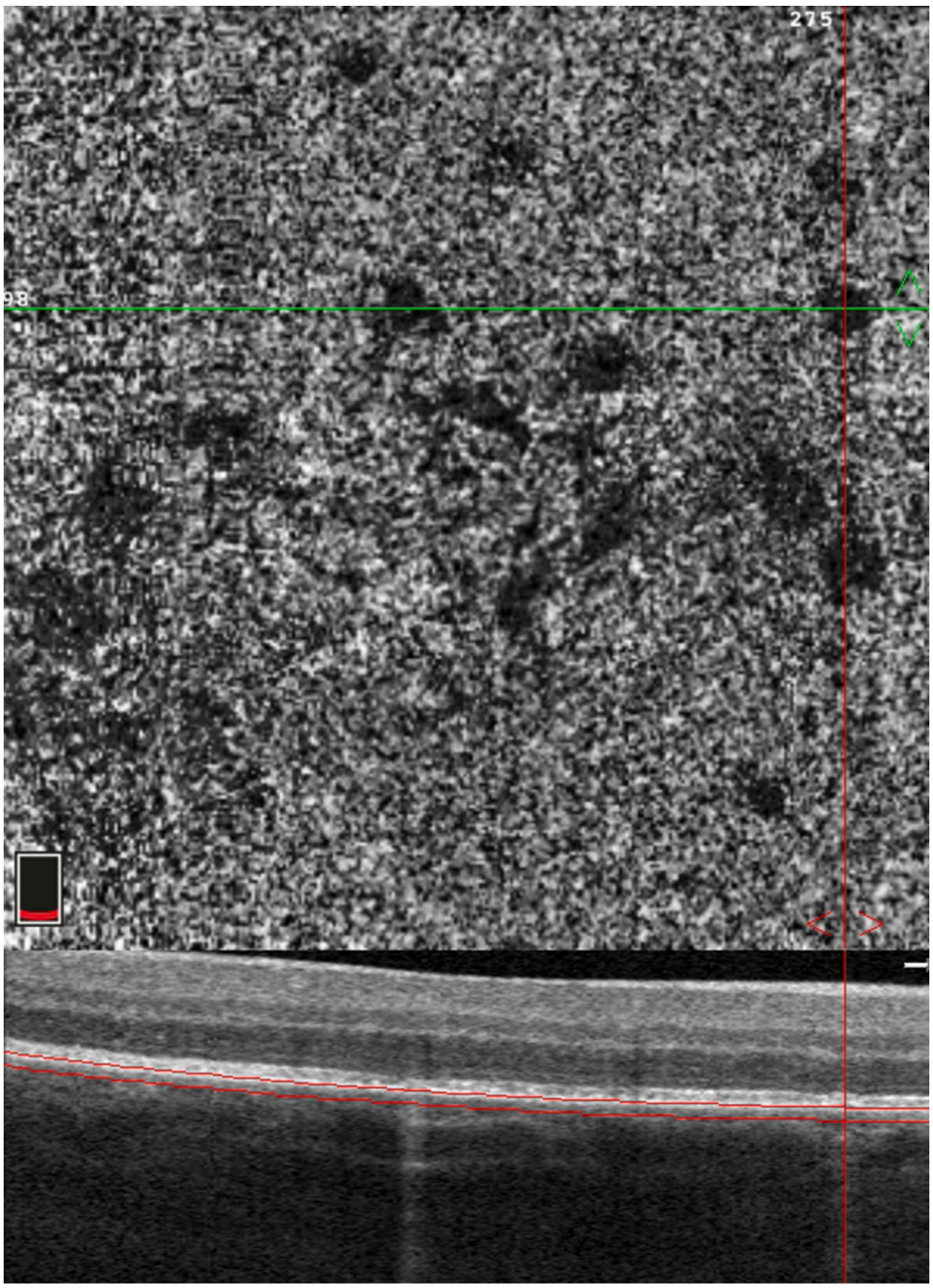

Fig. 2. 3 × 3mm *en face* OCT angiogram of the choriocapillaris revealing multiple flow deficit areas with a corresponding B-scan through two lesions showing hypertransmission.

the white lesions and the periphlebitis. Furthermore, CC hypoperfusion on OCTA found at both time points is not expected in this condition and should suggest a causative entity other than MEWDS.

Prior reports consistently note that the CC is not involved in MEWDS. In fact, it was not until the advent of OCTA that contending hypotheses of the pathogenesis in MEWDS could be resolved. Recent studies using OCTA show normal CC flow in MEWDS even in areas of corresponding ICG hypocyanescence, supporting the idea that these MEWDS lesions are attributed to injured photoreceptors and RPE cells, the latter of which are unable to absorb the ICG molecule.[3–5] There has been one case reported of a patient with MEWDS found to have hyporeflectivity on OCTA in the CC, but on further review of this report, it is not clear that this was indeed an area of true hypoperfusion and not actually an area of shadowing due to RPE changes.[9] Furthermore, studies have not found any alteration to the retinal vascular plexi on OCTA imaging in cases of MEWDS, either.[5,10]

Contrary to MEWDS, the CC is known to be affected in sarcoidosis, as granulomas often localize there. Choroidal flow will be preserved in the presence of small granulomas, while larger, full thickness granulomas can lead to flow deficits due to compression of surrounding vasculature.[8] A recent study comparing qualitative grading of OCTA images to FA in posterior segment ocular sarcoidosis found CC flow deficits in about 40% of the cases, which the authors attribute to active granulomas, chronic tissue damage secondary to previously active granulomas, or the presence of focal choroidal arteriolitis.[11]

There are other disease entities under the constellation of white dot syndromes that can present with CC flow deficits, which should be considered in the differential diagnosis. Although their lesions often have unique funduscopic characteristics, acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and serpiginous choroiditis

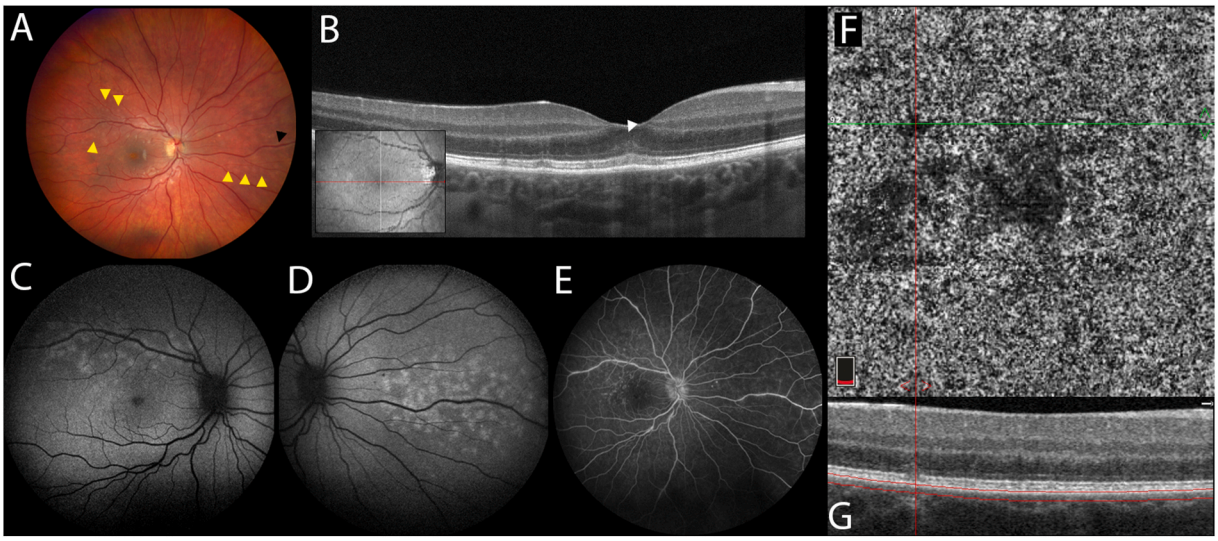

Fig. 3. Color fundus photograph of the right eye showing multiple white dots (yellow arrowheads) and periphlebitis at the mid-nasal periphery (black arrowhead) (A). Structural OCT B-scan showing EZ attenuation and ELM disruption (white arrowhead) (B). Inset depicts en face OCT with a red line through the fovea to denote the location of the B-scan. Fundus autofluorescence revealing prominent peripheral hyperautofluorescent dots following the topography of the superior temporal and nasal veins (C and D respectively). Fluorescein angiography showing punctate hyperfluorescence, diffuse staining of the superior temporal and inferior nasal vein, and focal staining at the other arcades, consistent with periphlebitis (E). 3 × 3mm *en face* OCTA of the choriocapillaris revealing several flow deficit patches (G), with a corresponding B-scan through a lesion showing hypertransmission (H). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

both manifest CC flow deficits on OCTA in areas of activity that correspond with hypocyanesence on ICG. Repeat OCTA imaging in these two disorders has been deemed a useful tool to monitor progressive, recurrent, and recovery of CC flow deficits to obviate the need for repeat dye-based angiography.[4,9,12,13] OCTA has also been found to help distinguish inflammatory from neovascular CC lesions in multifocal choroiditis (MFC) and punctate inner choroidopathy (PIC), two other diseases on the white dot syndrome spectrum.[12,14] The utility of OCTA in assessing uveitic syndromes in general extends to quantifying peripheral perfusion in recurrent retinal vasculitis.[12]

A recent case series has identified multiple cases in which presentations consistent with a diagnosis of MEWDS in fact unfold to reveal a more serious inflammatory, infectious, or neoplastic disease with more extensive workup and longer follow-up, including sarcoidosis. Other masqueraders of MEWDS in which CC hypoperfusion may occur include placoid syphilis and idiopathic retinal periphlebitis.[8] We hypothesize that MEWDS masquerading occurred in this patient as well.

In summary, the finding of CC hypoperfusion on OCTA should point one away from the diagnosis of MEWDS and instead prompt additional investigation for other conditions known to be MEWDS masqueraders, such as sarcoidosis, in which OCTA changes in the CC are indeed expected.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

Disclosures

This case was presented at the Atlantic Coast Retina Club and Macula 2020 meeting on January 10th, 2020 in New York, NY.

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Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

Declaration of competing interest

CRB has received speaker fees from Carl Zeiss Meditec, Optovue, Genentech, and Allergen. NKW has consulted for Topcon, Genentech, Regeneron, Apellis, Astellas, Boehringer Ingelheim, and Novartis; has served an advisory role for Genentech, Apellis, Astellas, Boehringer Ingelheim, Novartis, Topcon, and Carl Zeiss Meditec; is the officer of entity at Gyroscope; has stock in the Boston Image Reading Center, Ocudyne. All other authors report no conflicts of interest.

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