Secondary Multiple Evanescent White-Dot Syndrome and Multimodal Imaging

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ABSTRACT

Purpose: Secondary multiple evanescent white-dot syndrome (MEWDS) is an epiphenomenon that can occur during or following an underlying chorioretinal disease. In a 22-year-old male patient who presented blurred vision in the right eye for 10 days, a granuloma-like lesion located adjacent to inferotemporal optic disc and accompanying multiple, scattered and deep-seated white dots around the posterior pole were detected; thus, the patient underwent multimodal imaging methods. A combination of oral trimethoprim-sulfamethoxazole and azithromycin was administered empirically and systemic evaluation was performed at the same time. The infectious panel was found to be negative and the diagnosis of secondary MEWDS secondary to the unilateral granuloma was established. A month later, the final visual acuity improved to 10/10 from the baseline visual acuity of 4/10 in the patient. The granuloma site was recovered with a choroidal excavation. Secondary MEWDS is a relatively less known entity seen in many chorioretinal diseases in addition to the original lesion.

Conclusion: Secondary MEWDS is observed in addition to the lesions associated with a great deal of chorioretinal diseases. It is a new entity with good visual results with targeted therapy with exclusion of infectious pathologies.

Keywords: Fluorescein angiography, Indocyanine green angiography, MEWDS, Optical coherence tomography, Optical coherence tomography angiography.

INTRODUCTION

Multiple Evanescent White Dot Syndrome (MEWDS) was first described by Jampol et al. in 1984.[1] The MEWDS is an unilateral disease seen with well-defined lesions (approximately 100-200 µm in size) at retinal pigment epithelium (RPE) or at the level of outer retina, which characterized by gray-to-white, crown-like lesions starting from perimacular area to mid-periphery to retina.[2,3]

Based on **THE STANDARDIZATION OF UVEITIS NOMENCLATURE (SUN) Work Group,** the diagnostic criteria for MEWDS include multiple, gray-to-white chorioretinal dots, granular appearance at fovea, crown-like hyper-fluorescein lesion on fluorescein angiography (FA) or hyper-reflective lesion from RPE to ellipsoid zone, and minimal or no reaction in anterior chamber and vitreous . The exclusion criteria for MEWDS are positive Treponemal test for syphilis, hilar lymphadenopathy or biopsy-proven sarcoidosis findings and bilateral involvement at baseline.[3]

The term "secondary MEWDS" is used in clinical presentation where MEWDS is seen together with some posterior segment disorders. It is highly rare entity and can be defined by meticulous observation. The posterior segment disorders accompanied by secondary MEWDS include Best's vitelliform dystrophy, angiod streaks, history of retinal detachment, macular neovascularization (MNV), choroidal rupture and multi-focal choroiditis (MFC).[4-8] Association with MFC is more common.[9]

CASE REPORT

In December, 2020, a 22-years old male patient presented to our clinic with blurred vision in the right over 10 days. In his history, it was found that he had Familial Mediterranean Fever (FMF) and were on colchicine. The patient had no history of previous COVID-19 disease and no COVID-19 vaccine. In ophthalmological examination, best-corrected visual acuity was 4/10 in the right eye and 10/10 in the left eye. Anterior segment examination and intraocular pressure were found to be normal in both eyes.

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In the fundus examination of the right eye, granuloma-like lesion at the infero-temporal vicinity to optic disc and multiple white, punctate lesions while fundus examination was normal in the left eye (Figure 1A-1B). On fluorescein angiography (FA) of right eye, scattered, hypo-fluorescent punctate areas around posterior pole and a smooth, relatively hypo-fluorescent lesion at infero-temporal vicinity of optic disc were detected at early phase while it was seen that punctate areas and lesion at infero-temporal vicinity of optic disc appeared hyper-fluorescent at mid-phase and late phase. On spectral-domain and swept source optical coherence tomography (OCT), a granuloma-like lesion and involvement in outer retinal layers at infero-temporal to optic disc were detected (Figure 2A-B-C-D).

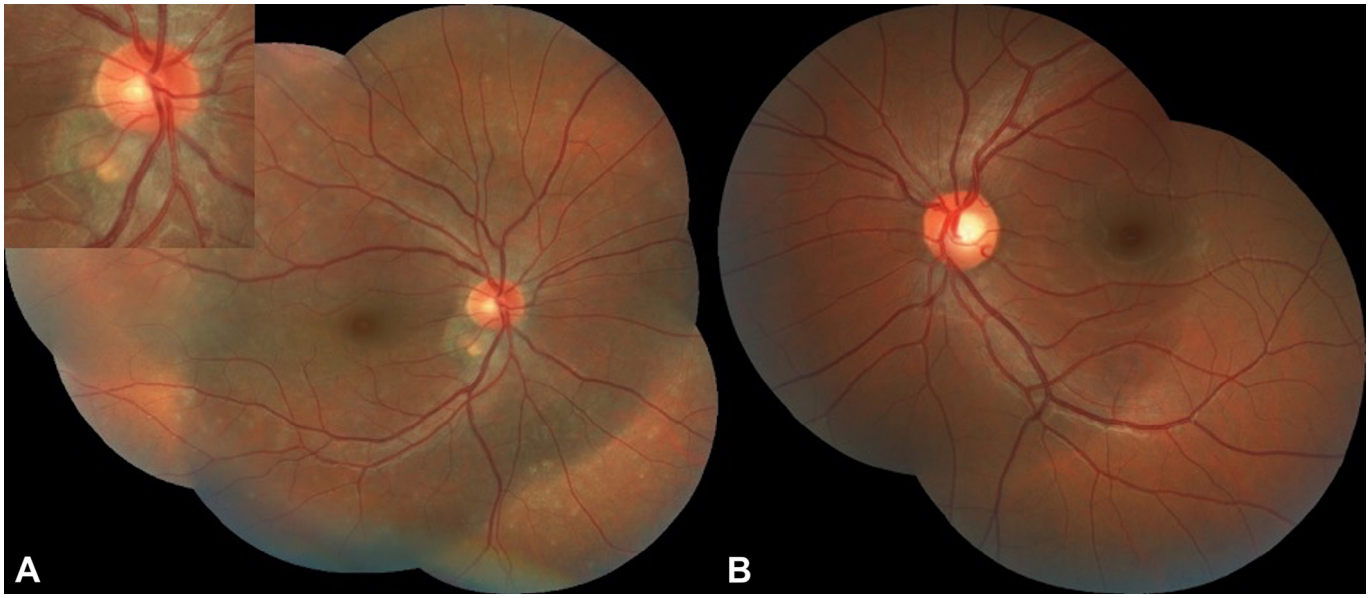

Figure 1A-B: *In the fundus examination of the right eye, granuloma-like lesion at the infero-temporal vicinity to optic disc and multiple white, punctate lesions* **(A)** *while fundus examination was normal in the left eye* **(B)**.

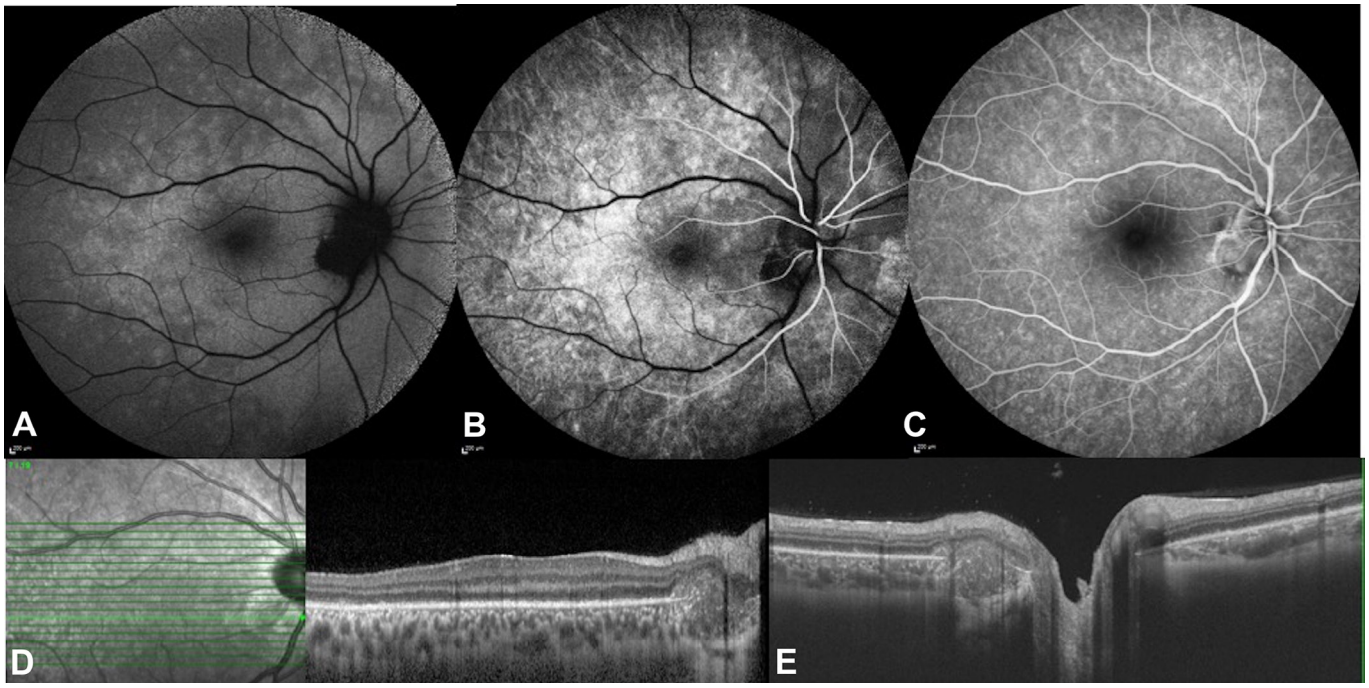

Figure 2A-B-C-D-E: *On FA of right eye, scattered, hypo-fluorescent punctate areas around posterior pole and a smooth, relatively hypo-fluorescent lesion at infero-temporal vicinity of optic disc were detected at early phase* **(A)** *while it was seen that punctate areas and lesion at infero-temporal vicinity of optic disc appeared hyper-fluorescent at mid-phase and late phase* **(B)**.*On spectral-domain and swept source optical coherence tomography (OCT), a granuloma-like lesion and involvement in outer retinal layers at infero-temporal to optic disc were detected* ***(D-E)***.

On indocyanine green angiography, scattered hypo-cyanininen dots and a hypo-cyanininen lesion at infero-temporal to optic disc was observed, which were subtle at early phase and became more prominent towards late phase (Figure 3A-B-C). On "en phase" images from OCT angiography (OCTA), it was seen that the lesion at infero-temporal to optic disc appeared as hypo-intense (Figure 3D-E). Trimethoprim-sulfamethoxazole 800/160 (2x1, 30 days) and azithromycin 500 mg 1x1, 9 days) was prescribed empirically with consideration of potential infectious disease and systemic evaluation was performed at the same time. However, infectious panel (toxoplasmosis, syphilis, Bartonella and Quantiferon tests) were negative. In addition, PCR test for COVID-19 disease was also negative. On the control visit at month 1, visual acuity was found as 10/10 in the right eye. In the fundus examination and FFA, it was seen that white dots in the right eye were markedly resolved and activity in the peripapillary lesion was decreased and transformed into chorioretinal scarring. On OCT, it was seen there was resolution in outer retinal layers and lesion at inferior nasal to optic disc led to a choroidal excavation (Figure 4 A-B-C).

DISCUSSION

The entity defined secondary MWDS is a clinical Figure with increasing awareness in recent years; however, its pathogenesis hasn't been fully understood. In a review by Pearlman et al., it was proposed that secondary MWDS develops through an immune-mediated mechanism caused by immunogenic triggers together with underlying potential genetic predisposition.[10] In addition, systemic fungal, bacterial and viral infections as well as vaccines are among triggers of secondary.[10]

Secondary MEWDS is characterized by gray-white lesions recovered spontaneously without causing anatomic and functional impairment. It is seen together with an underlying retinal disease. In the literature, Byran et al. are first authors described MEWDS together with underlying macular.[4] In a 29-years old healthy woman with history of

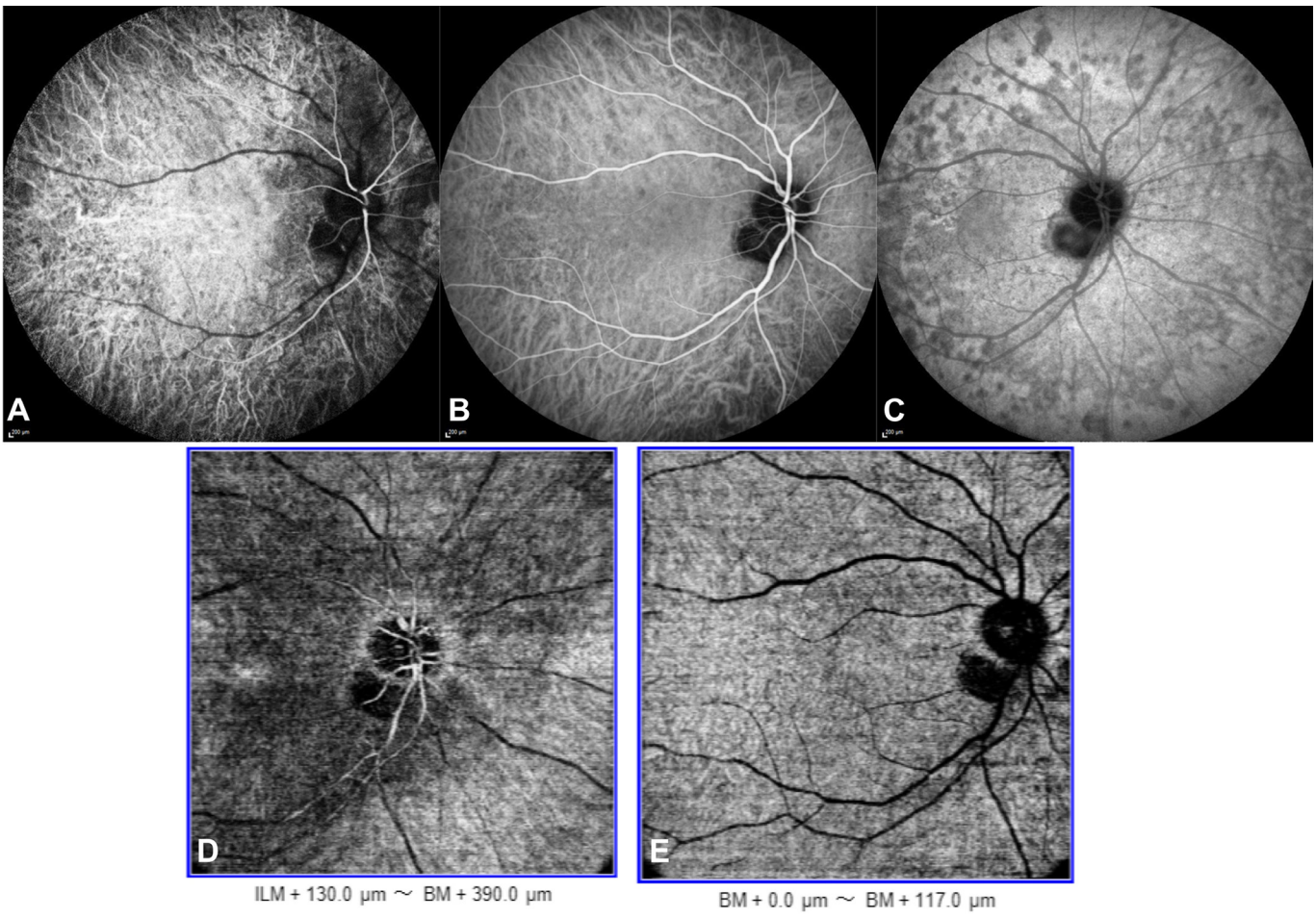

Figure 3A-B-C-D-E: *On ICGA, scattered hypo-cyanininen dots and a hypo-cyanininen lesionat infero-temporal to optic disc was observed, which were subtle at early phase and became more prominent towards late phase ICGA* (**A-B-C.** *On "en phase" images from OCT angiography (OCTA), it was seen that the lesion at infero-temporal to optic disc appeared as hypo-intense* **(D-E)**.

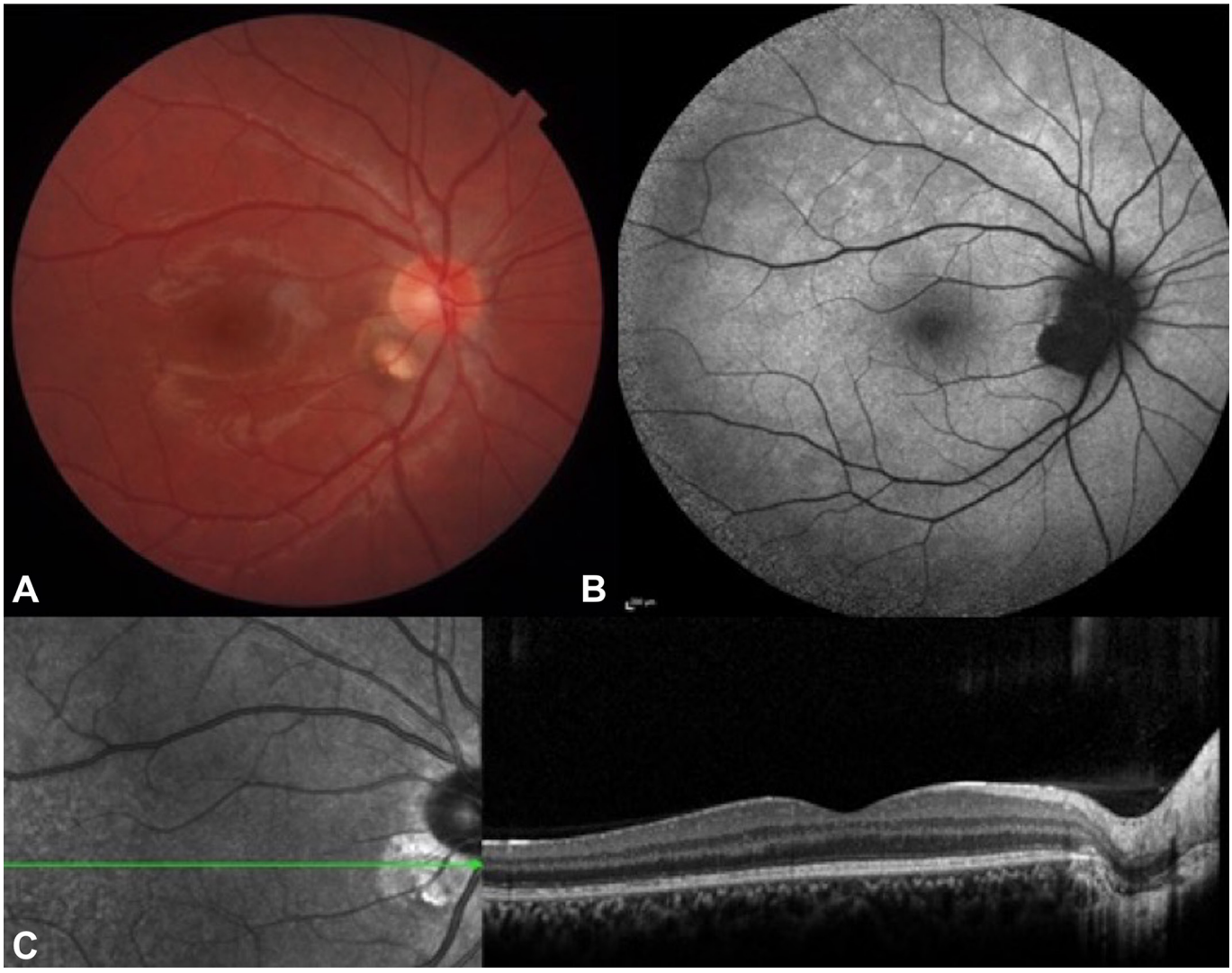

Figure 4A-B-C: *In the fundus examination and FFA, it was seen that white dots in the right eye were markedly resolved and activity in the peripapillary lesion was decreased and transformed into chorioretinal scarring* **(A-B)**. *On OCT, it was seen there was resolution in outer retinal layers and lesion at inferior nasal to optic disc led to a choroidal excavation* **(C)**.

Best disease who presented with acute loss of visual field in one eye and photopsia, central scarring and multiple, atrophic, pigmented scars were detected inferior were detected. It was observed white dots appeared at inferior and posterior pole were resolved spontaneously within two weeks. It is thought that the disease develops as an epiphenomenon by disrupted blood-retina barrier and triggered inflammatory process as a result of impaired Ruyschiana layer, choriocapillaris, Bruch's membrane, retinal pigment epithelium due to primary pathological lesion .[11,12]

When compared to secondary MEWDS, a good anatomical recovery is generally observed within weeks or months with identification of underlying retinal disease, exclusion of infectious etiologies and targeted therapy.

Essilfie et al. described 18 cases with MEWDS secondary to MFC.[9] In two cases, juxtapapillary chorioretinal lesion was reported but no detailed data was provided. In our case, secondary MEWDS was diagnosed in the patient with peripapillary granuloma-like lesion and impaired outer retinal layer. This case was presented as it is relatively newer clinical presentation.

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