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Multiple evanescent white dot syndrome masquerading as atypical optic neuritis: a case report

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Abstract

Background Multiple evanescent white dot syndrome is a rare posterior uveitis that presents with transient white dots in the retina, which may not always be visible at the time of diagnosis. The disease can mimic atypical optic neuritis owing to overlapping symptoms such as central visual field defect, relative afferent pupillary defect, and optic disc swelling. Here, we report a case of multiple evanescent white dot syndrome masquerading as atypical optic neuritis in a young female patient.

Case presentation A 23-year-old female patient of Korean ethnicity presented with ocular pain and visual field defect in her left eye for 1 week. Her best corrected visual acuity was 20/20 in her right eye and 20/30 in her left eye. Pupillary size was 3 mm for both eyes. Relative afferent pupillary defect was detected in the left eye. The color vision test was normal for both eyes. A visual field test revealed blind spot enlargement in the left eye. On fundus examination, disc swelling was found in the left eye. Other abnormalities were not found. The patient was suspected of having atypical optic neuritis. Fluorescein angiography showed hyperfluorescent spots in the posterior pole and leakage from the disc in the left eye. Orbital magnetic resonance imaging did not show any abnormal findings or enhancement. A multifocal electroretinogram showed reduced amplitude for the involved area. There were relatively hyperautofluorescent lesions outside the fovea and hypoautofluorescent fovea on the blue-light fundus autofluorescence image. *En face* optical coherence tomography revealed multiple hyporeflective dots at the ellipsoid zone. Swept-source optical coherence tomography showed irregular cells in the ellipsoid zone with increased outer retinal thickness. On repeated fundus examination, multiple white dots were found (vaguely). The patient was diagnosed with multiple evanescent white dot syndrome and was able to recover in 6 weeks.

Conclusion Patients with multiple evanescent white dot syndrome who present with disc swelling, ocular pain, and relative afferent pupillary defect might be misdiagnosed as having optic neuritis. In atypical optic neuritis, *en face* optical coherence tomography, blue-light fundus autofluorescence, and swept-source optical coherence tomography can aid in the differential diagnosis.

Keywords Multiple evanescent white dot syndrome (MEDWS), Optic neuritis, Optical coherence tomography (OCT)

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Background

Multiple evanescent white dot syndrome (MEWDS) is a rare posterior uveitis, characterized by numerous pale whitish dots seen in the posterior pole and the midperiphery [1]. It is a disease that is sometimes difficult to diagnose owing to the characteristic of evanescent fundal white dots, which might not be present during the visit. MEWDS can be misdiagnosed as atypical optic neuritis when patients present with central visual field defect, a relative afferent pupillary defect (RAPD), and optic disc swelling [2, 3].

Atypical optic neuritis typically presents with more significant vision loss, often accompanied by pain on eye movement and more pronounced color vision defects. Magnetic resonance imaging (MRI) findings can often help differentiate optic neuritis from MEWDS, as optic nerve enhancement is frequently seen in optic neuritis but not in MEWDS [4].

Here, we report a patient who had MEDWS masquerading as atypical optic neuritis, which was confirmed by *en face* optical coherent tomography (OCT), swept-source OCT (SS-OCT), and multifocal electroretinogram (mfERG).

Case presentation

A 23-year-old female patient of Korean ethnicity presented with ocular pain and visual field defect in her left eye for 1 week. Her best corrected visual acuity was 20/20 in the right eye and 20/30 in the left eye. Pupillary size was equal in both of her eyes. Relative afferent pupillary defect was detected in the left eye. The color vision test and slit-lamp examination were normal for both eyes. A visual field test revealed blind spot enlargement in the left eye. On fundus examination, disc swelling was found in her left eye. Other abnormalities were not found (Fig. 1). The patient was suspected of having atypical optic neuritis. Fluorescein angiography showed faint hyperfluorescent spots and dots in the posterior pole in the early and late phases, leakage of the disc, and peripapillary perivascular staining after the intermediate phase in her left eye (Fig. 2A, E). There were relatively hyperautofluorescent lesions outside the fovea and hypoautofluorescent fovea on the blue-light fundus autofluorescence (BL-FAF) image. Orbital magnetic resonance imaging did not show any abnormal findings or enhancement. Amplitudes of the multifocal electroretinogram (mfERG) were markedly reduced in the area corresponding to the paracentral scotoma and moderately reduced in other regions of the central field of the affected eye

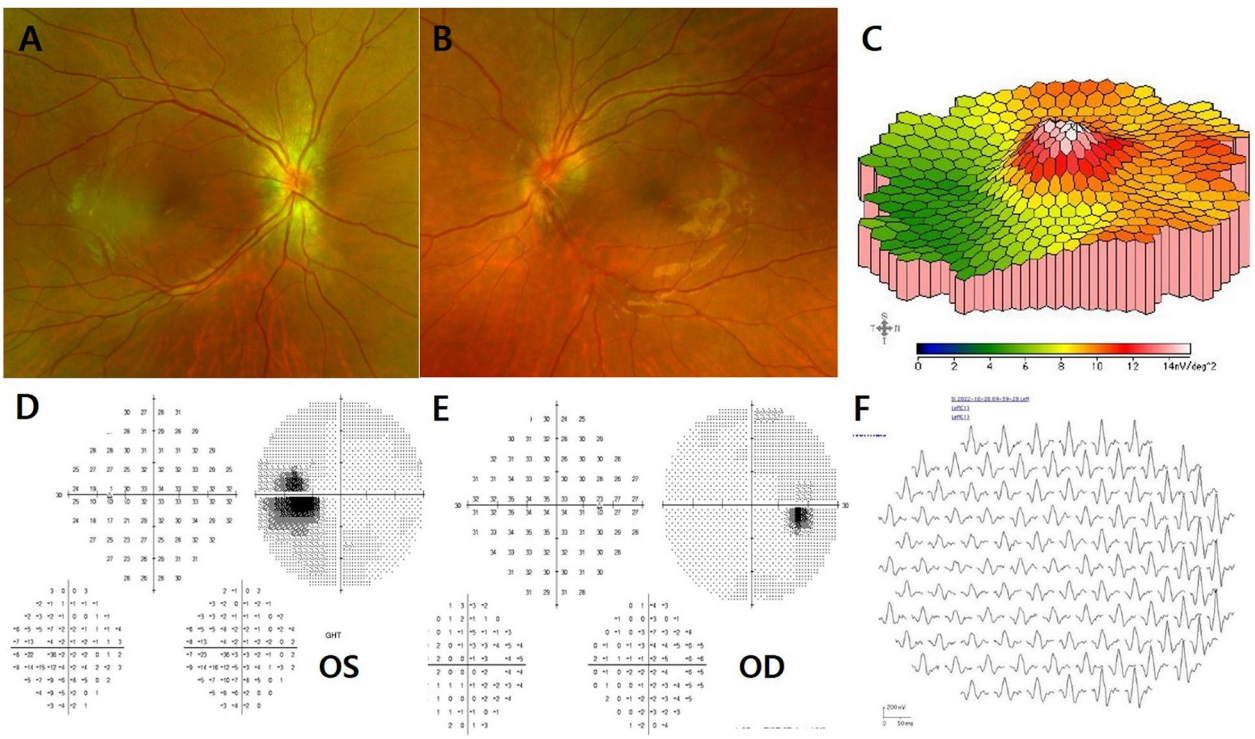

Fig. 1 Initial investigations suggesting atypical optic neuritis: left optic disc swelling was noted on fundus examination (**A**, **B**) and a dense paracentral scotoma was visible on the Humphery visual field test (**D**, **E**). Multifocal electroretinography showing reduced N1 and P1 responses in the nasal paramacular area (**C**, **F**)

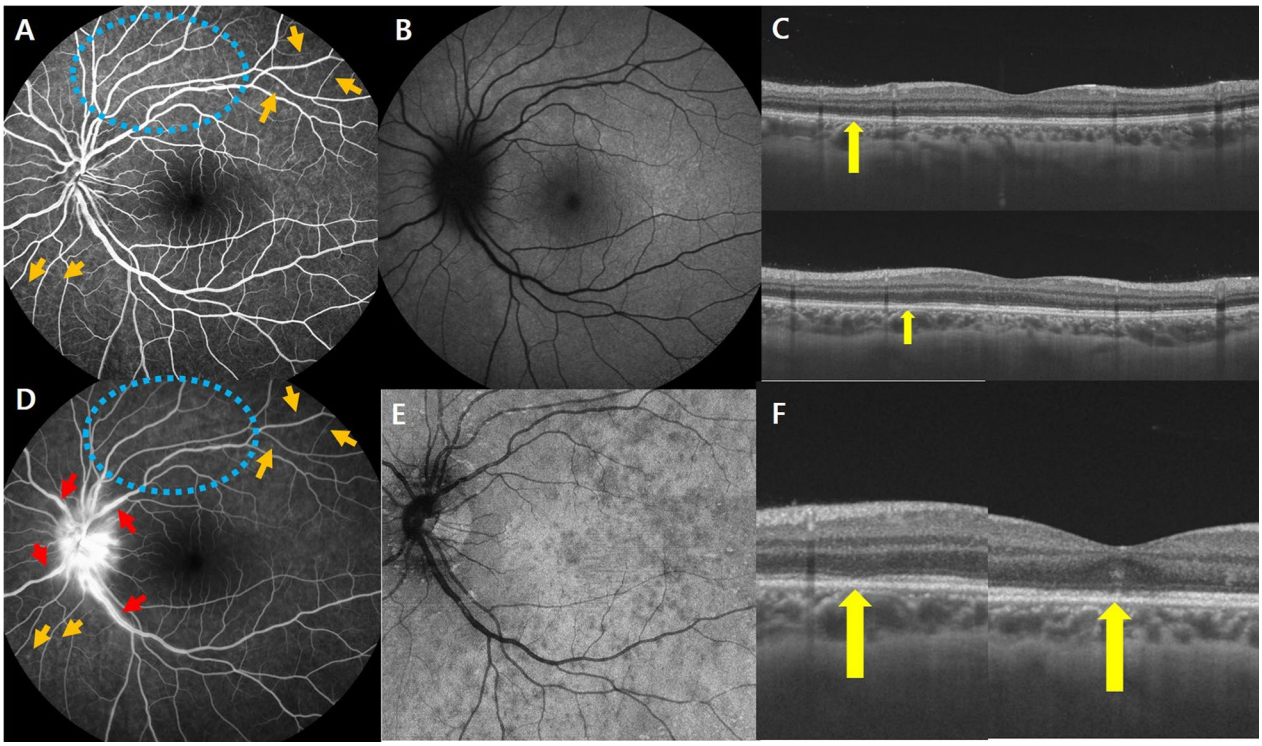

Fig. 2 Fluorescein angiography revealing scattered faint hyperfluorescent dots and spots over the posterior pole in the early phase (**A**), indicated by orange arrows and a blue circle, with disc leakage (red arrows) and peripapillary perivascular staining (orange arrows) in the late phase (**D**). Blue-light autofluorescence imaging showing hyperautofluorescent lesions outside the fovea (**B**). *En face* optical coherence tomography displaying scattered hyporeflective dots and a peripapillary hyporeflective area (**E**). Swept-source optical coherence tomography demonstrating disruption of the foveal photoreceptor outer segments and the accumulation of dome-shaped hyper-reflective material above the retinal pigment epithelium (**C**, **F**), marked by yellow arrows, corresponding to areas of reduced function seen on the multifocal electroretinogram

(Fig. 2B, C, F, G). *En face* optical coherent tomography (OCT) revealed multiple scattered hyporeflective dots and a peripapillary hyporeflective area at the level of the ellipsoid zone (EZ) (Fig. 2D). SS-OCT showed attenuation or disruption of the EZ and interdigitation zone (Fig. 2H). A subfoveal hyperreflective lesion extending into the inner retina and some dome-shaped hyperreflective lesions at the dot lesion were also observed. Multiple white dots were detected (vaguely) on repeated fundus examination. The patient was diagnosed with MEWDS. She was able to recover spontaneously in 6 weeks.

Discussion

MEWDS is an uncommon entity first described in 1984 by Jampol *et al.* as unilateral visual acuity loss notable for white dots of the "the retinal pigment epithelium (RPE) or deep retina and a granularity of the fovea." [5]. MEWDS is unilateral, causes visual loss, and occurs predominantly in young women. Thus, it might be confused with optic neuritis, especially when patients present with ocular pain, disc swelling, and RAPD [6].

The exact pathogenesis is unknown. Several past and present publications have classified MEWDS in the subgroup of primary inflammatory choriocapillaropathies [7, 8]. Recent studies have reported that the photoreceptor layer is damaged in MEWDS, and that photoreceptor loss is at the origin of the typical hyperautofluorescent areas seen on blue-light fundus autofluorescence (BL-FAF), which characterize MEWDS. However, this layer is only damaged secondarily owing to choriocapillaritis [4].

An infectious etiology is thought to be involved in the pathogenesis of MEWDS since there is a viral prodrome [9]. The proposed mechanism is that MEWDS is triggered by an autoimmune response following infection with viruses similar to those noted in acute zonal occult outer retinopathy (AZOOR) complex disorders [10]. Another hypothesis is that inflammation and autoimmune diseases are discrete entities. Their presentation is based on the interaction of genetics, immune system pathways, and environmental triggers (for example, viral infection, immunization, stress, and female sex) [11]. This patient also had symptoms related to an upper respiratory infection 1 month prior to her visual symptoms.

Several clinical elements are helpful in the diagnosis, including a flu-like viral episode preceding symptoms

(photopsias and subjective scotomas), fundal yellow-white dots, granularity of the fovea, mild vitreous cells, mild disc edema, and a highly variable decrease in visual acuity and visual field impairment, both of which can be very severe depending on the degree of severity of choriocapillaris nonperfusion [1, 12, 13]. Multimodal imaging has contributed significantly to an easier diagnosis. Visual field testing might reveal an enlarged blind spot. Fluorescein angiography shows early wreath-like discreet hyperfluorescence with late staining in the involved area. Indocyanine green angiography (ICGA) reveals hypocyanescent spots that are usually more numerous than the white spots noted on examination, indicating choriocapillaris hypo- or nonperfusion. SS-OCT of MEWDS shows disruption mainly of the ellipsoid zone (EZ-photoreceptor outer segments) and interdigitation zone (IZ) complex throughout the posterior pole. Posterior vitreous cells might also be visible on OCT imaging. The combination of ICGA, blue-light fundus autofluorescence (BL-FAF), and SD-OCT represents an extremely forceful triad complementing clinical findings in the diagnosis of MEWDS [14]. Although ICG was not tested in this patient, *en face* OCT revealed hyporeflective spots corresponding to white dots noted on fundus examination.

Optic neuritis and MEWDS can be differentiated by the lack of ocular pain aggravated by eye movement in MEWDS compared with optic neuritis, the more pronounced loss of color vision and contrast sensitivity in optic neuritis compared with MEWDS, and the presence of a RAPD evident in optic neuritis (although subtle RAPD can be observed, it is uncommon in MEWDS). Patients with optic neuritis complain of blurry vision and impaired color vision, whereas patients with MEWDS complain of central/paracentral scotoma [2]. RAPD in our patient initially led to a misdiagnosis of optic neuritis, similar to cases in Dodwell *et al.*, where three out of five patients also exhibited RAPD [6]. Finkelstein *et al.* described a similar case with mild RAPD, where further imaging confirmed MEWDS [2]. In our case, the combination of RAPD and disc swelling suggested optic neuritis, but multimodal imaging, including *en face* OCT and BL-FAF, ultimately confirmed MEWDS. Although neither Dodwell *et al.* nor Finkelstein *et al.* reported pain exacerbated by eye movement, which is typical for MEWDS, our patient experienced this symptom, complicating the diagnosis [2, 6]. Despite this, faint white dots and detailed imaging were crucial in distinguishing MEWDS from optic neuritis, emphasizing the variability in MEWDS presentations and the critical role of imaging for accurate diagnosis.

Conclusion

Patients with MEDWS who present with disc swelling, ocular pain, and RAPD can be misdiagnosed as having optic neuritis. When suspecting atypical optic neuritis, a detailed retinal examination should be performed, and *en face* OCT, BL-FAF, and SS-OCT can aid in the differential diagnosis.

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Author contributions
KSJ and LSM are responsible for the acquisition of the clinical information. KSJ and HKE are responsible for manuscript preparation. CHY and CJH are responsible for reviewing the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials
All data have been presented within the manuscript and in the form of images.

Declarations

Ethical approval and consent to participate
The Institutional Review Board of Pusan National University Yangsan Hospital approved the case report in compliance with the Helsinki Declaration (IRB no. 55-25024-048). Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest, other equity interest, or nonfinancial interest in the subject matter or materials discussed in this manuscript.

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