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# Multiple evanescent white dot syndrome following influenza immunization - A multimodal imaging study

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ABSTRACT

*Purpose:* To describe the multimodal imaging (MMI) findings and clinical course of a case of Multiple Evanescent White Dot Syndrome (MEWDS) following immunization with inactivated intra-dermal influenza virus, and to explore whether similarities exist with other, previously reported cases.

*Observations:* A 34-year-old Caucasian man presented with unilateral onset of para-central scotomata, photopsias, and dyschromatopsia two weeks after administration of an influenza vaccine. Clinical examination and MMI were indicative of MEWDS. The patient's MMI abnormalities and symptoms resolved spontaneously after four weeks.

*Conclusion and importance:* This is the first reported case of MMI of post-influenza vaccination-associated MEWDS. Comparison with eight previously reported cases of MEWDS following various immunizations revealed that subjects tended to be healthy, young to middle age women with a median time to onset of two weeks. Vision tended to recover spontaneously over one to three months.

## 1. Introduction

There is growing awareness regarding an association between vaccinations and uveitis.[1–3] While the vast majority of cases have been associated with anterior uveitis, selected reports of posterior uveitis following immunization have also appeared. To the best of our knowledge, eight cases of vaccination-associated multiple evanescent white dot syndrome (MEWDS) have been reported previously.[4–11] We add here the description of a ninth case of MEWDS following immunization with inactivated intra-dermal influenza virus, and include for the first time full multimodal imaging (MMI) of such a case. Characteristics and outcomes of all nine cases are summarized and compared.

## 2. Case report

A 34-year-old Caucasian man with a prior myopic-photorefractive keratectomy presented with the chief complaints of para-central scotomata, grey haze, and central photopsias affecting his right eye for two weeks. Past ophthalmic, medical and surgical histories were otherwise unremarkable. Snellen visual acuity was 20/20+2 on the right and 20/13-1 on the left. Intraocular pressure was 18 mmHg on the right and 14 mmHg on the left. Pupils, extraocular motility, and confrontation visual fields were unremarkable. Anterior segment examination was normal. Examination of the right-sided posterior segment was notable for mild foveal granularity and small, grey, outer-retinal lesions centered around the optic nerve with extension to the mid-periphery (Fig. 1A). The posterior segment of the left eye was unremarkable. At the locations of the grey retinal lesions, spectral domain-optical coherence tomography (SD-OCT) showed focal areas photoreceptor disruption (Fig. 1B); fundus autofluorescence revealed hyper-autofluorescence (Fig. 1E); indocyanine green angiography showed late hypofluorescence (Fig. 1D), and fluorescein angiography revealed multiple punctate areas of staining organized in a well-recognized wreath-like pattern (Fig. 1C). Collectively, these clinical and MMI findings lead to the diagnosis of MEWDS.

Upon further inquiry, our patient denied any preceding viral symptoms, but did reveal that he received Flucelvax Quadrivalent® influenza vaccine (Seqirus, Holly Springs, North Carolina) two weeks prior to onset of symptoms. The patient was observed without intervention and at four-week follow-up his symptoms had resolved, as did the abnormalities identified with MMI. Best-corrected Snellen visual acuity

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improved to 20/16-1 in the right eye at this last visit.

## 3. Discussion

We describe a young, previously healthy man who developed photopsias, paracentral scotomata, and dyschromatopsia in the right eye two weeks following influenza vaccination. Clinical features and findings on MMI were consistent with MEWDS. The subject's symptoms and ophthalmologic findings resolved four weeks following presentation without intervention.

In 1984, Jampol and colleagues described a new chorioretinal disorder name Multiple Evanescent White Dot Syndrome (MEWDS).[12] While there have been no known racial or hereditary predilections, the disease is most commonly diagnosed in young to middle aged women. As many as 30% of affected patients report a viral prodrome. MEWDS is almost always a unilateral disease, and common symptoms include photopsias, dyschromatopsia, or paracentral scotomata. The disorder is thought to have a benign prognosis with spontaneous resolution after two to three months.[13]

To the best of our knowledge, there have been eight published case of MEWDS following various vaccinations, including rabies,[7] human papilloma virus,[8,9] hepatitis A,[6,10] hepatitis B,[11] meningococcal,[8] Yellow fever,[6] and influenza.[4,5] The demographics and clinical course of all published cases. Including the current, are summarized in Table 1. Our case is the first to employ MMI, and revealed findings typical for MEWDS. Collectively, patients with post-vaccine MEWDS tended to be healthy (77.8%), young to middle age (median 33 years; mean 31.7 years; range 16–53 years) women (66.7%). Racial classification was 44.4% Caucasian, 22.2% Asian, and 33.3% undisclosed. Symptoms manifested on average 13.3 days (median: 14; range: 1-30) after immunization. Mean presenting Snellen visual acuity was of 20/38 (median: 20/25-2, range: 20/16 to 20/200). Patients most commonly described photophobia (88.9%), followed by central or paracentral scotomata (44.4%) and dyschromatopsia (33.3%). Seven cases (77.8%) of post-vaccine MEWDS displayed spontaneous resolution back to baseline Snellen visual acuity over an average of 6.9 weeks (median: 6 weeks; range: 4–12 weeks). The patient with MEWDS following rabies vaccination refused oral corticosteroids, but agreed to receive peri-ocular corticosteroid as part of the treatment protocol. Ogino and colleagues described a case of MEWDS following human papilloma virus vaccine that appeared to have resolved without treatment in two months. Subsequently, the patient noted progressive peripheral vision loss over two years. Repeat imaging revealed mid-peripheral vascular leakage on fluorescein angiography. Due to an allergy to methylprednisolone, she was treated with high dose betamethasone and anti-histamines, leading to drastic reduction in leakage on FA. Unfortunately, the leakage recurred as patient was weaned off the corticosteroid. Given the atypical symptoms and examination findings, the authors discussed the possibility of a different concurrent disease entity, such as acute zonal occult outer retinopathy. Visual acuity at last vision in affected eyes had mean of 20/18.5, with median of 20/20 and range of 20/16 to 20/20.

The exact pathogenesis of MEWDS is yet to be fully elucidated. Most recent hypotheses suggest an immune-mediated mechanism occurring at either the outer retina,[12,14,15] the choriocapillaris/inner choroid,[16–18] or both in genetically predisposed individuals, and the occurrence of MEWDS following vaccination would tend to support such theories. Specifically, vaccines have been suggested to trigger an inflammatory response resulting in uveitis by means of molecular mimicry, or direct antigen-mediated cellular/humoral immune response, adjuvant-mediated inflammation.[2,3] As many as 160 million doses of influenza vaccine were administered in the United States for the 2019–2020 season,[19] and billions more have been given since the first report of vaccine-associated MEWDS in 1996. It remains possible, therefore, that the occurrence of MEWDS following immunization is coincidental. However, given the generally mild and self-resolving nature of MEWDS, it could also be that post-vaccination cases of MEWDS tend to go unrecognized and unreported. The benefits of continuing to follow established vaccination guidelines far outweigh the risks of uveitis for the vast majority of patients.[3]

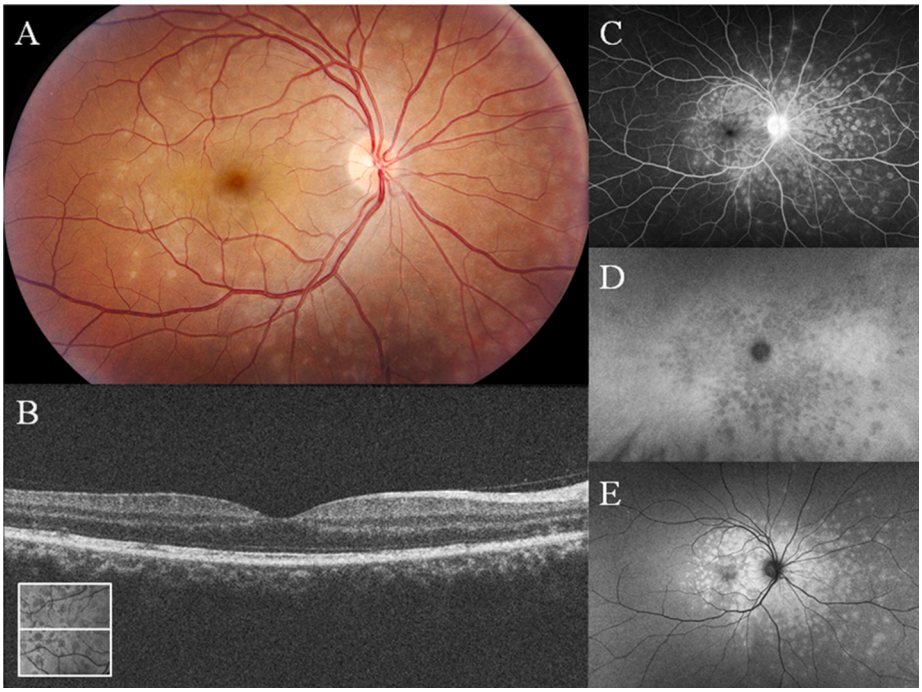


**Fig. 1.** Imaging on presentation: A - Color fundus photo, B – Spectral Domain-Optical coherence tomography, C - Early Fluorescein angiography, D - Late Indocyanine green angiography, E —- Fundus Autofluorescence. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

**Table 1**
Summary of all cases of MEWDS following Vaccination.

| Study | Age | Race | Gender | Vaccine Type | Time from Vaccination (days) | Laterality | Symptoms | Comorbidities | Presenting VA in affected eye (Snellen) | Vision at Last Visit in Affected Eye | Intervention | Time until Resolution (weeks) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ng et al., 2020 | 33 | Caucasian | M | Influenza (Flucelvax Quadrivalent® Seqirus) | 14 | Right | Paracentral scotomata, Photopsias, Grey haze | None | 20/20 + 2 | 20/16 | None | 4 |
| Yang et al., 2018 | 33 | Chinese | F | Rabies | 14 | Left | Large paracentral scotoma, Photopsias | None | 20/20 | 20/20 | Retrobulbar Triamcinolone Acetonide 40 mg | Partially resolved at 8 weeks |
| Abou-Samra et al., 2018 | 27 | Undisclosed | F | Influenza | 14 | Right | Central Photopsias | Stevens-Johnson Syndrome, Wolff-Parkinson-White Syndrome, vesicourethral reflux, mild chronic kidney disease, endometriosis, fibroadenomas, depression with anxiety. | 20/25-2 | undisclosed | None | 8 |
| Ogino et al., 2014 | 16 | Japanese | F | Human Papilloma Virus (Cervarix®, Glaxo Smith Kline) | 14 | Left | Throat pain, Headache, Photopsias, peripheral vision loss | None | 20/16 | 20/16 | None initially, Betamethasone and anti-histamine later for peripheral vascular leakage and associated visual field constriction | Retinal lesions resolved at two months; worsening peripheral vision loss for 2 years |
| Goyal et al., 2013 | 53 | Caucasian | M | Influenza | 10 | Right | Purple haze | Hepatitis B and C infection, Polysubstance abuse | 20/25-2 | 20/20 | None | 4 |
| Cohen, 2008 | 17 | Undisclosed | F | Human Papilloma Virus and meningococcal | 30 | Left | Photopsias, central and paracentral scotomata | None | 20/200 | 20/20 | None | 8 |
| Stangos et al., 2006 | 50 | Caucasian | F | Hepatitis A and Yellow fever | 10 | Left | Photopsias, paracentral scotomata | None | 20/40 | 20/20 | None | 6 |
| Fine et al., 2001 | 33 | Caucasian | M | Hepatitis A | 13 | Left | Photopsias, Grey haze | None | 20/25-2 | 20/20 | None | 6 |
| Baglivo et al., 1996 | 23 | Undisclosed | F | Hepatitis B booster | 1 | Left | Left Blurred vision, bilateral photopsias | None | 20/200 | Undisclosed -"recovery of vision" | None | 12 |
| n = 9 | Mean: 31.7 Median 33 Range: 16 - 53 | Caucasian: 44.4% Asian: 22.2% Undisclosed: 33.3% | M:F ratio 1:2 | | Median 14 Mean: 13.3 Range: 1 - 30 | OD:OS ratio 1:2 | Photopsias: 88.9% Central/Paracental Scotomata: 44.4% Dyschromatopsia: 33.3% | 77.8% None | Mean: 20/38 Median: 20/25-2 Range: 20/16 - 20/200 | Mean: 20/18.5 Median: 20/20 Range: 20/16 - 20/20 | 77.8% None | Mean: 6.9 Median: 6 Range: 4 - 12 |

## 4. Conclusion

We present the first reported case of MMI of vaccination-associated MEWDS. Comparison with eight previously reported cases of MEWDS following immunization revealed that subjects tended to be healthy, young to middle age women with a median time to onset of two weeks. Vision tended to recover spontaneously over one to three months.

## Patient consent

The patient consented to publication of the case in writing.

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## Authorship

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

## Declaration of competing interest

None of the authors have any financial disclosures.

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