Abstract

Multiple evanescent white dot syndrome (MEWDS) is a self-limiting disease that affects the retinal pigment epithelium and outer retina. This teaching case report involving a patient diagnosed with MEWDS reviews clinical findings, differential diagnosis and management of this condition. The associated epidemiology, pathophysiology and risk factors are also discussed. Although MEWDS is relatively uncommon, it is important for optometrists to accurately diagnose it because other retinal conditions that present similarly may have different clinical courses and required treatment as well as poorer prognosis.

Key Words: white dot syndrome, MEWDS, viral prodrome, scotomas, macular granularity

Background

This case involves a 22-year-old Caucasian female diagnosed with multiple evanescent white dot syndrome (MEWDS). MEWDS is part of a group of inflammatory disorders known as white dot syndromes, which affect the retina, retinal pigment epithelium (RPE) and choroid. Often, symptoms of MEWDS are unilateral, have sudden onset, and include blurred vision, central or paracentral scotomas, enlarged blind spots, photopsia or dyschromatopsia. Observable ocular signs include multiple small, gray-white spots at the level of the RPE and outer retina. The most significant consequence of MEWDS is temporary vision changes, which usually spontaneously resolve. However visual field defects and photopias may persist. This teaching case report highlights the role of the primary care optometrist in the evaluation and management of MEWDS. It focuses on the importance of critical-thinking skills for accurate diagnosis as well as patient education. It is appropriate for use with optometry residents and students who have had some patient care experience and knowledge in ocular disease. At most colleges, it would be appropriate for third- and fourth-year optometry students.

Student Discussion Guide

Case description

Visit 1

A 22-year-old Caucasian female was referred by her primary care physician to the vision department as a new patient for same-day evaluation. She complained of a gray spot in her vision in her left eye, associated with blur and loss of vision in part of her visual field. She denied new flashing lights, movement of the “spot” throughout her visual field, new floaters, new headache, eye pain and sun-gazing. At her last eye exam with a different doctor 10 months prior, the patient reported an unremarkable ocular history and that she didn’t wear glasses or contact lenses. Her medical history was remarkable for seasonal allergies, migraines with aura, irritable bowel syndrome and a recent history of flu a few days before onset of vision changes. She did not experience symptoms of nausea or vomiting at the time of her reported flu. Her medications included birth control pills as well as Dayquil and acetaminophen at the time of flu. There were no known medication allergies.

| Table 1. | Click to enlarge |

<table>
<thead>
<tr>
<th>Anterior and Posterior Segment Evaluation</th>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uveal tissues</td>
<td>clear</td>
<td>clear</td>
</tr>
<tr>
<td>Conjunctiva</td>
<td>white, quiet</td>
<td>white, quiet</td>
</tr>
<tr>
<td>Sclera</td>
<td>clear, no tear</td>
<td>clear, no tear</td>
</tr>
<tr>
<td>Anterior-chamber</td>
<td>clear, quiet, no mela, no flare</td>
<td>clear, quiet, no mela, no flare</td>
</tr>
<tr>
<td>Iris</td>
<td>flat</td>
<td>flat</td>
</tr>
<tr>
<td>Lens</td>
<td>clear, no opacity</td>
<td>clear, no opacity</td>
</tr>
<tr>
<td>Fovea</td>
<td>clear, no cells</td>
<td>clear, no cells</td>
</tr>
<tr>
<td>Optic nerve</td>
<td>distinct margins, pink r/r, 0.30 mm x 0.30 mm</td>
<td>distinct margins, pink r/r, 0.30 mm x 0.30 mm</td>
</tr>
<tr>
<td>Macula</td>
<td>flat</td>
<td>flat</td>
</tr>
<tr>
<td>Posterior pole</td>
<td>clear</td>
<td>clear</td>
</tr>
<tr>
<td>Periphery</td>
<td>flat without retinal breaks, 360°</td>
<td>flat without retinal breaks, 360°</td>
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Uncorrected distance visual acuity (UCDVA) was 20/20 in each eye. Pupils, extraocular muscles and finger-counting confrontation fields were normal. Intraocular pressure was 16 mmHg in each eye. Undilated exam showed normal ocular health in each eye. The patient’s pupils were dilated with 1% tropicamide and 2.5% phenylephrine, and a 24-2 Sita Fast full-threshold automated Humphrey visual field (HVF) test was ordered for the patient to complete while dilating. After dilated retinal evaluation, optical coherence tomography (OCT) of the macula was ordered. Table 1 shows slit lamp findings and dilated fundus evaluation; Figure 1 shows HVF test results; and Figure 2 shows the OCT macular imaging.

The patient was diagnosed with central scotoma in the left eye secondary to MEWDS. She was shown her HVF and OCT test results and educated about MEWDS. The vision team explained that there are no treatment options for MEWDS and that symptoms should self-resolve without intervention. The patient was reassured that there were no signs of anterior or posterior...
segment inflammation, optic neuropathy or retinal breaks that would require treatment and that she’d be monitored closely for any changes. A two-week follow-up visit was recommended, and the patient was given an Amsler grid for monitoring her vision at home. She was offered the option of being evaluated by a retinal specialist at the two-week visit. She agreed and the referral was made.

Visit 2: one-day follow-up

Rather than wait for the two-week follow-up visit, the patient chose to be evaluated the next day by a retina specialist, who repeated dilated fundus evaluation with OCT and performed fluorescein angiography (FA). OCT findings were described as normal in the right eye, and ellipsoid zone disruption inferior to the fovea was observed in the left eye. On FA, there were no observable hyperfluorescent retinal lesions in either eye, confirming the absence of underlying vasculitis, leakage or optic nerve inflammation, ruling out several other potential white dot syndromes. Based on a granular macular appearance, OCT results and documented central scotoma, the ophthalmologist confirmed the diagnosis of MEWDS. The relevant patient education was delivered again: There are no proven treatments for MEWDS; it usually resolves on its own over several weeks; and, in the absence of underlying inflammation, follow-up in two weeks was an appropriate course of action.

Visit 3: two-week follow-up

The patient returned to the ophthalmology department for the two-week progress evaluation. Dilated examination showed stable ocular health and OCT findings. Continued monitoring with a follow-up examination in two months was recommended, but the patient was lost to follow-up.

Educator’s Guide

The Educator’s Guide includes the necessary information for teaching and discussing the case.

Key concepts

1. Hallmark symptoms and signs of MEWDS
2. Critical-thinking skills in diagnosis, using appropriate optometric tools when additional testing may guide to a
MEWDS: a Teaching Case Report

3. Management and clinical course of MEWDS
4. The role of communication throughout the exam: developing patient rapport, obtaining a thorough case history, patient education

Learning objectives

Upon conclusion of this case discussion, participants should be able to:

1. Describe the ocular signs of MEWDS
2. Apply critical-thinking skills to correlate symptoms with clinical findings
3. Describe various white dot syndromes, noting similarities and differences to MEWDS
4. Describe additional testing that can be performed to confirm the diagnosis of MEWDS
5. Understand the need to investigate further if the clinical picture does not match the patient’s complaints

Discussion questions

A. Knowledge, concepts, facts, information required for critical review of the case:

1. Describe classic presentation of MEWDS and compare to other white dot syndromes
2. Determine differential diagnoses by analyzing case history, risk factors and demographics
3. Describe MEWDS etiology and patient demographics
4. Discuss how recent flu impacted this case

B. Differential diagnosis:

1. What tests were used in this case to diagnose MEWDS?
2. What are differential diagnoses based on symptoms alone?
3. How were the clinical findings analyzed to rule out or support potential differential diagnoses?
4. At this time, are there other diagnoses one should consider?

C. Patient management and the role of the optometrist:

1. What are appropriate management options in this case?
2. What is an appropriate follow-up schedule?
3. What is the prognosis for a patient with MEWDS?
4. What are patient education strategies to reassure patients when their condition is self-limiting and/or no treatment is indicated?

D. Critical-thinking concepts:

1. How does entering visual acuity impact the provider’s decision-making in this case? Would it be different if vision were worse than 20/20?
2. What inferences are made in the determination of the diagnosis?
3. If any one particular test performed during the visit was not completed, would the provider have been able to make the diagnosis?
4. What are the potential implications involving the management of this patient?
5. What if symptoms worsen or do not improve?
6. How would management have been different if an ophthalmologist had not been as easily accessible to the patient?
7. What are some effective strategies to reassure patients with self-resolving conditions?

Teaching instructions and assessment methodology
The purpose of this case report is to help clinicians review the clinical features and course of MEWDS as well as develop strategies for reassuring patients at the end of a clinical encounter. Optometry students can be guided through a discussion in a classroom or clinical setting. They should be presented with case details in a stepwise fashion (i.e., case history, dilated fundus examination, automated threshold visual fields, OCT) to think critically through the clinical presentation, devise differentials and arrive at a diagnosis. The key aspects of patient education can be discussed, including delivery of the diagnosis, management options and ocular prognosis.

The keys to diagnosis in this case were a thorough case history including systemic history and review of systems, a comprehensive dilated ocular evaluation and critical-thinking skills to incorporate and interpret additional test findings (HVF and OCT) as part of the visit. It is important that clinicians make an accurate MEWDS diagnosis and rule out other sight-threatening retinal pathology that would require treatment. MEWDS management is generally observation, and the condition has a good prognosis. In contrast, other white dot syndromes require invasive treatment and have worse prognoses.

Discussion

White dot syndromes

MEWDS was first reported in 1984, described as a transient chorioretinopathy often preceded by a viral-like illness. It is noted to be a clinical entity distinct from other inflammatory white dot syndromes such as acute macular neuroretinopathy, acute posterior multifocal placoid pigment epitheliopathy (APMPPE), acute retinal pigment epitheliitis, birdshot choroidopathy, multifocal choroiditis (MFC) with panuveitis, and punctate inner choroidopathy.

This group of inflammatory disorders produces discrete, yellow/white retinal lesions in young adults, which can be differentiated by history, appearance, laterality and FA (Table 2). MEWDS commonly presents with macular granularity and “wreath-like” hyperfluorescence on FA. MEWDS generally affects healthy, myopic women (4:1 compared to males) in their third or fourth decade, but patients in their 50s have been reported. The annual incidence is 0.22 per 100,000. There are no known genetic or racial predilections. A viral prodrome has been reported in more than 50% of cases.

Etiology

The exact pathogenesis of MEWDS is unknown, but it is thought to be caused by an underlying autoimmune (non-infectious) mechanism. Suggested explanations include viral agents entering retinal receptor cells at the edge of the optic nerve and ora serrata, triggering an autoimmune response. An association with environmental triggers and human leukocyte antigen (HLA)-B51 has been reported. Cases have also presented after vaccinations for human papillomavirus, hepatitis A, and hepatitis B. One theory holds that choriocapillaris hypoperfusion or non-perfusion results in ischemic damage to the outer retina and RPE due to a vaso-occlusive process involving small vessels, whereas other white dot syndromes such as APMPPE and MFC involve larger blood vessels. Few reports provide an explanation for differences between retinal spots and dots. A recent report suggests a shallow infiltration of inflammatory cells within the inner choroid or outside the choriocapillaris, beneath the RPE, is what causes smaller retinal dots in MEWDS.

Clinical features

Patients with MEWDS may complain of sudden, unilateral changes in vision including decreased acuity, visual field defects consistent with enlarged blind spots or scotomas, photopsias or color vision changes. Visual acuity may vary, ranging from 20/20 to 20/400 in some cases.

Clinical manifestations include small, gray-white retinal dots and spots ranging in size from 100-200 µm. Some reports
have described differences between the retinal dots and spots based on their location; dots appear more anteriorly at the level of the outer retina and RPE, and spots appear deeper at the RPE and inner choroid. Dots may present greater in number around the optic nerve and nasal retina. The macular region may also have a fine, granular appearance, which has been reported to be pathognomonic for MEWDS. A relative afferent pupillary defect (RAPD) may be present, as well as mild optic nerve inflammation, mild vitreous cells and mild anterior chamber reaction.

Retinal lesions are usually transient and tend to resolve within 3-10 weeks, with larger spots resolving quicker than smaller dots. After the acute clinical phase and resolution of retinal lesions, minimally evident macular and paramacular granularity may persist.

**Differential diagnosis**

Clinicians must be diligent in ruling out potentially ominous causes of a patient’s perceived visual field defect, whether it be of ocular or neurological origin. Upon chief complaint of “gray spot” associated with blur and loss of vision, a broad range of differentials could be considered including ocular inflammation, optic neuropathy, macular disease and retinal detachment. A condition commonly encountered in clinic in young, healthy patients is central serous retinopathy (CSR). However, this patient did not fit the classic demographics of being a myopic male under recent stress or with Type A personality. Other retinal conditions that may cause a patient to present with a scotoma include MEWDS and central pigment epithelial detachment.

Given this patient’s history of migraine with aura, it is reasonable to consider an atypical ocular migraine as the cause of the symptoms, but this should be a diagnosis of exclusion, which was certainly ruled out with clinical exam. Classic symptoms of ocular migraine include flashing or shimering lights, blind spots, floating lines and zig-zag patterns, and symptoms may occur without headache. When questioned, the patient denied headache but reported recently having the flu, which was confirmed by her primary care physician and managed with over-the-counter medications.

MEWDS is diagnosed by clinical observation and can be confirmed with electrophysical and angiographic testing (Table 3). Careful case history, clinical appearance and ancillary testing help to differentiate MEWDS from other white dot syndromes. Testing may include:

- **OCT**: OCT may reveal disruption to the hyper-reflective band attributed to the photoreceptor inner segment/outer segment junction or dome-shaped subretinal hyper-reflective lesions. Increased reflectivity of the choroidal space has also been reported. OCT findings gradually resolve with resolution of the disease; however, outer nuclear layer thinning has been apparent in cases of recurrent disease, suggesting that repeated episodes may result in permanent retinal atrophy.

- **FA**: FA usually demonstrates early punctate hyperfluorescence corresponding to retinal dots and spots, with late staining of the lesions and optic nerve. Dots appear during the choroidal-filling and retinal artery perfusion phases, often in multiple clusters in a “wreath-like” pattern near the macula. Depending on duration of symptoms at presentation, variances in equipment and imaging modality,
and severity of the condition, FA appearance may also include hypofluorescent lesions or even appear normal. Resolution of FA findings correlate to resolution of retinal lesions.\textsuperscript{6}

- Indocyanine green angiography (ICGA): Hypofluorescence is evident in early and late phases. Multiple hyperfluorescent dots may appear in the late phase 20 minutes after injection, characteristically more numerous and less “wreath-like” than noted on clinical examination and FA.\textsuperscript{3-6}

- Fundus autofluorescence (FAF): In the acute phase, retinal dots and spots show up as increased areas of autofluorescence, and pinpoint areas of decreased autofluorescence around the disc and macula may be seen. As MEWDS resolves, hyperfluorescent lesions disappear and hyperfluorescent spots may lessen in number, resolve, become smaller in size, or have a more hypoa autofluorescent appearance (either a halo or throughout the lesion). FAF abnormalities may persist for months after diagnosis and after resolution of FA-ICGA abnormalities.

- Electrophysiologic testing: electro-oculogram (EOG) demonstrates reduced light-dark ratios, and electroretinogram (ERG) shows reduced a-waves and early receptor potentials.

- Visual field testing: Automated visual field testing may reveal an enlarged blind spot or scotomas (central, paracentral, temporal or scattered). Although not diagnostic, automated visual field testing may be useful in ruling out possible neurological causes for visual field reductions and ruling in retinal disease (especially with central 10-2 testing). Documentation of the visual field defect may be useful for patient education as well as monitoring disease course and symptoms.

- Fundus photography: While also not diagnostic, fundus photography may be useful in documenting the current status of the retina, which may change based on duration of disease. In early stages, photodocumentation of yellow-white retinal spots in the posterior pole and midperiphery is common. Lesions appear at the level of the outer retina, RPE and inner choroid. Foveal granularity described as small white or orange pinpoint specks may be pathognomonic for MEWDS. As the clinical course progresses, retinal dots and spots may fade or
appear more reddish/brown before resolving completely.

- There have been reports of MEWDS cases without dots or spots on clinical examination that were identified with both FA and ICGA as well as ICGA alone. There are few reports of cases without retinal spots and macular granularity alone, but this may represent differing timing in the clinical course. This case is one example of a MEWDS presentation with macular granularity as the only clinical sign on dilated examination, consistent with changes on OCT and HVF testing but not identified on FA.

**Management**

The prognosis for MEWDS is generally good with spontaneous resolution of retinal lesions within weeks to months (3-10 weeks). Symptoms generally improve shortly after; however, OCT, angiographic and visual field abnormalities may take longer to resolve. In some cases, visual field defects and photopsias may persist. Recurrence is rare, but is estimated to occur in approximately 10% of cases. An Amsler grid can be given to patients to monitor their vision at home. Treatment is not usually necessary; however, recurrent cases have been treated with cyclosporine, and rare incidents of choroidal neovascularization have been treated with intravitreal ranibizumab.

**Critical-thinking concepts**

Because the degree of visual acuity loss may vary in cases of MEWDS, ranging from 20/20 to 20/400, it should not be used as an indicator of disease. In this case, the patient’s UCDVA was 20/20 in each eye and thus did not lead to high suspicion of macular disease at the start of the examination. For this reason, color vision and Amsler grid testing were not performed at the initial visit. However, because color vision changes may be a presenting symptom, it may be helpful to perform color vision testing to document any defects as well as resolution of symptoms throughout the clinical course of MEWDS. Anterior segment slit lamp examination revealed no signs of corneal disease or anterior uveitis. Dilated fundus evaluation showed flat optic nerve heads, well-perfused with distinct margins in each eye. Thus, optic neuritis, optic atrophy and optic neuropathy were ruled out. Additionally, there were no signs of vitritis, serous detachments, pigment epithelial detachments or retinal breaks, thus CSR and retinal detachment were ruled out. The only remarkable retinal finding was a fine macular granular change outside the fovea of the left eye; there were no classic white retinal spots or dots. It is possible that retinal spots and lesions were present prior to the patient arriving for evaluation and had already self-resolved, revealing only granularity correlating to abnormal HVF and OCT test results.

This patient fits the classic profile of patients diagnosed with MEWDS. However, without a thorough case history revealing recent-onset flu and without a stepwise approach to investigating symptoms with careful dilated examination and the addition of HVF and OCT testing, the diagnosis may not have been made. In this case, the clinical picture did not include classic white spots/dots. Clinical pearls for students are to have a high level of suspicion when examination does not reveal obvious pathology and to order additional testing when clinical findings do not fully correlate with patients’ symptoms. In this case, HVF testing was performed to rule out any neurological etiology for the patient’s visual field complaints as undilated examination revealed no obvious pathology. As it turned out, the central visual field defect suggested macular pathology, and macular OCT was ordered while the patient’s pupils were dilating. Photoreceptor integrity line abnormalities on OCT correlated with fundus examination, HVF test findings and the patient’s complaint.
Although fundus photography may be useful in documenting the clinical course of MEWDS, and can be used as a visual aid during patient education, it was not performed at the initial visit due to minimal retinal changes observed on clinical examination as well as scheduling and billing/insurance constraints. Other tests that could have been ordered were FAF, FA, ICGA, and ERG/EOG; however, they were not available at the practice. The patient was referred to a nearby ophthalmology practice where OCT was repeated and FA was performed, ruling out underlying vasculitis or inflammation. Although FA often shows “wreath-like” hyperfluorescent dots corresponding to retinal dots observable in the acute phase of MEWDS, this patient did not present with retinal dots and thus there was no hyperfluorescence on FA. It is possible that retinal spots had already appeared and resolved in the 10 days prior to FA being performed. However, there have also been cases of MEWDS that present without retinal spots; therefore, FA should not be solely relied upon for making a MEWDS diagnosis.

Often, when health conditions are self-limiting or without clear cause, clinicians may attempt to reassure patients to decrease their concern or worry and improve outcomes. Clinicians may use several strategies including developing rapport with the patient, empathizing with him/her and providing accurate information and explanations about the condition. A six-step strategy for patient reassurance has been described (Table 4). Though there are many theoretical models of patient reassurance, the effectiveness of each approach has not been extensively studied and there are no standardized methods of delivering reassurance. Preliminary clinical trial evidence does suggest that a more cognitive approach (information, education) may be more effective than an affective approach (rapport building, empathy) in the long run. However, a mixture is commonly employed. Different patients may require different strategies for reassurance, thus a patient-centered approach should be considered in each case.

Conclusions

This case serves as a reminder that young, seemingly healthy patients without chronic systemic disease can have less commonly encountered retinal pathology. This patient experienced acute-onset viral symptoms followed by changes in vision caused by MEWDS. This case report is intended to educate eyecare providers on the clinical course and management of MEWDS, highlighting the importance of thorough case history, careful ophthalmic examination, and critical thinking in analyzing information throughout the examination. While MEWDS is uncommon and generally has a good prognosis, it is important that clinicians are able to accurately diagnose and educate patients on its course.

References


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