Acquired Vitelliform Lesions in the Setting of Nonexudative Age-Related Macular Degeneration

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Abstract
Introduction: Acquired vitelliform lesions (AVL) are unilateral or bilateral lesions found in a variety of macular conditions including age related macular degeneration. They can masquerade as a choroidal neovascular membrane leading to unnecessary referrals to specialists for further treatment.

Case Presentation: An 81-year-old male patient with a history of acquired vitelliform lesions and age related macular degeneration in both eyes presents for an examination complaining of decreased vision. Upon diagnostic imaging, the lesions were suspicious for a CNV and patient was referred to retina specialist for further workup.

Management and Outcome: The referral to the Ophthalmologist warranted both OCT angiography and fluorescein angiography that did not show leakage of the lesions and thus no evidence of a CNV in either eye.

Discussion: While a referral to a retina specialist is warranted for suspicious vision threatening lesions, a closer look at fundus examination and OCT diagnostic imaging is crucial in correctly diagnosing these lesions and differentiating them from a CNV.

Introduction
Vitelliform lesions are the result of the accumulation of lipofuscin, melanolipofuscin, melanosomes, and outer segment debris in the subretinal space between the retinal pigment epithelium (RPE) and the photoreceptor layer. The lesions appear as yellowish deposits in the macula.

Vitelliform lesions can be either inherited or acquired and the phenotype of the disease is shared between different retinal disorders with distinct genetics and etiologies. Vitelliform lesions in younger individuals usually occur in Best’s Macular Dystrophy, which is associated with a mutation of the bestrophin gene. Adult onset foveo-macular dystrophy is most common in individuals between 30 to 50 years of age and is associated with a mutation in peripherin 2 gene.

Acquired vitelliform lesions (AVLs) are most commonly seen in patients older than 60 years of age and do not have any genetic associations. They are associated with retinal diseases such as age-related macular degeneration (AMD), cuticular drusen, tractional maculopathies, pseudoxanthoma elasticum, and central serous chorioretinopathy. This paper reviews a case of AVLs and reviews the role of diagnostic imaging in their diagnosis.

Case Presentation
An 81-year-old Caucasian male presented with complaints of declining vision in his left eye over the past year. Past ocular history was remarkable for dry AMD and posterior subcapsular cataracts both eyes. Past medical history was remarkable for hypertension and atrial fibrillation and his medications included: AREDS 2, tamsulosin, metoprolol, and amlodipine.

On examination, best-corrected visual acuity (BCVA) was 20/25 in the right eye and 20/30 in the left. Pupils, extraocular motilities, and finger counting fields were all within normal limits. The patient denied any scotoma or metamorphopsia on Amsler grid testing. Anterior segment showed nuclear sclerosis and posterior subcapsular cataracts bilaterally. Dilated exam revealed scattered intermediate drusen, intraretinal pigment migration, retinal pigment epithelium (RPE) atrophy and central vitelliform lesions bilaterally.

Optical coherence tomography (OCT) testing in both eyes showed intact foveal contours without intraretinal edema bilaterally. The right eye showed a hyper-reflective lesion between the photoreceptor and RPE in the right eye and a heterogenous lesion between the RPE and photoreceptor layer with hyper- and hypo-reflective components in the left eye (Figure 1).

The hypo-reflective area in the left eye raised suspicion for subretinal fluid and choroidal neovascularization (CNV). The patient was referred for retinal consultation.
Figure 1. Presentation of acquired vitelliform lesions with spectral domain optical coherence tomography in right (1A) and left (1B) eyes. The blue arrows depict the hyperreflective material between the photoreceptor layer and the retinal pigment epithelium.

Figure 2. Presentation of optical coherence tomography angiography depicting transverse intensity image showing hyperreflectivity of the lesion consistent with vitelliform and corresponding B scan with flow overlay of the right eye (2A) and left eye (2B).

Figure 3. Presentation of fluorescein angiography depicting staining of vitelliform lesions without leakage of right eye (3A) and left eye (3B).

Upon retinal evaluation, OCT angiography (OCT-A) was performed and shown to be unremarkable with normal outer retinal layers and choriocapillaris; there was no evidence of CNV as shown in Figure 2.

Fluorescein angiography (FA), as seen in Figure 3, showed staining of the vitelliform lesions in the late phases without leakage to suggest CNV in either eye. Interpretation was limited by the noted posterior capsule opacities, however.

Discussion
This case highlights the characteristics of AVLs clinically and on multimodal imaging in the presence of AMD when the AVLs may appear suspicious for CNV. Recognizing AVLs will lead to the correct diagnosis and management.

Etiology of Acquired Vitelliform Lesions
Acquired vitelliform lesions occur due to the loss of apposition between the photoreceptors and the RPE leading to the dysfunction of the RPE. The yellowish appearance of the vitelliform lesion on funduscopic examination is thought to be pigment laden macrophages, RPE cells, and the loss of apposition between the photoreceptors and the RPE. The pathophysiology includes the disruption of phagocytosis that occurs in the photoreceptors shed outer segments.

Diagnostic Testing
The advent of the OCT, OCT-A and FA imaging modalities has made identification of macular lesions much more accurate as seen in Table 1 below. The OCT reveals a hyper-fluorescent material within the subretinal space primarily between the RPE and Ellipsoid zone. The macular layers will show the hyper reflective material within the subretinal space, thickening of the intact IS/OS junction, preservation of the external limiting membrane, and mild thinning of the outer nuclear layer. A split between the retinal pigment epithelium-basal laminar-Bruch's membrane band on OCT may indicate CNV.

Complications
Due to the disruption of the outer retinal layers, there is always a risk for CNV in more severe macular disease. If the AVLs are present without other macular findings, the risk of CNV is low. However, in the presence of other macular pathology like AMD, there is a higher risk of CNV. The risk for a CNV is thought to be due to lesions being rich in lipids of lipoprotein origin which are pro-angiogenic and pro-inflammatory when oxidized. Drusen and basal linear deposit are also biomechanically fragile and provide a cleavage plane for invading the choriocapillaris.
The pathophysiology of drusen accumulation includes components of complement proteins that promote choroidal neovascularization. If CNV occurs, it is most often during the resorption phase of the vitelliform life cycle.\(^5\) The resorption phase may be associated with mechanical interruptions in Bruch’s membrane, which allows for pathologic angiogenesis to extend from the choroid into the sub-RPE space.\(^5\) Evaluating Bruch’s membrane, which allows for pathologic angiogenesis phase may be associated with mechanical interruptions in atrophy.\(^5\) Patients with AVLs and dry AMD should be followed for VA outcomes in eyes with AVLs was the presence of foveal atrophy.\(^5\) The most significant factor predictive of VA outcomes in eyes with AVLs was the presence of foveal atrophy.\(^5\) Patients with AVLs and dry AMD should be followed for PER-AREDS2 management recommendations.

**Outcomes**

Elderly individuals with AVLs have an equal gender distribution and commonly present with good visual acuity (VA).\(^4\) However, there is an inverse correlation of the relationship between visual acuity and the integrity of the ellipsoid zone. Disruption of the outer segments on SD OCT is responsible for VA loss in patients with AVLs.\(^1\) In eyes with AVL and CNV, pre-treatment ellipsoid zone and external limiting membrane zone integrity rather than initial VA were significant predictors of final BCVA or change in BCVA.\(^5,7\) The most significant factor predictive of VA outcomes in eyes with AVLs was the presence of foveal atrophy.\(^5\) Patients with AVLs and dry AMD should be followed for PER-AREDS2 management recommendations.

**Conclusion**

Age-related macular degeneration is a common retinal disease that may present with concomitant macular lesions including AVLs. In the setting of AMD, eyes with AVLs have a higher risk of developing CNV. Clinical examination and diagnostic imaging facilitate the correct diagnosis and management of AVLs. Nonetheless, a referral to a Retina specialist is always important if the diagnosis of AVL vs CNV is uncertain.

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**References**


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**Table 1. Diagnostic Imaging Results of Macular Lesions**

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Clinical presentation</th>
<th>OCT(^a)</th>
<th>OCT-A(^b)</th>
<th>FA(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drusen</td>
<td>Small yellow deposits with distinct or hazy borders</td>
<td>Hyper-reflective deposits between the RPE and Bruch’s membrane</td>
<td>Hyper-reflective deposits between the RPE and Bruch’s membrane</td>
<td>Early phase: Small hyperfluorescent spots that are well contoured Late phase: spots fade away with choroidal fluorescence</td>
</tr>
<tr>
<td>Acquired Vitelliform Lesions</td>
<td>Yellow circular deposits</td>
<td>Hyper-reflective deposits between the RPE and Photoreceptor layer</td>
<td>Hyper-reflective deposits between the RPE and Photoreceptor layer</td>
<td>Early phase: blocked fluorescence of by material within the subretinal space Late phase: diffuse staining of AVL</td>
</tr>
<tr>
<td>Inherited Vitelliform Dystrophy</td>
<td>Yellow circinate deposit, worsening with advance stage</td>
<td>Thickening of the cone outer segments</td>
<td>Thickening of the cone outer segments</td>
<td>Early Phase: hypo-fluorescence Late Phase: hyper-fluorescence as the disease progresses</td>
</tr>
<tr>
<td>Pigment Epithelial Detachments</td>
<td>Yellow-white elevations of the RPE with brown or grey pigmentation</td>
<td>Detached, reflective RPE band</td>
<td>Detached, reflective RPE band</td>
<td>Early phase: faint hyper-fluorescence that increases throughout stages without leakage</td>
</tr>
<tr>
<td>Choroidal Neovascular Membrane</td>
<td>Grey-green elevated lesion or retinal hemorrhage</td>
<td>Retinal edema with disruption of Bruch’s membrane</td>
<td>Neovascular complex between RPE and Bruch’s membrane</td>
<td>Early phase: macular hyper-fluorescence Late phase: leakage from CNVM</td>
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Table 1: \(a=\) optical coherence tomography; \(b=\) optical coherence tomography angiography; \(c=\) fluorescein angiography

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