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Case report

Macular hole and serous pigment epithelial detachment in bilateral acquired vitelliform lesions

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ABSTRACT

Purpose: Acquired vitelliform lesions (AVLs) are associated with age-related macular degeneration and other variable macular disorders. AVLs often lead to outer retinal atrophy, sometimes accompanying a macular hole and choroidal neovascularization. The purpose of this study was to report a rare case with bilateral AVLs, in which one eye had accompanied a macular hole and the second eye a serous pigment epithelial detachment (sPED).

Observations: A 66-year-old woman complained of bilateral metamorphopsia. AVLs were observed in the right eye and a flat sPED in the left eye. The best-corrected visual acuity (BCVA) was 20/17 in both eyes. Fluorescein angiography revealed local leakage in the right eye and pattern dystrophy-like hypofluorescence in both eyes. The sPED progressed with AVLs in the left eye and was treated with a combination therapy of intravitreal aflibercept, a sub-Tenon's injection of triamcinolone acetonide, and photodynamic therapy (IVA/STTA/PDT), which successfully flattened the sPED and sustained good vision for 4 years. The right eye was treated with intravitreal ranibizumab and tissue plasminogen activator, which enhanced absorption of the vitelliform material. However, 14 months later, a macular hole with typical metamorphopsia formed above a subretinal fibrotic scar at the vitelliruptive stage. Although pars plana vitrectomy closed the macular hole, enlargement of the outer retinal atrophy worsened the BCVA to 20/100.

Conclusions and importance: We successfully treated one eye with a sPED with AVLs using the combination therapy of IVA/STTA/PDT, while the second eye with a macular hole secondary to AVLs ultimately developed outer retinal atrophy with visual loss.

1. Introduction

Subretinal yellowish vitelliform lesions are observed in eyes with Best disease, adult-onset foveomacular vitelliform dystrophy (AOFVD), and acquired vitelliform lesions (AVLs).[1–3] Best disease is an autosomal dominant disease with a mutation in the *bestrophin 1* (*BEST1*) gene.[1,4] AOFVD typically is included in disease subtypes associated with a mutation in the *peripherin 2* (*PRPH2*) gene such as retinitis pigmentosa and macular pattern dystrophy.[1,4,5] AVLs are related to aging retinal disorders including age-related macular degeneration (AMD), central serous chorioretinopathy, cuticular drusen, and angioid streaks, among others.[2,3,6]

Vitelliform lesions typically evolve to outer retinal atrophy through pseudohypopyon and a scrambled egg appearance and sometimes accompany a macular hole and choroidal neovascularization (CNV).[1,2,7–9] There currently are no recommended treatments for vitelliform lesions, while CNV and macular holes can be treated with anti-vascular endothelial growth factor (VEGF) therapy and vitrectomy, respectively.[7–10]

We recently experienced a rare case with bilateral AVLs and atypical complications. In this case, a macular hole formed in one eye when the AVLs were resolving, while the second eye had AVLs with a serous retinal pigment epithelial detachment (sPED).

2. Case report

A 66-year-old woman was referred to our hospital from a private clinic with suspicion of AMD in March 2015. She reported bilateral metamorphopsia; the best-corrected visual acuity (BCVA) was 20/17 in both eyes. In the right eye, submacular vitelliform lesions were

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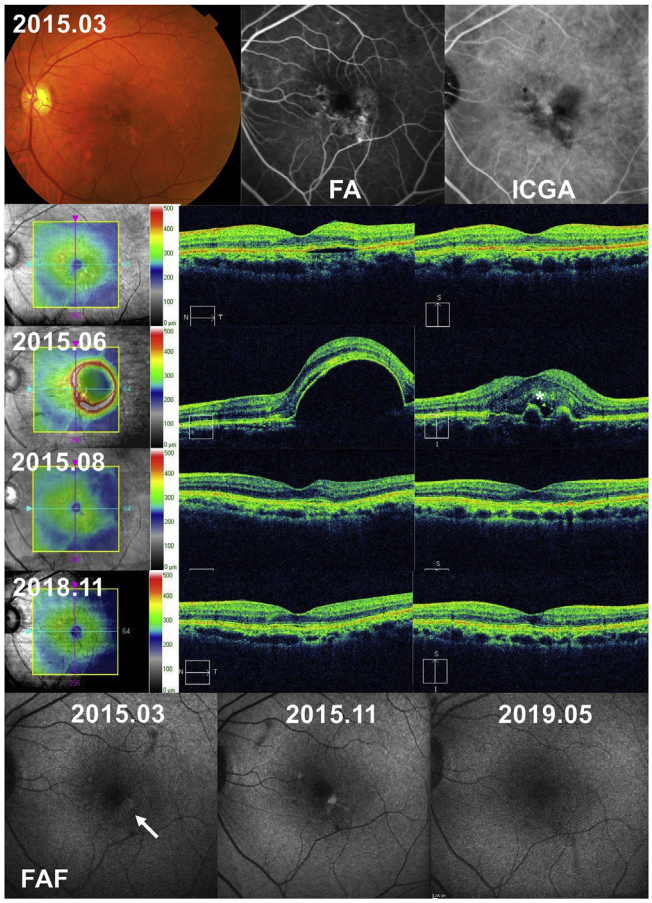

Fig. 1. The left eye with acquired vitelliform lesions (AVLs) and a serous pigment epithelial detachment (sPED). At the first visit (March 2015), pachychoroid pigment epitheliopathy was diagnosed in the left eye, while indocyanine green angiography (ICGA) showed bilateral pattern dystrophy-like pigment alteration. Fluorescein angiography (FA) and ICGA showed neither active leakage nor choroidal neovascularization. Three months later (June 2015), AVLs (asterisk) with a sPED developed. In July 2015, the combination therapy of intravitreal aflibercept, a sub-Tenon's injection of triamcinolone acetonide, and photodynamic therapy was administered, and the sPED was promptly flattened (in August 2015) and the AVLs resolved. On fundus autofluorescence imaging (FAF), hyperautofluorescent lesions corresponding to the AVLs (arrow) gradually disappeared without the development of atrophy-related hypofluorescent spots. Good vision has been maintained over 3 years with no remarkable fundus changes. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

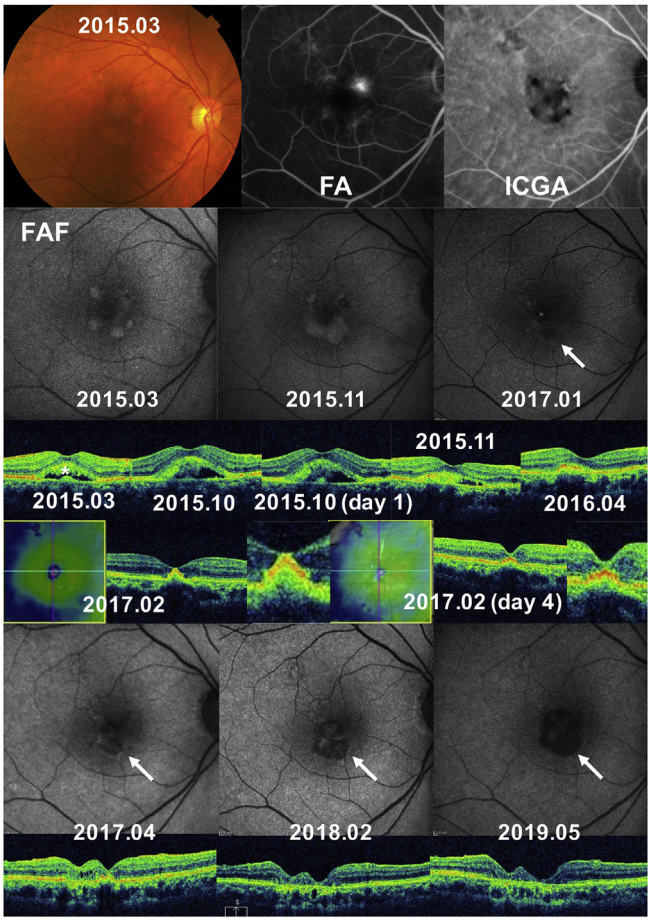

Fig. 2. The right eye with acquired vitelliform lesions (AVLs) and central serous chorioretinopathy. At the first visit (March 2015), ALVs (asterisk) with central serous chorioretinopathy are observed. Immediately after intravitreal ranibizumab and tissue plasminogen activator were administered in October 2015, the ALVs at the pseudohypopyon stage decreased the reflectivity, possibly accelerating the following absorption. One year later, a fibrotic scar at the vitelliruptive stage protruded through the external limiting membrane, resulting in formation of a small macular hole with metamorphopsia. In February 2017, a pars plana vitrectomy with internal limiting membrane peeling was performed. Retinal thickness maps on OCT showed centripetal contraction of the macula, leading to the macular hole closure. However, the ALVs led to the atrophic stage with enlargement of the atrophy of the outer nuclear layer and retinal pigment epithelium (arrows) and decreasing vision.

observed with hyperautofluorescence; in the left eye, a flat sPED was observed. The pachychoroid seen in both eyes exceeded 300 μm. Fluorescein angiography (FA) showed bilateral pattern dystrophy-like hypofluorescence and a local leakage point of fluorescent dye in the right eye, which led to a diagnosis of AVLs complicated by central serous chorioretinopathy in the right eye and atypical pachychoroid pigment epitheliopathy in the left eye (Figs. 1 and 2).

In June 2015, the sPED became enlarged and bullous in the left eye and was accompanied by AVLs with hyperautofluorescence (Fig. 1). Therefore, in July 2015, intravitreal aflibercept (IVA) (Eylea, Regeneron Pharmceuticals, Tarrytown, NY) and a sub-Tenon's injection of triamcinolone acetonide (STTA) were administered followed by photodynamic therapy (PDT) the following day. One month after IVA/STTA/PDT, the sPED flattened with no recurrence, and good vision was preserved. The BCVA at the final visit in November 2019 was 20/13.

Because the patient expected the persistent AVLs in the right eye to be treated, intravitreal ranibizumab (Lucentis, Genentech Inc., South San Francisco, CA) and tissue plasminogen activator (IVR/tPA) were administered in October 2015 after the patient provided informed consent (Fig. 2). Immediately after IVR/tPA was administered, the subretinal hyperreflective material seen on an optical coherence tomography (OCT) image started to resolve. The AVLs shrank, and the BCVA was maintained at 20/20. However, a resultant subfoveal protruding mass, possibly comprised of migrated retinal pigment epithelial (RPE) cells and other materials, breached the outer retina and subsequently a small macular hole with characteristic metamorphopsia developed, and the vision decreased to 20/40 15 months after IVR/tPA. Therefore, pars plana vitrectomy was performed in February 2017. Although the macular hole closed, the BCVA remained 20/40. Furthermore, macular atrophy, the end stage of the AVLs, developed and progressed after vitrectomy, and the BCVA decreased to 20/100 at the final visit.

3. Discussion

Vitelliform lesions are observed in association with Best disease, AOFVD, and AVLs. Best disease is associated with autosomal dominant

mutations in the *BEST1* gene.[1] Generally, the onset is at an early age (< 40 years).[1,4] In contrast, AOFVD is an adult-onset disease (> 40 years of age) related to a mutation in the *PRPH2* gene and interphotoreceptor matrix proteoglycans encoded by the *IMPG1* and *IMPG2* genes as well as the *BEST1* gene.[1,4,5] AVLs may overlap the pathological background with AOFVD, although AVLs are supposed to be hemilateral or bilateral findings related to other age-related diseases, such as AMD.[2,3,6] In the current case, bilateral specific RPE atrophy resembling PRPH2-associated pattern dystrophy and typical vitelliform lesions in the right eye may be diagnosed as AOFVD, while a vitelliform lesion accompanied central serous chorioretinopathy in the right eye and a sPED in the left eye.[11] Nevertheless, other tests including electrooculography and genetic testing should be performed for definitive diagnosis.

Vitelliform lesions generally evolve to the pseudohypopyon, vitelliruptive, and atrophic stages.[12] To date, there are no justifiable therapeutic modalities for treating vitelliform lesions. Intravitreal ranibizumab was reported to be ineffective for AVLs associated with a sPED.[11] Vitelliform lesion-associated CNV generally is treated with anti-VEGF therapy, while PDT is not recommended for type 1 CNV associated with AOFVD because of enhancement of RPE atrophy and poor visual outcomes.[1,13] Based on those previous reports, AVLs complicated by central serous chorioretinopathy in the right eye of the current patient were treated with IVR/tPA. We previously reported the effect of IVR/tPA on fibrinous and fibrous subretinal hyperreflective material.[14] In the current case, the AVLs in the right eye started to resolve immediately after IVR/tPA. Because fibrinous material in eyes with typical AMD and polypoidal choroidal vasculopathy completely resolve even 1 day after IVR/tPA,[14] the most part of AVLs may be composed of other materials. Nevertheless, the impacts of tPA on AVLs and the long-term visual prognosis remains to be determined. On the other hand, multimodal imaging of the left eye showed atypical pachychoroid pigment epitheliopathy. Because pachychoroid spectrum diseases occur predominantly in Asian populations and are treatable by PDT, the combination therapy of IVA/STTA/PDT was administered. While type 1 CNV and/or pattern dystrophy should not be treated with PDT,[1,13] AVLs with a sPED and pachychoroid may be treatable by IVA/STTA/PDT.

Vitelliform lesions are sometimes complicated by a macular hole and CNV.[1,2,7–9] A macular hole tends to be large when it develops at the atrophic stage of vitelliform macular dystrophy (Fig. 3). In contrast, in this case, a small macular hole developed above the fibrotic scar at the vitelliruptive stage in the right eye. At the atrophic stage, the large loss of photoreceptors and concomitant breach of the external limiting membrane and the tangential force of the vitreous may lead to the formation of a large macular hole. At the vitelliruptive stage, the fibrotic scar, anterior migration of RPE cells, or both may locally breach the external limiting membrane and the outer nuclear layer inward, leading to formation of a small macular hole.[15,16] Clues to predict the development of a small macular hole at the vitelliruptive stage may be acquired by the Amsler test as well as OCT showing the inward breach of the macula. Although a small macular hole can be treated by conventional vitrectomy with internal limiting membrane peeling, the transition to the atrophic stage may worsen the long-term visual outcome.

4. Conclusions

We successfully treated one eye with a sPED with AVLs using the combination therapy of IVA/STTA/PDT, while the second eye with a macular hole and AVLs ultimately led to outer retinal atrophy with visual loss despite macular hole closure after vitrectomy. As reported previously, vitelliform lesions are sometimes accompanied by a macular hole. Although a macular hole can be closed by vitrectomy, the VA may decrease at the atrophic stage of vitelliform lesions. The combination therapy of IVA/STTA/PDT may be effective in limited cases with early-stage vitelliform lesions. Nevertheless, because PDT is not recommended generally because of possible worsening of the RPE atrophy, the efficacy of PDT should be carefully investigated in the future study.

Consent to publish

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for

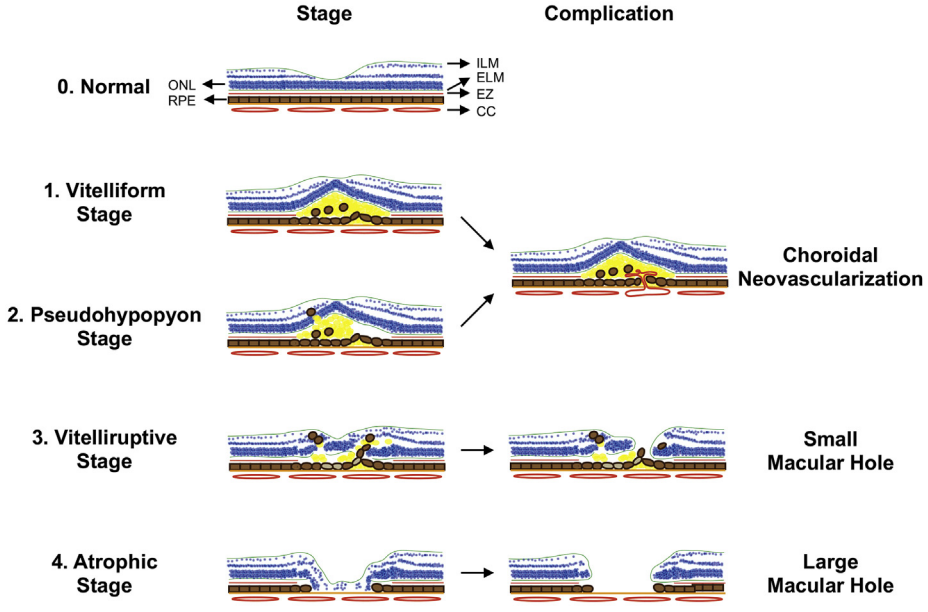

Fig. 3. Stages of vitelliform lesions and complications. Vitelliform lesions (*yellow*) form in the subretinal space, partially including the retinal pigment epithelial (RPE) cells (*brown*) and the rare complication of choroidal neovascularization (*red*). Some RPE cells migrated anteriorly through the external limiting membrane (ELM) (*green line*). A local breach of the ELM and the tangential force of the vitreous may lead to small macular hole formation, while the large loss of the outer nuclear layer (ONL) at the atrophic stage may cause large macular hole formation. ILM = internal limiting membrane (*green line*); EZ = ellipsoidal zone (*red line*); CC = choriocapillaris. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

authorship.

Declaration of competing interest

The following authors have no financial disclosures: (N·Y., T.Y., M.K., Y·H., Y·O.).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2020.100628.

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