the ipsilateral eye. Multimodal retinal imaging including UWF ICGA and fundus autofluorescence can facilitate identification of these abnormalities, which can be complicated by the development of pigmentary alterations and even serous retinal detachment with the potential to cause vision loss.

Meira Fogel-Levin,* Alice Wong,* Srinivas R. Sadda,* 3 K Bailey Freund,1,4 David Sarraf* 1,4

*Stein Eye Institute, University of California–Los Angeles School of Medicine, Los Angeles, Calif; 1Doheny Eye Institute, Los Angeles, Calif; 3Vitreous Retina Macula Consultants of New York, New York, NY; 4New York University Grossman School of Medicine, New York, NY; 5Greater Los Angeles VA Healthcare Center, Los Angeles, Calif.

Correspondence to David Sarraf, MD; dsarraf@ucla.edu.

References


Correspondence

Meira Fogel-Levin: none. Alice Wong: none. Srinivas R. Sadda is a consultant for Amen, Allergan, Novartis, Roche/Genentech, Regeneron, Bayer, 4DMT, Astellas, Apellis, Iveric, Centervue, Heidelberg, and Optos. He has received speaker fees from Carl Zeiss Meditec, Nidek, Topcon, Optos, Heidelberg Engineering, and Novartis. He has received research instruments from Carl Zeiss Meditec, Nidek, Topcon, Optos, Heidelberg Engineering, and Centervue. K. Bailey Freund is a consultant for Heidelberg Engineering, Zeiss, Allergan, Bayer, Genentech, and Novartis and receives research support from Genentech/Roche. David Sarraf is an advisory board member (Optovue), consultant (Amen, Bayer Healthcare, Genentech, Novartis, Optovue, and Iveric Bio), investigator (Amen, Genentech, Heidelberg, Optovue, and Regeneron), receiver of grants/honoraria (Amen, Bayer Healthcare, Genentech, Iveric Bio, Novartis, Optovue, and Regeneron), speaker (Optovue), equipment receiver (Heidelberg, Optovue, and Topcon), and stock owner (Optovue).

Footnotes and Disclosure

Retinal pigment epithelium apertures associated with subretinal fluid and acquired vitelliform lesions in non-neovascular age-related macular degeneration

Classic features of non-neovascular age-related macular degeneration (AMD) include drusen, drusenoid retinal pigment epithelial (RPE) detachment, and RPE atrophy. More recent studies have shown that intra- and subretinal fluid also may complicate the non-vascular form of AMD.1

RPE aperture has been described as an atypical feature of eyes with non-neovascular AMD. Querques et al.2 studied 10 eyes, most with drusenoid pigment epithelial detachment (PED) that developed such RPE defects. Similarly, Giannakaki-Zimmermann et al.3 reported 7 eyes with apertures, of which 4 displayed drusenoid PED, whereas Yoshinaga et al.4 studied 5 cases of RPE defect all associated with drusenoid PED.

In this correspondence, we describe 7 cases of RPE aperture that developed in eyes with acquired vitelliform lesions and subretinal fluid in the absence of drusenoid PED at the time of presentation. In this retrospective case series, eyes with RPE aperture associated with subretinal fluid (SRF) secondary to non-neovascular AMD were captured. The study was approved by the institutional ethics committee and adhered to the tenets of Declaration of Helsinki. Inclusion criteria were age greater than 55 years, presence of classic features of non-neovascular AMD including macular drusen and/or outer retina and RPE atrophy associated with an RPE aperture, and the absence of macular neovascularization (MNV) with multimodal imaging including optical coherence tomography (OCT; Spectralis, Heidelberg Engineering, Heidelberg, Germany, or Avanti, Optovue, Calif.), OCT angiography (Spectralis, Heidelberg Engineering or
Table 1—Patient Demographics and Imaging Characteristics of Eyes with RPE Defect Secondary to Non-neovascular AMD

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Sex</th>
<th>Intravitreal injection before defect</th>
<th>BCVA before defect</th>
<th>BCVA at defect</th>
<th>Follow-up after defect, mo</th>
<th>Drusen RPE atrophy</th>
<th>Intraretinal HRF</th>
<th>Vitelliform deposition</th>
<th>Choroidal thickness</th>
<th>Fellow eye findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>73</td>
<td>F</td>
<td>IVB</td>
<td>20/100</td>
<td>20/200</td>
<td>24</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>278</td>
</tr>
<tr>
<td>2</td>
<td>70</td>
<td>M</td>
<td>IVB</td>
<td>20/100</td>
<td>20/200</td>
<td>12</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>290</td>
</tr>
<tr>
<td>3</td>
<td>78</td>
<td>M</td>
<td>No</td>
<td>20/100</td>
<td>20/100</td>
<td>3</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>299</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>F</td>
<td>No</td>
<td>20/32</td>
<td>20/40</td>
<td>12</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>250</td>
</tr>
<tr>
<td>5</td>
<td>87</td>
<td>M</td>
<td>No</td>
<td>20/32</td>
<td>20/40</td>
<td>12</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>288</td>
</tr>
<tr>
<td>6</td>
<td>85</td>
<td>F</td>
<td>No</td>
<td>20/100</td>
<td>20/400</td>
<td>15</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>150</td>
</tr>
<tr>
<td>7</td>
<td>64</td>
<td>F</td>
<td>IVR</td>
<td>20/32</td>
<td>20/100</td>
<td>15</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>352</td>
</tr>
</tbody>
</table>

RPE, retinal pigment epithelial; AMD, age-related macular degeneration; BCVA, best corrected visual acuity; HRF, hyper-reflective foci; F, female; M, male; IVB, intravitreal bevacizumab; PED, pigment epithelial detachment; cRORA, complete retinal pigment epithelium and outer retinal atrophy; SRF, subretinal fluid; MNV, macular neovascularization; iRORA, incomplete retinal pigment epithelium and outer retinal atrophy; IVR, intravitreal ranibizumab.

Fig. 1—(A) Fundus autofluorescence, (B) spectral domain optical coherence tomography, and (C, D) optical coherence tomography angiography imaging 1 year before baseline presentation in a 70-year-old man showing subretinal vitelliform material without macular neovascularization and no evidence of a drusenoid pigment epithelial detachment. (E) Fundus autofluorescence and (F) optical coherence tomography images 1 year later (i.e. baseline presentation) showing the formation of an RPE aperture associated with subretinal fluid.
Avanti), and fluorescein angiography (Heidelberg Retina Angiograph, Heidelberg Engineering). Eyes with retinochoroidal disorders other than AMD were excluded. RPE aperture was defined as an abrupt discontinuity of the RPE with a preserved overlying ellipsoid zone and external limiting membrane in the absence of retracted or scrolled RPE suggestive of an RPE tear.

Seven eyes of 7 patients including 3 males and 4 females with an age range of 64–87 years were included. Table 1 summarizes the demographics and imaging findings. Best-corrected (Snellen) visual acuity was 20/32–20/100. Follow-up visits were available for 5 eyes. The visual acuity decreased in 3 eyes and remained stable in 2 other eyes. MNV was not detected at any of the baseline or follow-up visits.

All 7 eyes presented with RPE aperture associated with SRF and an intact overlying ellipsoid zone and external limiting membrane (Figs. 1 and 2). None of the eyes displayed evidence of macular hemorrhage or MNV with clinical examination or with OCT or OCTA imaging. All eyes displayed macular drusen and evidence of intraretinal hyper-reflective foci with OCT. Six of the 7 eyes showed evidence of associated acquired vitelliform lesions. Choroidal thickness ranged from 150 to 352 μm. Typical features of non-neovascular AMD were identified in 6 fellow eyes.

Three patients presented with a history of prior intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections. OCT and FA images were available for these 3 eyes before injections and before the development of an RPE aperture. Two of these 3 eyes displayed drusenoid PED with vitelliform material, and the other eye exhibited an acquired vitelliform lesion. None of these eyes had evidence of MNV before anti-VEGF injections.

In this correspondence, we describe 7 eyes with RPE aperture associated with SRF and acquired vitelliform lesion (AVLs) in the setting of non-neovascular AMD. Drusenoid PED is an invariable association of aperture formation in prior studies but was not observed at the time of baseline presentation in this study and was noted in 2 of 7 cases with prior images. MNV was absent in all eyes using multimodal imaging. From a total of 22 reported cases of RPE aperture in the literature, 19 were associated with drusenoid PED. The exact mechanism of development of this characteristic RPE defect is not clear. Querques et al. suggested that drusen regression in the context of drusenoid PED results in a sharply demarcated area of round RPE atrophy. In this study, AVL, not drusenoid PED, was the typical lesion type associated with the development of RPE atrophy, although it is possible that drusenoid PED was present in these eyes predating patient baseline visits. AVL is a known risk factor for the development of RPE atrophy, similar to drusenoid PED, and is an indicator or biomarker of RPE impairment and disruption. Subsequent development of RPE dehiscence therefore is not a surprising finding.

RPE apertures should be differentiated from an RPE tear. RPE tears occur most commonly in eyes with neovascular AMD and large PEDs (>500 μm in height) after anti-VEGF therapy as a result of a combination of contractile and hydrostatic forces in the vascularized PED. Unlike apertures that typically develop near the apex of the PED, tears develop near the base of the PED, where the contractile forces are greatest. Non-neovascular fluid, acquired vitelliform lesions, and RPE apertures are all the result of RPE dysfunction and disruption. The greatest risk of decompenation of the RPE may relate to its separation distance from the underlying choroid that supports and nourishes the

![Fig. 2—(A) Fundus autofluorescence, (B) fluorescein angiography, (C, D) en face optical coherence tomography angiography, and (E, F) spectral domain optical coherence tomography in a 75-year-old woman showing evidence of a retinal pigment epithelium aperture associated with an acquired vitelliform lesion in the absence of a drusenoid pigment epithelial detachment. No macular neovascularization is evident with (C) outer retinal and (D) choriocapillaris en face optical coherence tomography angiography slabs.](image)
overlying pigmented layer. This may explain the propensity for non-neovascular fluid, AVLs, and apertures to develop at the apex of a large drusenoid PED. The presence of AVL alone, however, is a sign of RPE impairment and a risk factor for the development of RPE aperture and/or atrophy.

Khalil Ghasemi Falavardjani,* Pasha Anvari,* Riccardo Sacconi,1 Giuseppe Querques,1,2 David Sarraf1,3

*Eye Research Center, The Five Senses Health Institute, Iran University of Medical Sciences, Tehran, Iran; 1Vita-Salute, San Raffaele University, Milan, Italy; 2IRCCS San Raffaele Scientific Institute, Milan, Italy; 3University of California Los Angeles, Los Angeles, Calif; 4Veterans Administration Greater Los Angeles Healthcare System, Los Angeles, Calif.


Correspondence to Khalil Ghasemi Falavardjani, MD; drghasemi@yahoo.com.

References

Footnotes and Disclosure
None of the authors has any conflict of interest in the subject matter of this paper. David Sarraf has received research grants from Amgen, Boehringer, Genentech, Heidelberg, Optovue, Regeneron, and Topcon and is a consultant for Amgen, Bayer, Genentech, Iveric Bio, Novartis, and Optovue and a paid speaker for Optovue.

Papilledema associated with COVID-19 multisystem inflammatory syndrome in children

Multisystem inflammatory syndrome in children (MIS-C), also called pediatric inflammatory multisystem syndrome, is characterized by a wide range of symptoms and can present a diagnostic challenge given its myriad presentations. On top of the more well-known inflammatory manifestations of MIS-C, recent reports have also surfaced of MIS-C causing increased intracranial pressure.1,2 MIS-C can present similarly to other systemic inflammatory disorders such as Kawasaki disease and can be especially difficult to distinguish from Kawasaki disease if a Kawasaki-like presentation is accompanied by a positive test for coronavirus disease 2019 (COVID-19).3

In adults, ocular manifestations of COVID-19 include nonspecific symptoms such as conjunctival hyperemia, chemosis, epiphora, and increased secretions.4 However, there is a relative paucity of literature regarding ocular manifestations of COVID-19 in children relative to adults. Some documented pediatric symptoms include a similar conjunctivitis presentation, along with increased conjunctival discharge, ocular pain, and eyelid swelling,5 but pediatric MIS-C is far from completely characterized.

Here we present a pediatric patient who developed bilateral papilledema and abducens nerve palsy in the setting of MIS-C to highlight the potential increased intracranial hypertension and neurologic complications of this inflammatory condition. Institutional review board approval was obtained at the Washington University in St. Louis, and consent was provided by the patient’s parents.

A 12-year-old boy with no past medical history and a past ocular history of myopia, astigmatism, and mild amblyopia OD presented to our institution in May 2020 with fever, vomiting, and diarrhea. These symptoms were accompanied by headache, fatigue, dysgeusia, photophobia, and 2 episodes of epistaxis on the day of presentation. The patient’s father had experienced similar symptoms and anosmia following recent domestic travel but was not tested for COVID-19. The patient did not have any respiratory or ophthalmic symptoms at presentation. Rapid streptococcal antigen and COVID-19 reverse transcription polymerase chain reaction tests were performed, both of which were negative, and the patient was discharged home. The patient returned 3 days later for persistent intermittent fever and diarrhea and was admitted. An infectious disease panel was notable for positive severe acute respiratory syndrome coronavirus 2 IgG.