Abstract: PURPOSE: To report a recently observed association of macular vitelliform detachment and subretinal drusenoid deposits (reticular pseudodrusen). METHODS: Clinical and multimodal imaging data of patients with acquired vitelliform lesions in association with subretinal drusenoid deposits were reviewed. Acquired vitelliform lesions were defined as subretinal accumulations of yellow material that developed in adulthood. Subretinal drusenoid deposits were diagnosed as being present if there were drusen-like accumulations that colocalized with aggregates of subretinal material as seen by multimodal imaging including spectral-domain optical coherence tomography, autofluorescence, and near-infrared imaging. RESULTS: Seven eyes of 6 patients with a mean age of 85 years, all of whom were white, were found to have vitelliform material in association with subretinal drusenoid deposits. The median visual acuity was 20/30. The vitelliform material was hyperautofluorescent and was in all eyes located in the subretinal space between the inner segment/outer segment junction and the retinal pigment epithelium. This material had the same color, autofluorescence, and optical coherence tomographic characteristics as the vitelliform material seen in association with cuticular drusen. CONCLUSION: Acquired vitelliform lesions can occur in association with subretinal drusenoid deposits. Subretinal drusenoid deposits might be mistaken for cuticular drusen because of their similar appearance in color fundus photography but can be easily distinguished with multimodal imaging because they lie above the retinal pigment epithelium. Subretinal drusenoid deposits may reflect abnormalities in the function of the retinal pigment epithelium and their presence may interfere with photoreceptor outer segment turnover, leading to an accumulation of vitelliform material.

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structure and classification are under flux.\textsuperscript{4-7} This report describes the association of vitelliform detachment in adults with subretinal drusenoid deposits using multimodal imaging.

Patients, Material, and Methods

This is a retrospective study of patients with vitelliform detachment and subretinal drusenoid deposits in the same eye examined in a private retinal referral practice between January 2008 and December 2009. The Institutional Review Board of the Lenox Hill Hospital approved this retrospective review (IRB L09.09.71E). Each patient underwent a complete ophthalmologic examination, including color, red-free fundus photography, autofluorescence, near-infrared pictures, SD-OCT, and fluorescein angiography, as indicated to rule out possible choroidal neovascularization. Eyes with signs of choroidal neovascularization were not included in this study. The SD-OCTs of the eyes were obtained with the Heidelberg Spectralis (Version 5.1.3.0; Heidelberg Engineering, Heidelberg, Germany) as viewed with the contained Heidelberg software (Spectralis Viewing Module 4.0.0.0; Heidelberg Engineering). The near-infrared pictures are routinely obtained with SD-OCT (Spectralis HRA-OCT, Heidelberg Engineering). In each patient, 31 to 37 B-scans were obtained within a 20° x 25° or 30° x 25° rectangle to encompass the macula, including the area between the temporal arcades. Autofluorescence images were obtained using either a confocal scanning laser ophthalmoscope (Heidelberg Retina Angiograph, Heidelberg Engineering) with an excitation light with a wavelength of 488 nm and an emission band-pass filter starting at 500 nm or a fundus camera (Topcon Medical System, Paramus, NJ) with a band-pass filter for excitation light with a bandpass of 535 nm to 585 nm and a matched barrier filter with a bandpass of 605 nm to 715 nm.

The diagnosis of subretinal drusenoid deposits was based on clinical examination, autofluorescence, near-infrared imaging, and SD-OCT. At least 5 definite drusenoid accumulations above the RPE in more than on B-scan on SD-OCT had to be observed to be considered as having subretinal drusenoid deposits.\textsuperscript{5} The presence of basal laminar drusen was based on finding small densely packed drusen causing a starry-sky appearance by fluorescein angiography. Soft drusen were determined from color fundus photographs and confirmed by SD-OCT. Acquired vitelliform lesions were considered to be present if there were subretinal accumulations of yellow material in the macular region. Central geographic atrophy was considered present if there were confluent areas of depigmentation of the RPE larger than one fourth of disk diameter in size in which the underlying choroidal blood vessels were plainly visible. The presence of subretinal and intraretinal fluid at the initial visit and at the most recent follow-up was recorded.

Results

We evaluated 7 eyes of 6 patients with acquired vitelliform lesions and subretinal drusenoid deposits. There were 2 male and 4 female subjects with a mean age of 85 ± 7.6 years. All the patients in this study were whites. Their best-corrected visual acuity ranged from 20/20 to 20/60 (median 20/30; logMAR = 0.2) at the initial visit and did not change during a mean follow-up of 11 months. Subretinal drusenoid deposits were located above the level of the RPE, in the subretinal space, ranging in their configuration from relatively flat aggregates to conical mounds breaking through the boundary between the inner and outer segments of photoreceptors in the SD-OCT examination. Cuticular drusen were not observed in any of the cases. In addition to the subretinal drusenoid deposits, a cluster of soft drusen in the central macular region was observed in 3 eyes (Figure 1). In 1 eye, the subretinal drusenoid deposits were noted to overlie soft drusen (Figure 1).

In all eyes, the vitelliform material was clinically apparent as a yellowish lesion in the central macula in color fundus photography, hyperautofluorescent and located between the RPE layer externally and the boundary between the inner and outer segments of the photoreceptors internally (Figures 1–3), and did not change over the follow-up period. The vitelliform material was noted in the central or paracentral macula in all patients. In Figure 3, a 91-year-old patient had central and paracentral accumulations of subretinal material. Increased pigment adjacent or within the yellow material was present in all eyes in color fundus photographs, was hyperautofluorescent, and corresponded to hyperreflective areas in the near-infrared imaging noted as focal areas of thickening above the RPE band on the SD-OCT within the vitelliform lesion. Subretinal fluid and intraretinal fluid were each noted in one eye. During the mean follow-up of 11 months, none of the patients developed choroidal neovascularization or geographic atrophy within the macula.

Discussion

The present series of cases demonstrate subretinal drusenoid deposits associated with acquired
vitelliform lesions. The material had the same yellow color, autofluorescence characteristics, and location in the subretinal space as does the vitelliform material in association with cuticular drusen. Although the location of the associated drusen is different, the similarities of the deposition may suggest similarities in pathophysiology.

Cuticular drusen are located under the RPE, while the vitelliform material is above the RPE. Because of the intense autofluorescence at wavelengths similar to that used for detection of RPE lipofuscin, the composition of the yellow vitelliform material in cuticular drusen has been proposed to contain retinoids derived from shed outer segments of the photoreceptors. By analogy, the intensely autofluorescent material in association with subretinal drusenoid deposits suggests the presence of retinoids as well.

The accumulation of the material in this subretinal space causes the shared similarities in appearance, although the exact reason for the accumulation may not necessarily be the same in cuticular drusen as compared with subretinal drusenoid deposits. In cuticular drusen, subretinal fluid has been seen in some cases, which along with the presumed accumulation of outer segments, and may suggest abnormal RPE function. The simple presence of subretinal fluid has been associated with the accumulation of yellow highly autofluorescent material in a number of diseases ranging from central serous chorioretinopathy to vitelliform macular dystrophy. Accumulation of autofluorescent material because of defective phagocytosis occurs in the RCS rat. While the exact reasons for the accumulation in association with cuticular drusen is not known, it may involve the contributing factors of subretinal fluid and decreased phagocytosis. In addition to abnormalities in the RPE function, the accumulation of vitelliform material in eyes with subretinal drusenoid deposits may be related to another factor. Both SD-OCT and electron microscopic examinations have shown the deposition of material related to the subretinal drusen. This material is not autofluorescent, does not contain opsins, but does have cholesterol and cholesterol esters. The physical interposition of this material between the RPE and the outer segments may prevent proper phagocytosis of shed outer segments.
Fig. 2. A. Color fundus photograph of the right eye of a 94-year-old woman showing a large subfoveal vitelliform detachment (arrow) in association with fine subretinal drusenoid deposits. B. In the left eye, there is a much smaller amount of yellow subretinal material (arrow). C. The autofluorescence image of the right eye shows a large collection of intensely hyperautofluorescent material. D. There were many more subretinal drusenoid deposits in the left eye as compared with the right eye. Note the small hyperautofluorescent accumulations in the macula of the left eye. E. The SD-OCT shows a large accumulation of material in the subretinal space. This material has a similar gradient in intensity as sometimes seen with vitelliform material associated with cuticular drusen. F. The arrowheads highlight the subretinal drusenoid deposits. G. The subretinal vitelliform material is highlighted by the arrow.
Accumulation of shed, but not phagocytized outer segments, would lead to the formation of autofluorescent yellow material as has been described in other entities. This report has the typical weaknesses of retrospective studies and has a very small sample size. As with any study appearing to show an association, and this includes those involving cuticular drusen and vitelliform material, an observed association does not mean that there is a causal link. However, observation of multimodal imaging characteristics of these eyes does supply interesting information, and there are biologically plausible mechanisms that may explain, in part, the accumulation of subretinal material in patients with subretinal drusenoid deposits.

**Key words:** autofluorescence, cuticular drusen, reticular pseudodrusen, spectral-domain optical coherence tomography, subretinal drusenoid deposits, vitelliform macular detachment.

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