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Case Report

Reticular Pseudodrusen Voids after Rhegmatogenous Retinal Detachment

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Keywords
Reticular pseudodrusen · Drusen disappearance · Retinal detachment · Age-related macular degeneration · Dissolved drusen · Subretinal drusenoid deposits

Abstract
We present a case of reticular pseudodrusen (RPD) regression on multimodal retinal imaging following a rhegmatogenous retinal detachment. Two mechanisms of action can be postulated. The subretinal deposits dissolve due to voluminous subretinal fluid during retinal separation from the retinal pigment epithelium and are in turn mechanically cleared during retinal re-attachment surgery. Alternatively, an RPD clearance is facilitated by enhanced phagocytic activity of macrophages and microglial cells as a response to acute retinal stress.

Introduction

Reticular pseudodrusen (RPD) are typically associated with age-related macular degeneration, infrequently occurring in the absence of other retinal pathology [1]. RPD constitute accumulations of extracellular material in the subretinal space, which in advanced stages can extend into the photoreceptor layers, the outer nuclear layer, and beyond the outer limiting membrane [1–3]. RPD are dynamic structures that may spontaneously regress through reabsorption and migration within inner retinal layers [4–6]. Color fundus photography displays RPD as clustered, yellowish-white lesions in the outer macula. Enhanced RPD detection requires multimodal retinal imaging, including optical coherence tomography (OCT), scanning laser ophthalmoscopy with infrared reflectance (IR), and fundus autofluorescence (FAF) [7].

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Case Presentation

A 76-year-old man with a history of mild mitral valve insufficiency and permanent atrial fibrillation presented with a macula off rhegmatogenous retinal detachment (RRD) of 4 clock hours (1–5) in his left eye. Visual acuity at presentation was finger counting at 1 m. The RRD was treated 3 days after central vision loss with phacovitrectomy, endo photocoagulation of a superior retinal tear, and 30 percentage SF6 endo-tamponade. Bilateral RPD were evident on swept source (SS) – OCT, IR, and FAF 4 weeks after re-attachment surgery (Fig. 1a, c, d). Additionally, twelve subretinal vertical voids extending into the ellipsoid zone were visible on SS-OCT of the re-attached retina (Fig. 1a). The exact location of these voids corresponded with a relative hyperreflectivity on IR (Fig. 1c). Three months after retinal re-attachment, all of the subretinal voids on SS-OCT had disappeared, and 2 years following retinal re-attachment, nearly full disappearance was also evident on FAF. On FAF of macular areas that were not involved in the detachment, the RPD density increased inferiorly, whereas a density decrease occurred superiorly (Fig. 1d, e). Visual acuity was logMAR 0.2 at 4 weeks and logMAR 0.1 2 years after re-attachment surgery.

The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531676). IR and FAF images were obtained using the Heidelberg Spectralis HRA (Heidelberg Engineering GmbH, Heidelberg, Germany) and SS-OCT images using the Topcon DRI OCT Triton (Topcon Corp., Tokyo, Japan).

Discussion

We present a case of RPD regression on multimodal retinal imaging after the event of a RRD. We suggest that the accumulation of subretinal fluid (SRF) during the detachment contributed to this phenomenon. RPD are hydrophobic due to rich content of neutral lipids [3, 8]. Solubility of the subretinal material may nevertheless increase in the presence of voluminous SRF, over time. Dissolution of the RPD in SRF would allow for a mechanical clearance through SRF drainage during retinal re-attachment surgery. An alternative mechanism of action could be a result of the acute oxidative stress and substantial photoreceptor apoptosis induced by the RRD. These factors lead to increased activation and migration of macrophages and microglial cells [9, 10], and macrophages also infiltrate the subretinal space during RRD [11, 12]. Pro-inflammatory cytokine concentrations increase in the SRF during RRD and enhance the phagocytic ability of migrated macrophages [13]. Thus, a possible explanation of RPD regression in the detached areas is a retinal clearance mediated by activated macrophages or resident microglia and retinal pigment epithelium cells.

Drusen that are located beneath the retinal pigment epithelium have also been reported to regress after RRD [14]. As migrating macrophages infiltrate the injured area from the choroid and through Bruch's membrane [11, 12], the proposed mechanism of a phagocytic clearance would also apply to this scenario.

The theory of RRD-mediated RPD regression is supported by the observation that the voids occurred in the formerly detached macular areas, in contrast to minor morphologic changes observed in the non-detached areas, and their shape resembling the conical stage 3 RPD (Fig. 1). Additionally, several voids on cross-sectional OCT co-localized with fading target aspects on IR images, a key characteristic of RDP. It is, however, a possibility that spontaneous regression occurred [5, 6]. SRF blebs are frequently observed after re-attachment surgery for RRD and were present 1 month after re-attachment in our case (Fig. 1a) [15]. The SRF blebs could have merged with the RPD voids, and may, in theory, have been confused with RPD

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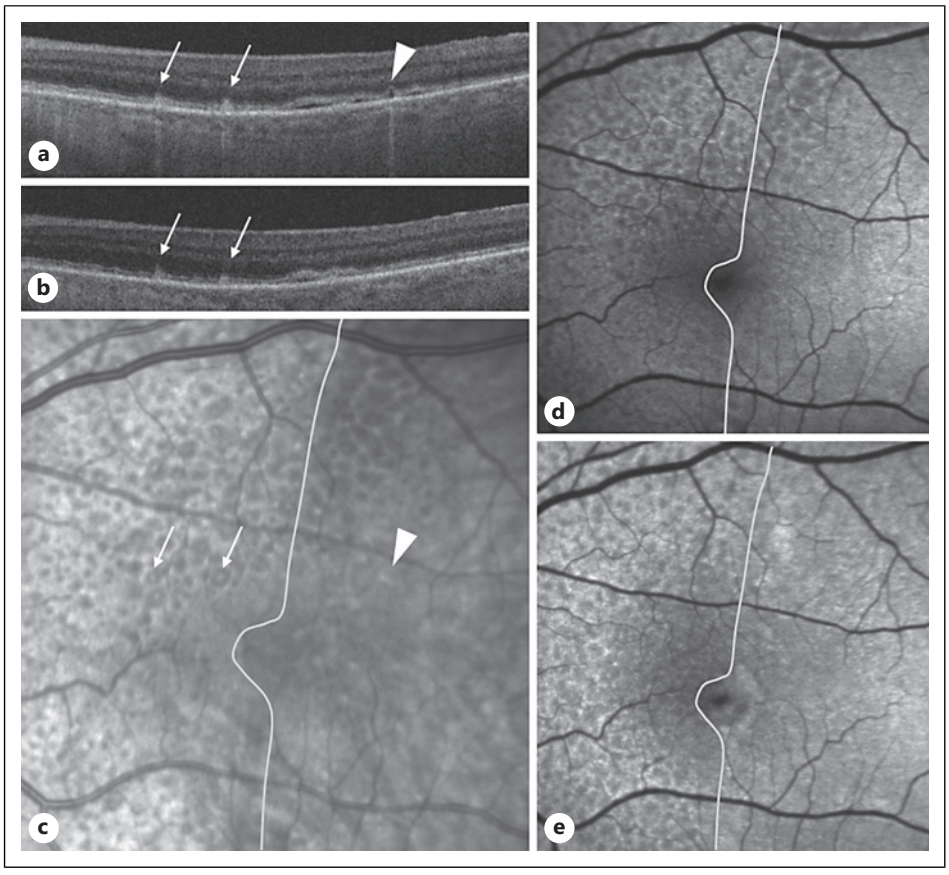

Fig. 1. a SS OCT cross-sectional scan 1 month after retinal re-attachment. Arrows represent RPD with conical hyperreflectivity penetrating the EZ in attached retina. The arrow head shows a subretinal vertical void resembling the shape of a RPD in the re-attached retina. **b** Same area scanned 3 months after re-attachment. The arrows point to the same RPD as in image (**a**). The subretinal vertical void seen in image (**a**) is absent. **c** IR 1 month after re-attachment. Line represents the border between attached to the right and re-attached retina to the left. Arrows represent the same RPD in the attached retina as in images (**a**, **b**). Typical target-like appearance of RPD with an isoreflective core surrounded by a hyporeflective halo. Arrow head represents the site of a presumed clearance of RPD in the re-attached retina. The previous core of the RPD presents as relative hyperreflectivity, and the previously hyporeflective halo blends in with the relative hyporeflective re-attached retina. **d** FAF 1 month after re-attachment reveals hypofluorescent reticular pseudodrusen, mainly in the superior macula, affecting attached and re-attached retina. **e** FAF 2 years after re-attachment. In the re-attached retina the RPD have nearly completely regressed. In the non-detached retina the RPD density is reduced in the superior macula and increased in the inferior macula. EZ, ellipsoid zone.

voids. We suppose the two entities can be differentiated by their relation to the retinal layers, where the SRF blebs do not extent beyond the ellipsoid zone, in contrast to the RPD voids that do so. Additionally, the SRF blebs persisted up to 6 months, compared to only 1 month regarding the RPD voids. A limitation to the case report is the lack of pre RRD images.

This case illustrates a proposed RRD mediated clearance of RPD. Further research is necessary to verify our findings and its potential therapeutic implications.

Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images. The patient has signed a written informed consent for participation in a prospective observational study on RRD adhering to the Declaration of Helsinki, approved by the Regional Committee for Medical and Health Research Ethics, South-East Norway (2017/730) and registered in ClinicalTrials.gov (NCT03187613).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

V.A.F. and V.M.T. contributed equally to the drafting of the manuscript and follow-up of the patient.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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