Reticular pseudodrusen: a tale of two species?

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Abstract

Introduction The anatomic localization of reticular pseudodrusen (RPD) has been an important area of research study.

Methods A multimodal imaging analysis was conducted of two patients who were classified as having presumed RPD.

Results Analysis of case 1 lends credence to original histopathologic evidence suggesting a choroidal origin of RPD, and analysis of case 2 supports RPD as originating above the RPE.

Conclusion This case series demonstrates that RPD may represent a compilation of diseases rather than one distinct clinical entity.

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Introduction

Reticular pseudodrusen (RPD), originally described as ‘les pseudodrusen bleus’ due to their enhanced visibility using blue light,¹ refer to a yellowish interlacing macular pattern distinguished from true drusen by their characteristic fundus appearance and their initial distribution in the superior macula sparing the fovea. RPD have been associated with conferring a heightened risk of progression in age-related macular degeneration.²

Since its initial description, multiple studies have focused on further characterizing RPD. Unlike true drusen, which have been well characterized as focal depositions between the RPE basal lamina and the inner collagenous layer of Bruch’s membrane, RPD have evaded precise localization. Despite the advent of newer imaging techniques, the quandary remains

unsettled, and the myriad shifts in nomenclature have perhaps served as an intrinsic barometer of this.

After initial clinical descriptions, RPD were considered to originate below the RPE-like typical drusen, and in fact were termed ‘reticular drusen’ in the Wisconsin age-related maculopathy grading system.³ Arnold *et al.*² subsequently performed the first histopathologic study of an eye with the clinical diagnosis of RPD and noted loss of middle choroidal small vessels and increased spacing of choroidal veins. They postulated that RPD originated as choroidal disease, perhaps by loss of choroidal vessels being accompanied by fibrous replacement of the choroidal stroma in a reticular pattern.² The advent of spectral-domain OCT (SD-OCT) clearly demonstrated hyperreflective material above the RPE, leading Zweifel *et al.*⁴ to coin the term ‘subretinal drusenoid deposits.’ They proposed an elaborate grading scheme based on SD-OCT, with stage 1 characterized as diffuse deposition of granular hyperreflective material between the RPE and IS/OS boundary, stage 2 with mounds of accumulated material sufficient to alter the contour of the IS/OS boundary, and stage 3 with thicker material breaking through the IS/OS boundary.

Notably absent from these grading schemes was any specific sub-RPE alterations associated with RPD, in sharp contrast to initial histopathologic suggestions of a choroidal origin of RPD, perhaps further accentuating the conundrum of RPD’s origin. More recently, a study of ICGA and EDI SD-OCT characterized choroidal changes of RPD by demonstrating reticular ICGA patterns correlating with OCT subretinal deposits and also demonstrated a thinner choroid associated with RPD.⁵ We report the multimodal imaging of two cases that would have been classified as RPD but each case was different from the other and thus try to show that this rubric might actually be used for a compilation of diseases.

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Case reports

Case 1

A 68-year-old woman presented to our retina clinic for evaluation of a suspicious choroidal nevus. Visual

acuity were 20/20 in the right and 20/25 in the left, and anterior segment examination was unremarkable except for PCIOL in the right and 2+ nuclear sclerosis in the left. Posterior segment examination revealed optic disc drusen in both eyes and a choroidal nevus in her left eye.

Figure 1 (a) Fundus photo right eye demonstrating no evidence of reticular pseudodrusen or true drusen. (b) SD-OCT demonstrating no evidence of reticular pseudodrusen, with notable absence of any granular hyperreflective material between the RPE and IS/OS boundary or any IS/OS junction alterations. (c) ICGA (Late) demonstrating a reticular hyperfluorescent pattern consistent with reticular pseudodrusen.

Figure 2 (a) Fundus photo right eye demonstrating an yellowish interlacing pattern more prominent in the superior macula and predominantly sparing the fovea. (b) SD-OCT demonstrating an undulating pattern of OS/IS junction with intact RPE. (c) ICGA (Late) demonstrating absence of reticular hyperfluorescent pattern.

Fundus examination revealed no evidence of true macular drusen or reticular pseudodrusen (Figure 1a). SD-OCT similarly showed no evidence of RPD, with notable absence of diffuse granular hyperreflective material between the RPE and IS/OS boundary or any IS/OS junction alterations (Figure 1b). ICGA demonstrated a reticular hyperfluorescent pattern, consistent with previous descriptions of RPD (Figure 1c). This is the first case to the authors' knowledge demonstrating isolated involvement of RPD on ICGA, without any involvement noted on fundus examination or SD-OCT.

Case 2

A 73-year-old woman presented to our retina clinic for evaluation of age-related macular degeneration. Visual acuities were 20/60 in the right and 20/30 in the left. Anterior segment examination was unremarkable except for 2+ nuclear sclerosis cataract in the right and 1+ nuclear sclerosis cataract in the left. Posterior segment examination revealed extensive RPD in both eyes as well as basal laminar drusen (Figure 2a). SD-OCT demonstrated undulating appearance of the OS/IS junction (Figure 2b). ICGA demonstrated no reticular pattern (Figure 2c). This case demonstrated clinically obvious RPD with OCT findings most consistent with Stage 2 RPD according to Zweifel *et al*'s⁴ recently proposed classification.

Discussion

These two cases representing presumed RPD clearly demonstrated very different properties by imaging. In reviewing the images, the fundus photos are unremarkable in case 1, and demonstrate extensive RPD in case 2. The OCT is unremarkable in case 1, but demonstrates extensive OS/IS junction undulation in case 2. The ICG very clearly demonstrates a reticular pattern in case 1, but is unremarkable in case 2. Although RPD are evident in each clinical case, the fundus photos, OCT findings, and ICG findings are each very different.

Case 1 represents the first case to the authors' knowledge demonstrating isolated involvement of RPD on ICGA, without any involvement noted on fundus examination or SD-OCT. Case 2 is more typical of cases described as stage 2 RPD in Zweifel's recently proposed classification.⁴ Case 1 may lend credence to original histopathologic evidence suggesting a choroidal origin of RPD,² and case 2 may support RPD as originating above the RPE.

Taken together, these cases may uphold a previous report suggesting that RPD is a dynamic entity, with preferential involvement at different depths in the retina and choroid.⁶ However, the imaging properties of RPD in each of these cases are so different that we need to consider the possibility that these are in fact two separate entities. What is currently known as RPD may actually represent an umbrella term for at least two separate entities with two separate anatomic origins. Appropriate diagnosis of which type of RPD may require a multimodal imaging approach as evidenced by this case series.

Clearly, further studies are necessary to characterize RPD. This remains an elusive clinical entity of uncertain origin with a broad spectrum of clinical and imaging characteristics. An improved understanding of RPD and its pathophysiology may illuminate mechanisms leading to its association with accelerated progression to advanced AMD.

Summary

What was known before

- Controversy exists about the precise anatomic localization of RPD.

What this study adds

- Multimodal imaging analysis in this case series demonstrates that RPD may actually represent a compilation of diseases.

Conflict of interest

The authors declare no conflict of interest.

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