

Drusenoid retinal pigment epithelium detachments

Descolamento do epitélio pigmentar da retina tipo drusenóide

Miguel Hage Amaro¹, Mario Martins dos Santos Motta², Jorge Mitre³, João Jorge Nassaralla Junior⁴, Angelo Leite⁵, Teruo Aihara⁶

ABSTRACT

The authors make a review of drusenoid retinal pigment epithelium detachments (DPEDs), a form of retinal pigment epithelium detachment (PED) that evolves from confluent and large soft drusen. Drusenoid retinal pigment epithelial detachments are a recognized element of the “dry” AMD. Until now, no treatment is indicated in drusenoid PEDs. The authors describe the clinical characteristics of drusenoid retinal pigment epithelium detachments (DPEDs) and make a review of the DPEDs related in the international literature. We related in this revision paper the multimodal advanced image exams in two cases of drusenoid retinal pigment epithelium detachments (DPEDs) and the general characteristics of this finding associated with Dry Macular degeneration. Upon examination of the ocular fundus DPEDs emerge as well-circumscribed yellow or yellow–white elevations of the RPE that are usually found within the macula. They may show scalloped borders and a slightly irregular surface. When visualized using fluorescein angiography (FA), DPEDs are typically described as faint hyper-fluorescent in the early phase followed by a slow increase in fluorescence throughout the transit stage of the study without late leakage. With optical coherence tomography (OCT), drusenoid PEDs usually show a smooth contour of the detached hyperreflective RPE band that may have an undulating appearance. Drusenoid PEDs encompass far above the ground possibility type of “dry” AMD that develops in relationship with large confluent soft drusen. At this point no treatment is utilized in drusenoid retinal pigment epithelium detachment (DPEDs).

Keywords: Macular degeneration; Retinal detachment; Retinal drusen; Fluorescein angiography ; fundus oculi; Aged; Age factors

RESUMO

Os autores fazem uma revisão do descolamento do epitélio pigmentar tipo drusenóide e apresentam dois casos desta patologia associada à degeneração macular relacionada à idade descrevendo seus achados em avançados exames com imagem da retina. Neste artigo de revisão da literatura sobre os achados característicos do descolamento do epitélio pigmentar tipo drusenóide e sua evolução descrevemos os achados de dois casos associados à degeneração macular relacionada à idade, forma seca, utilizando exames como SD-OCT, fundus autofluorescência e angiografia com indocianina verde, além de retinografia colorida e fluoresceínica. O descolamento do epitélio pigmentar tipo drusenóide evolui a partir de drusas moles confluentes presentes na degeneração macular relacionada à idade e é também associado a outras doenças retinianas. Até este momento não há tratamento para esta forma da doença.

Descritores: Degeneração macular; Descolamento retiniano; Drusas retinianas; Angiofluoresceinografia; Fundo de olho; Idoso; Fatores etários

¹ Instituto de Olhos e Laser de Belém, Belém, PA, Brazil.

² Universidade do Rio de Janeiro, RJ, Brazil.

³ Faculdade de Medicina do ABC, Santo André, SP, Brazil.

⁴ Instituto de Olhos de Goiânia, Goiânia, GO, Brazil.

⁵ Clínica CEOFT, Belém, PA, Brazil.

⁶ Hospital da Irmandade da Santa Casa de Misericórdia de São Paulo, São Paulo, SP, Brazil.

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INTRODUCTION

A retinal pigment epithelial detachment (PED) is the separation of the retinal pigment epithelium (RPE) from Bruch's membrane^{1,2}.

Age-related macular degeneration (AMD) is a frequently associated^{1,2}. Drusenoid retinal pigment epithelial detachment (DPED) is the form of PED that evolves from confluent and large soft drusen²⁻⁴. In particular, drusenoid retinal pigment epithelial detachments (DPEDs) are a recognized element of the "dry" AMD.

Other types of PED observed in AMD are serous, vascularized, or mixed categories²⁻⁴. Furthermore, it is not unusual to see more than one type of PED in AMD²⁻⁵. In addition, Drusenoid PEDs encompass far above the ground possibility type of "dry" AMD that develops in relationship with large confluent soft drusen.

Drusenoid PEDs may also occur in other retinal disorders including: cuticular drusen^{6,7}, the maculopathy associated with Type II membranoproliferative capillary glomerulonephritis^{8,9}, choroidal nevi¹⁰ and mallealeventinese.¹¹

In a prospective study¹², a total of 311 eyes (from 255 participants) with DPEDs were followed for a median of 8 years subsequent to the initial detection of a DPEDs. Of the 282 eyes that did not show advanced AMD at baseline, 119 eyes (42%) developed advanced AMD within 5 years, with 19% progressing to central geographic atrophy (CGA) and 23% progressing to neovascular age-related macular degeneration (NV-AMD). In the eyes that did not develop advanced AMD, progressive changes occurred in the fundus, including the development of calcified drusen and pigmentary changes. In addition, 40% of all eyes showed decreases in visual acuity by >5 letters at 5-years follow-up; overall, mean visual acuity decreased from 76 letters (20/30) baseline to 61 letters (20/60) over 5 years. Five-year decreases in mean visual acuity averaged 26 letters for eyes progressing to advanced AMD and 8 letters for non-progressing eyes.

In a retrospective study¹³ evaluated the likelihood of progression to advanced AMD form in 61 eyes with drusenoid PEDs with a mean follow-up of 4.6 years. The outcomes fell into one of three categories: persistent drusenoid PED (38%), the development of geographic atrophy (49%), or the development of choroidal neovascularization (CNV) (13%). At 10 years, visual outcomes were poor, with progression to geographic atrophy in 75% of eyes and to CNV in 25% of eyes. The authors also noted IDPED size >2 disk diameters (DD) and the presence of metamorphopsia upon presentation were associated with an increased likelihood of progression to highly developed AMD.

It is not rare to detect the presence of a compartment of subretinal fluid in DPEDs, in the absence of CNV; in such cases a analysis with advanced multimodal imaging, such as indocyanine green angiography (ICGA) can be used to exclude CNV^{5,14}.

Acquired vitelliform lesions is any times a finding in DPEDs⁵. According any reports, the vitelliform lesions were related with various forms of AMD, including: subretinal drusenoid deposits¹⁵, cuticular drusen¹⁶, large drusen^{16,17} and non neovascular AMD¹⁶. Researchers putted that RPE gradual dysfunction was the mechanism for the development of subretinal fluid or vitelliform lesions in the avascular DPEDs^{3-5,17-19}.

Upon examination of the ocular fundus the researchers

describe¹⁻⁵ that DPEDs emerge as well-circumscribed yellow or yellow-white elevations of the RPE that are usually found within the macula. They may show scalloped borders and a slightly irregular surface. The presence of a speckled or stellate pattern of brown or gray surface pigmentation on their surface is typical. They are often surrounded by large soft drusen and may be undistinguishable from a solitary large drusen in eyes with confluent drusen.

The age-related eye disease study defined a large drusen as measuring 125 μm or greater and a drusenoid PED as measuring 350 μm or greater¹².

When visualized using fluorescein angiography (FA), DPEDs are typically described as faint hyperfluorescent in the early phase followed by a slow increase in fluorescence through out the transit stage of the study without late leakage⁵. Focal hypofluorescence is often due to the blocking effect of overlying pigment hyperplasia, where as focal hyperfluorescence typically represents window defects caused by RPE atrophy³⁻⁵. Authors³⁻⁵ stated that the interpretation of FA findings for DPEDs may be challenging because it is difficult to distinguish characteristic angiographic patterns from those seen with vascularized PEDs although the latter exhibits more intense late staining or obvious leakage. Comparison of FA findings with spectral domain – optical coherence tomography (SD-OCT) and ICGA^{5,15} analyses may help differentiate drusenoid from vascularized PEDs. With ICGA using a confocal scanning laser ophthalmoscope (SLO) system, the content of the drusenoid PED will block the fluorescence emitted from the underlying choroidal vasculature and, therefore, the PED will appear as an homogeneous hypofluorescent lesion during the early phase and remain hypofluorescent through out the transit^{5,20,21}. When ICGA is used with a traditional fundus camera-based system, the DPED may appear isofluorescent or slightly hypofluorescent through out the sequence. Discrepancies may exist in findings obtained using fundus camera-based ICGA versus the confocal SLO-based ICGA because the absorption, diffraction, polarization, and scatter of light are different in the two systems^{5,20,21}. One of the primary differences relates to the confocal aperture of the SLO system that blocks the scattered light and allows transmission only of the images from the focused planes^{5,20,21}. With either system, there is absence of a hyperfluorescent hot spot or plaque at the border or within the drusenoid PED, which helps to rule out the presence of associated CNV^{5,20,21}.

Drusenoid PEDs may exhibit decreased fundus autofluorescence (FAF) but they are isofluorescent or hyperautofluorescent^{5,22}. In some cases, the degree of FAF may represent different stages of progression toward atrophy of the elevated RPE⁵. Drusenoid PEDs often show a slight, evenly distributed increase in the FAF signal surrounded by a well-defined, hypofluorescent halo delineating the entire border of the lesion^{5,22-24}. In some cases, areas of increased FAF can be observed overlying or adjacent to drusenoid PEDs these correspond to focal hyperpigmentation or pigment clumping that can be observed via color photography and funduscopic examination^{5,22-24}. This finding may correspond to pigment hyperplasia or RPE cells or macrophages containing lipofuscin or melanin lipofuscin that have migrated into the retina or subretinal space⁵. In some eyes with drusenoid PEDs, it is unclear whether the FAF signal originates from the RPE itself, the material beneath the RPE, or associated vitelliform material in the subretinal space above the PED^{5,21-23}. The spontaneous flattening of drusenoid PEDs can be associated with RPE atrophy and decreased autofluorescence at the former site of the PED^{5,22-24}.

FAF is a useful indicator of the health of the RPE and may help predict those PEDs evolving toward atrophy⁵. In the conventional and enhanced depth imaging optical coherence tomography⁵ drusenoid PEDs usually show a smooth contour of the detached hyperreflective RPE band that may have an rolling appearance. Pigment clumping lying immediately a top the drusenoid PED is not uncommon and will demonstrate hyperreflective signals with SD-OCT with posterior shadowing⁵.

Drusenoid PEDs are typically not associated with overlying subretinal or intraretinal fluid⁵. A retrospective series¹³ found that the presence of subretinal or intraretinal fluid and the increase in material hyporeflectivity under the PED were associated with CNV. However, the presence of a hyporeflective area between the neurosensory retina and the elevated RPE line with SD-OCT does not necessarily mean that there is an associated CNV^{5,13}. Instead, this signal may result from a small pocket of benign subretinal fluid or an acquired vitelliform lesion⁵. If the presentation of the drusenoid PED is typical, with the SD-OCT showing homogeneous hyperreflective content of the PED without intraretinal fluid, it is unlikely that ICGA will show CNV. However, if the content of the drusenoid PED appears heterogeneous or increasingly hyporeflective on SD-OCT during the follow-up, or if there is evidence of significant subretinal or intraretinal fluid, then it may be helpful to perform ICGA to rule out the presence of CNV⁵.

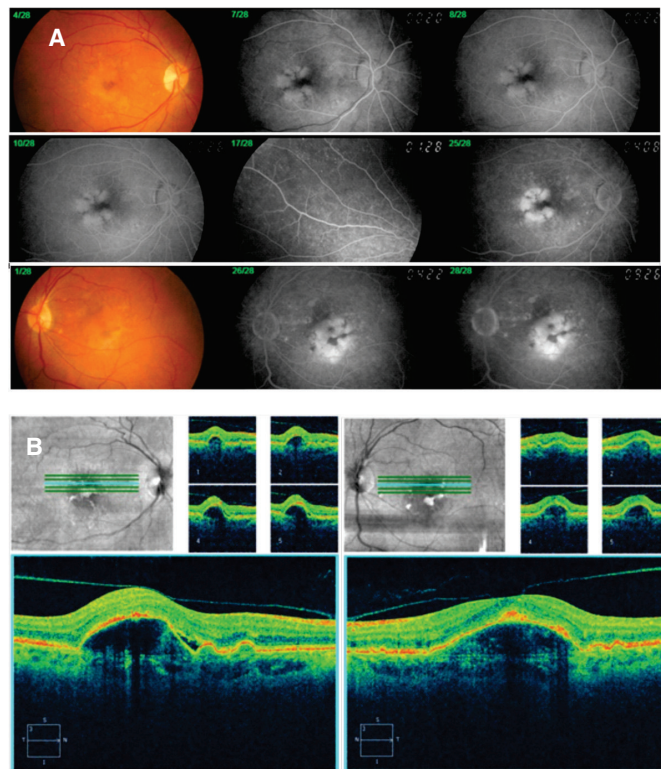


Figure 1: (A) The color photograph shows a yellow macular lesion surrounded by multiple soft drusen in both eyes and elevated in right eye. The FA shows early hyperfluorescence and late staining (B) The SD-OCT shows a DPED with a pocket of associated subretinal fluid.

In some eyes, soft drusen may become confluent, forming RPE detachments in the absence of CNV⁵. It is hypothesized that progressive accumulation of lipids within Bruch membrane over time may cause it to become increasingly hydrophobic^{5,25,26}. An increasingly stressed RPE pump is unable to adequately move

fluid and debris across Bruch membrane, leading to accumulation of fluid and debris in the sub-RPE space and enlargement of drusen^{5,26}. Authors²⁶ analyzed a series of clinical and clinicopathological cases with drusen and found that “the larger and more fluid the soft drusen has become, the finer the particles into which the original amorphous hard drusen material is found to have disintegrated and the more rapidly the drusen develop and fade, more often leading to geographic atrophy than choroidal neovascularization. The conclusions of researchers^{25,26} in this clinicopathological analysis suggests that the larger size and more fluidic content of DPEDs may both be predictors of their evolution toward RPE atrophy.

Until now, no treatment is indicated in drusenoid PEDs.

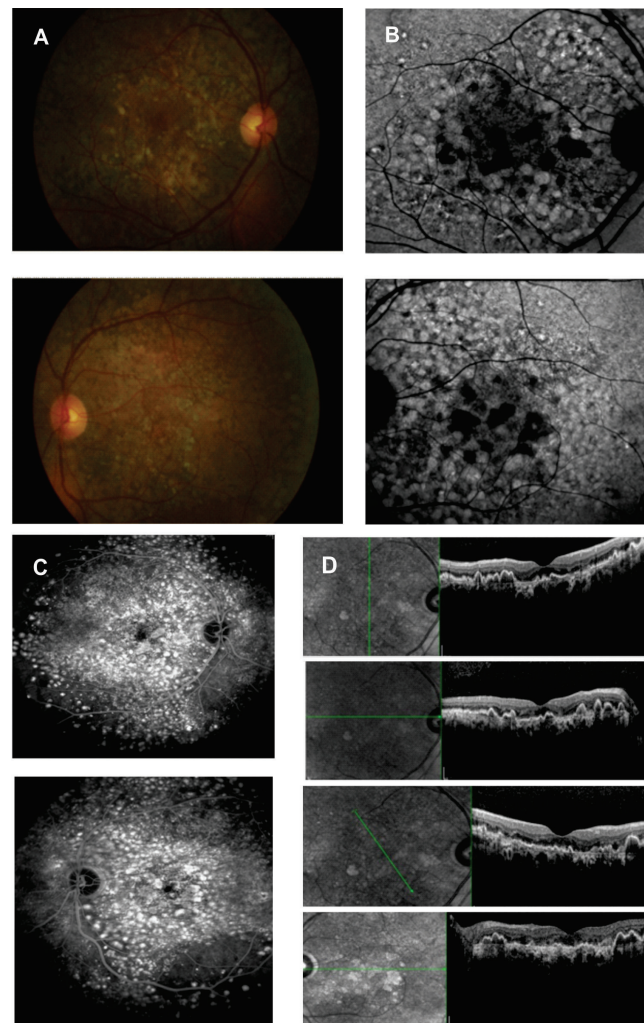


Figure 2: (A) Color photograph shows multiple and confluent drusen in both eyes. (B) FAF shows hyperautofluorescence and hypoautofluorescence consistent with soft drusen and early focal atrophy. (C) FA shows late multiple hyperfluorescence drusen in both eyes. (D) SD-OCT shows multiple DPEDs in both eyes.

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Corresponding author:

Miguel Hage Amaro

Address: Trav: Quintino Bocaiúva, 516 - Bairro Reduto - Belém - Pará - Brazil - CEP.: 66053-249

E-mail: miguelhamaro@yahoo.com.br