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Subretinal fluid overlying a drusenoid pigment epithelial detachment in an eye with dry age-related macular degeneration

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Introduction

Age-related macular degeneration (AMD) is the fourth leading cause of irreversible blindness worldwide.[1] The condition is more prevalent in European and North American populations than in some other populations.[2] The prevalence of AMD is increasing in the aging population and is estimated to grow from 196 million people worldwide in 2020 to 288 million by 2040.[3] AMD is a multifactorial disease increasing the risk of functional disability.[4] The disease can be classified into two general subtypes: dry (non-neovascular) AMD, characterized by the late development of geographic atrophy of the retinal pigment epithelium (RPE) and outer retinal layers, and wet (neovascular) AMD, characterized by the formation of new vessels invading the subretinal space. The presence of subretinal fluid (SRF) has been correlated to a diagnosis of wet AMD; however, SRF has also rarely been associated with dry AMD.[5] We report the case of a patient with dry AMD, who had a drusenoid PED in one eye with overlying SRF but no identifiable macular neovascularization (MNV).

Case Report

A 68-year-old pseudophakic female with a family history of AMD presented with a large drusenoid PED in the left eye. Best-corrected visual acuity (BCVA) was 20/32 in both eyes. The anterior segment was normal, and dilated fundus examination showed evidence of confluent drusen and a large subfoveal serous PED but no heme or exudate. Intraocular pressures were normal. Optical coherence tomography (OCT) demonstrated soft drusen

and a small drusenoid PED without fluid or hemorrhage in the right eye (Figure 1). OCT of the left eye demonstrated a larger drusenoid PED with a small pocket of overlying SRF and some subretinal hyperreflective material (SHRM), but no hemorrhage or intraretinal fluid (Figure 2a).

The right eye was diagnosed with dry AMD, and wet AMD was initially suspected in the left eye. The patient declined further imaging and treatment. Observation was recommended.

Over the following six months, the BCVA remained stable in both eyes with no heme or exudates noted on ophthalmoscopy. The OCT of the right eye remained unchanged, while the left eye showed no change in the PED but an increase in the overlying SRF (Figure 2b). Further observation was elected.

Twelve months after presentation, BCVA and clinical findings remained stable in both eyes. OCT of the left eye showed decreased height of the drusenoid PED and increased SRF (Figure 2c). The patient consented to fluorescein angiography (FA) but was unable to complete the imaging due to marked light sensitivity. Available images did not demonstrate clear evidence of MNV. OCT angiography was not available.

Three years after presentation, the BCVA and clinical findings remained stable. OCT findings in the left eye showed a continued decrease in the drusenoid PED height with minimal overlying SRF (Figure 2e). Observation was recommended.

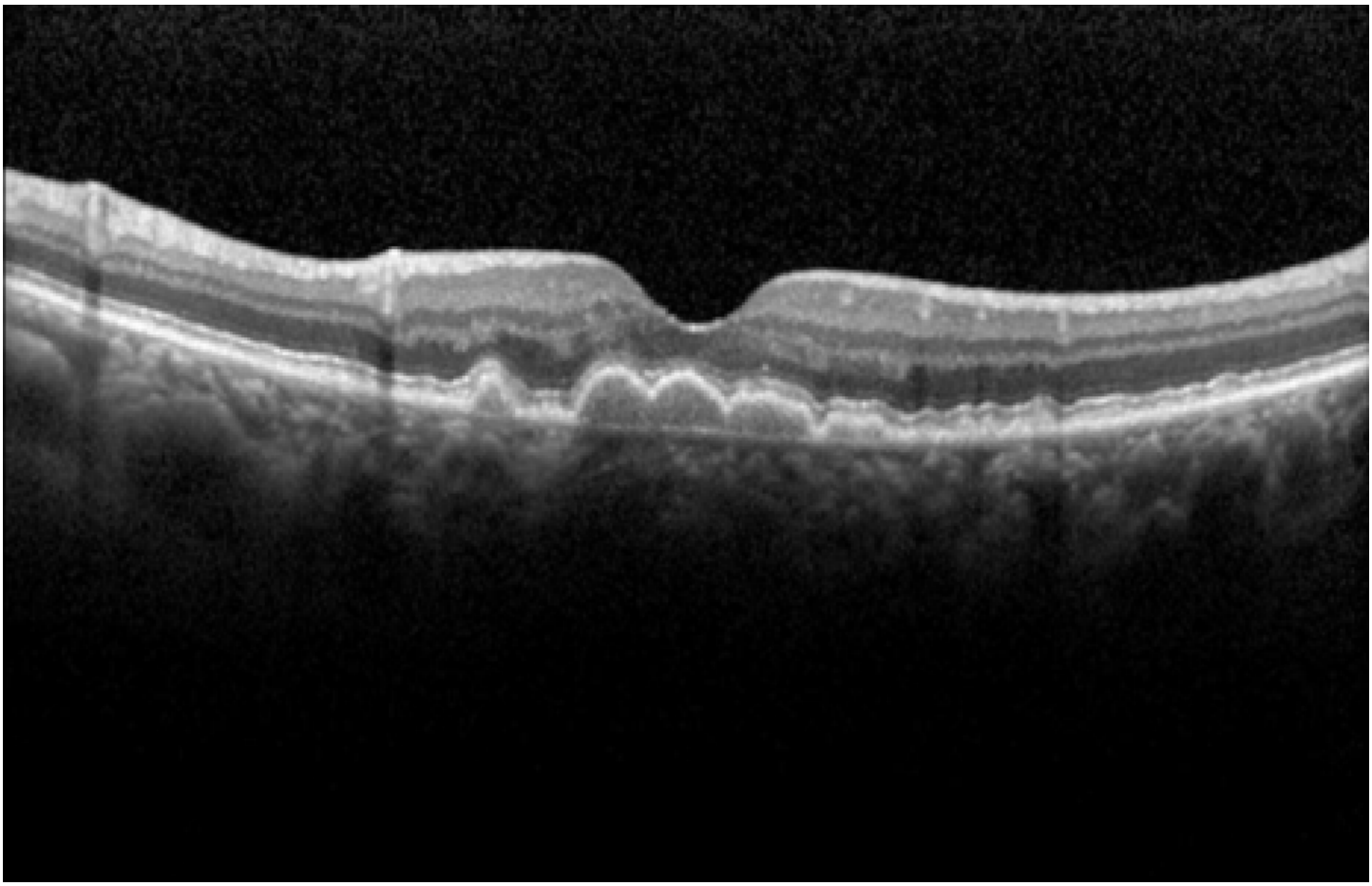

Figure 1. Multiple drusen and a low-lying pigment epithelial detachment without fluid or hemorrhage was present in the right eye.

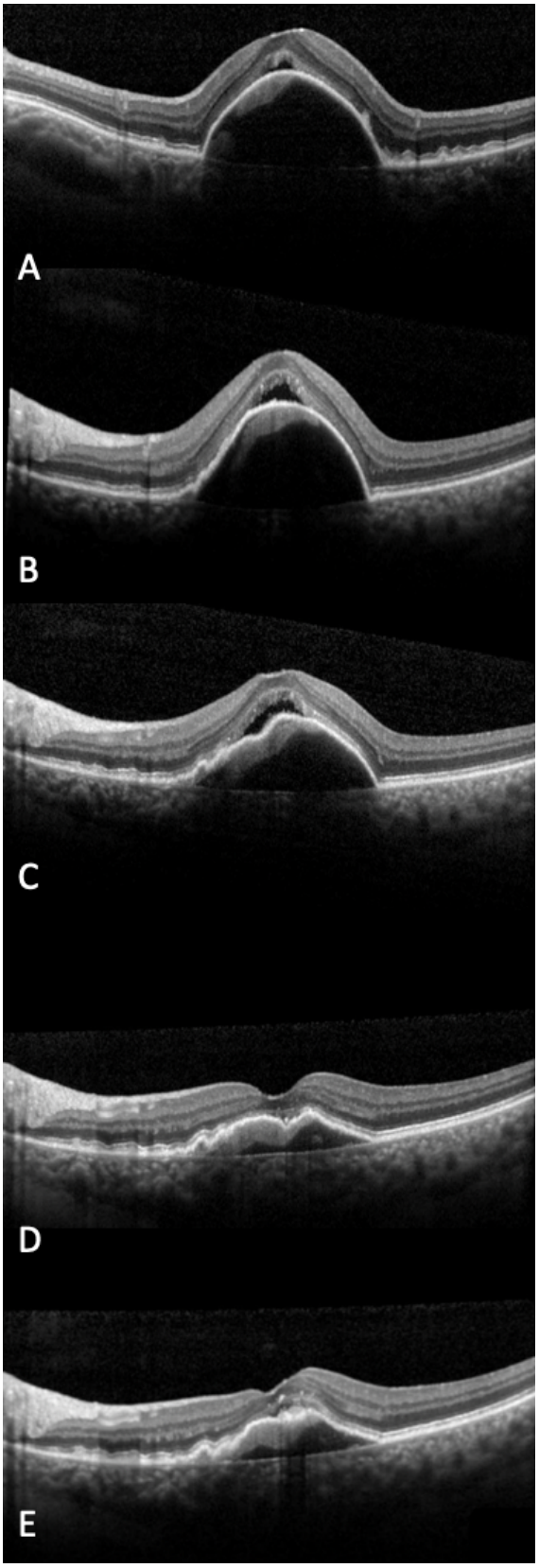

Figure 2. Serial spectral-domain optical coherence tomography images of the left eye demonstrating the longitudinal evolution of a drusenoid pigment epithelial detachment. A. At presentation, a large drusenoid pigment epithelial detachment was observed with overlying subretinal fluid and focal subretinal hyperreflective material. B. Six months after presentation, increased subretinal fluid was noted overlying a relatively stable drusenoid pigment epithelial detachment. C. Twelve months after presentation, the pigment epithelial detachment has decreased in size, with a concomitant increase in overlying subretinal fluid. D. Two years after presentation, continued flattening of the drusenoid pigment epithelial detachment was evident, with minimal residual subretinal fluid. E. Three years after presentation, optical coherence tomography demonstrated remodeling of the outer retinal layers surrounding the pigment epithelial detachment.

Discussion

The diagnosis of neovascular AMD is based on the identification of MNV. Macular neovascularization is classified into three subtypes according to its anatomical location. Type 1 neovascularization consists of vessels originating from the choriocapillaris that proliferate into the sub–RPE space. Type 2 neovascularization also arises from the choriocapillaris but penetrates the RPE and extends into the subretinal space. Type 3 neovascularization, also known as retinal angiomatous proliferation, originates from the deep retinal capillary plexus and progresses toward the outer retina, eventually breaching Bruch membrane in the advanced stages and leading to RPE detachment and secondary MNV.[6] One of the hallmark clinical signs suggestive of MNV is the presence of SRF, detectable on fundoscopic examination or OCT.[5] Fluorescein angiography may help identify occult or Type 1 MNV as either fibrovascular PEDs with ill-defined areas of irregular elevation that may stain with "stipples" of hyperfluorescence or as late leakage of undetermined source with poorly demarcated areas of leakage, which appear at the level of the RPE in the late phase. Angiography may also demonstrate classic or Type 2 MNV as well-demarcated areas of intense hyperfluorescence on early frames that show progressive leakage. Type 3 MNV may appear as a focal area of hyperfluorescence on FA.[7] OCT angiography (OCTA) is a non-invasive technology that uses motion contrast to create a three-dimensional analysis of the retinal and choroidal vasculature and can be segmented to view each of the retinal vascular plexuses individually to detect MNV.[8]

This case highlights the uncommon finding of SRF in an eye with a drusenoid PED, which can prompt the initiation of unnecessary anti-VEGF therapy. Our patient did not have clinical evidence of MNV with long-term

clinical stability observed over several years. In untreated wet AMD, persistent SRF would generally be expected to show progression over time, or be accompanied by additional exudative or hemorrhagic signs. The absence of such progression in this patient further reinforced that the SRF was not secondary to active MNV but rather associated with the underlying drusenoid PED in the setting of dry AMD. The presence of SRF in eyes with dry AMD has been previously reported by various authors, proposing different mechanisms for its origin.[5,6,9] Potential mechanisms for the development of SRF in eyes with dry AMD include mechanical strain on the outer retinal layers resulting in fluid from coalescent drusen[5,9] or the formation of an avascular but serous PED.[10] In a prospective case series of 12 eyes with intermediate dry AMD with SRF but no MNV, only one eye developed MNV during a 36-month period after the identification of SRF.[11] Another retrospective series of 45 eyes with dry AMD reported 27 eyes with SRF but no MNV. Of these 27 eyes, 57.8% also had large drusenoid PEDs that eventually collapsed and became atrophic.[5] This sequence, initial RPE thickening followed by atrophy, has been considered a primary mechanism leading to SRF in such eyes. The atrophy breaks the barrier between the neurosensory retina and the underlying choroid, facilitating the accumulation of SRF.[11] Another proposed mechanism suggests that age-related dysfunction of the RPE may impair the clearance of photoreceptor outer segments and reabsorption of SRF. This dysfunction can lead to the accumulation of vitelliform material and fluid in the subretinal space even before RPE cell death occurs,[12] further explaining the observation of SRF in eyes with dry AMD.

Conclusion

This case highlights the importance of distinguishing between dry and wet AMD prior to initiating anti-VEGF therapy. Accurate determination of the etiology of SRF is critical for appropriate classification and management. In this patient, prolonged observation over several years without significant progression or development of MNV supported a diagnosis of dry AMD. Careful longitudinal follow-up and, when available, multimodal imaging can help avoid misclassification and unnecessary treatment.

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Statement of Ethics

This case series adheres to patient confidentiality and ethical principles in accordance with the guidelines of the Declaration of Helsinki and relevant local regulations. Consent was obtained from the patient for the publication of this case report.

Conflict of Interest Statement

Authors declare no conflicts of interest related to this topic.

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