Case Reports in Ophthalmology

Case Rep Ophthalmol 2023;14:48–55
DOI: 10.1159/000528834
Received: September 24, 2022
Accepted: December 16, 2022
Published online: February 14, 2023

Case Report

The Development of Suspended Scattering Particles in Motion in a Patient with Exudative Reticular Pseudodrusen

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Keywords

Suspended scattering particles in motion · Exudative reticular pseudodrusen · Multimodal imaging · Optical coherence tomography angiography · Pseudoflow

Abstract

The development and characteristics of suspended scattering particles in motion (SSPiMs) in a patient with exudative reticular pseudodrusen (ERPD) are reported using multimodal imaging modalities. An 82-year-old woman was referred because of persistent macular edema during intravitreal injections of bevacizumab. ERPD associated with types I and II (mixed type) macular neovascularization in both eyes was diagnosed. Bilateral flat irregular pigment epithelial detachments were associated with macular neovascularization in both eyes by optical coherence tomography. An intense oval hypersignal was found at umbo in her right eye, as detected by *en face* optical coherence tomography angiography. This avascular hypersignal at umbo was SSPiM. No change was noticed in the appearance of SSPiM after intravitreal injection of aflibercept. However, intraretinal hemorrhage developed in Henle's fiber layer a month after the second intravitreal injection of aflibercept. Then, several SSPiMs were unveiled in a perifoveal location a month after uncomplicated cataract surgery. The SSPiMs that developed after cataract surgery were connected to the capillaries in the deep retinal vascular plexus. Temporary SSPiMs could be seen during injections of anti-vascular endothelial growth factor and after cataract surgery in the same eye of a patient with ERPD. SSPiMs detected by optical coherence tomography angiography were neither artifacts nor hypersignals due to neovascularized vessels. SSPiMs were considered to be a unique phase colloidal phenomenon generating pseudoflow in exudative macular disorders.

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Introduction

Reticular pseudodrusen (RPD), also known as subretinal drusenoid deposits (SDD), are considered to belong to a unique subgroup of age-related macular degeneration (AMD) [1, 2]. Reticular macular disease, pseudodrusen, and reticular drusen are also used to describe this disease. Optical coherence tomography (OCT) analysis of the eyes can disclose that pseudodrusen are located between the retinal pigment epithelium (RPE) and the ellipsoid zone [3]. The histopathology of pseudodrusen or SDD indicates that they are composed of membranous debris, unesterified cholesterol, and complement [2].

A strong association was found between RPD and late AMD [2]. In fellow eyes of participants in the Comparison of Age-related Macular Degeneration Treatments Trials, dot pseudodrusen were associated with neovascular AMD, whereas confluent pseudodrusen were associated with geographic atrophy [4]. Thus, RPD is an independent risk factor for disease progression leading to visual impairment [2]. Remarkable changes in RPD have been seen in the choroid layer [5, 6]. The presence of RPD in patients with AMD is an indicator of poor choroidal perfusion or choroidal ischemia and carries a high risk of development of choroidal neovascularization in 66% of patients [5]. The formation of SDD in patients with RPD may be related to dysfunction of active bidirectional transport mechanism moving cholesterol and polyunsaturated fatty acids from the RPE to the Müller cells and inner segments [2].

Optical coherence tomography angiography (OCTA) is a non-invasive dye-less imaging technique, which acquires volumetric OCT B-scans that reveal segmentation of the chorioretinal layers and analyzes the decorrelation signal between sequential scans [7]. In addition to its unique advantages, the limitations of OCTA include inability to disclose leakage, limited field of view, and artifacts (blinks, movement, and vessel ghosting) [7]. Suspended scattering particles in motion (SSPiM) is a new OCTA non-projection imaging artifact created by the extravascular motion signal of the particulate matter, which may occur in certain retinal diseases, including diabetic retinopathy, retinal vein occlusion, and neovascular AMD [8]. Recently, we suggested that the altered lipoprotein turnover in subretinal space during the healing period after intravitreal injection of aflibercept might have provoked the enhancement of SSPiM in Henle's fiber layer (HFL) and the subretinal space in a patient with exudative cuticular drusen [9]. The avascular ovoid hypersignals appearing at HFL and the subfoveal space during the acute phase of the healing period could be considered as pseudoflow [8, 9]. Meticulous interpretation of the results of OCTA for patients with exudative AMD during follow-up is crucial to the differential diagnosis because the hypersignals generated could be indicative of neovascularization, artifact, or SSPiM.

A case of bilateral exudative RPD (ERPD) in a woman who developed SSPiM during follow-up in one eye is presented here. Consensus-based clinical case reporting guideline was enclosed as a supplementary file (CARE checklist) of our manuscript.

Case Report

A retired high school teacher was referred because of reduced vision in her left eye in 2012. She did not have a previous health issue, other than some memory difficulties. She was previously a heavy smoker for more than 3 decades. Her sister and brother had AMD. She was diagnosed as exudative AMD in her left eye and atrophic AMD in her right eye by clinical examination and OCT. Four intravitreal injections of bevacizumab (IVB) were given in the left eye. The data were assessed solely by the author.

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At the initial presentation, her right eye was dry, but exudative changes in the macula developed 2 years later in 2014. OCT disclosed the double-layer sign and hyporeflective cysts inferiorly in the left eye (not shown). Three injections of IVB were given in her right eye, then she discontinued her treatment for social and financial reasons. Another ophthalmologist at a different hospital gave her six injections of IVB in her right eye until 2016. Timolol/brinzolamide eye drops (twice daily) were initiated in her right eye as she developed unilateral glaucoma. As her ophthalmologist told her that her vision in her right eye had deteriorated because of macular edema, she was referred again. Her visual acuity was 20/40 in the right eye and 20/200 in the left eye. Fundus recording (Kowa VX-20; Kowa Company Ltd., Japan) disclosed macular edema and geographic atrophy at the inferior macula and multiple paramacular SDDs extending superior to the retina in the right eye (Fig. 1a). Reticular-type fundus autofluorescence was observed (Fig. 1b). OCT (RTVue XR Avanti; Optovue, Inc., Fremont, CA, USA) revealed an oval-shaped semi-reflective lesion at umbo, hyperreflective lesions at the outer plexiform layer, double-layer sign, subretinal hyporeflective cavities, and SDDs at the macular/paramacular regions (Fig. 1c). OCTA (AngioVue RTVue XR Avanti; Optovue, Inc., Fremont, CA, USA) showed a hyperflow signal (Fig. 1d, e). This signal was located at HFL, as shown by cross-sectional 3-mm OCTA (Fig. 1d). On the same day, fundus fluorescein angiography (FA) in the right eye showed diffuse macular hyperfluorescence in late phase due to leakage of macular neovascularization (Fig. 1f). No hyperfluorescence at umbo in the right macula was observed during the venous phase of FA (Fig. 1f), which cannot disclose the SSPiM observed during OCTA (Fig. 1d, e). The appearance of SSPiMs after the first intravitreal injection of aflibercept (IVA) did not change (not shown). However, intraretinal hemorrhage developed in the HFL, causing her visual acuity to decrease to 20/200 1 month after the second injection of IVA (Fig. 2a). Because of intraretinal hemorrhage at the fovea, blocked hypofluorescence was noticed by FA (Fig. 2b). OCT revealed increased macular thickness due to intraretinal hemorrhage and edema, an oval-shaped semi-reflective lesion at umbo, exudative macular detachment, double-layer sign, and intra/subretinal hyporeflective cavities (Fig. 2c). However, *en face* and cross-sectional 3-mm OCTA showed a diminished hyperflow signal at umbo (Fig. 2d). Six IVA injections were given in her right eye. Because of a developing cataract, uncomplicated phaco + intra-ocular lens implantation was performed in 2018 in the right eye. SSPiMs appeared 1 month after uncomplicated cataract surgery in a perifoveal location as noted by *en face* and cross-sectional 3-mm and 2-mm OCTA (Fig. 3a, b), respectively. Figure 3c is an inverted *en face* OCTA image of Figure 3b. The SSPiMs were connected to the capillaries in deep retinal vascular plexus (Fig. 3b, c). The mid-venous phase of FA showed window defects due to RPE atrophy and perimacular hypofluorescence (Fig. 3d). Extensive punctate paramacular hyperfluorescence and perifoveal petaloid hyperfluorescence and striation were prominent at the late phase of FA (Fig. 3e). The period between the appearance and disappearance of hypersignals was around 6 months for SSPiMs (Fig. 3f). The patient was followed for 4 more years. At her final visit in August 2022, the final visual acuities were 20/400 in the right eye and 20/200 in the left eye.

Discussion

Pseudodrusen are best visible in blue- and red-free light during fundus photography but do not show hyperfluorescence on FA [2, 4]. Infrared reflectance of SDD is hyporeflective [2]. Hypoautofluorescence of SDD might be caused by light scattering [2]. During FA, SDD colocalizes choroidal filling defects [2]. The appearance of hypofluorescence on SDD at the middle and late phases of indocyanine green angiography is a common finding [6]. OCT is crucial for the definitive diagnosis and staging of RPD [2]. Recently, the field of adaptive optics,

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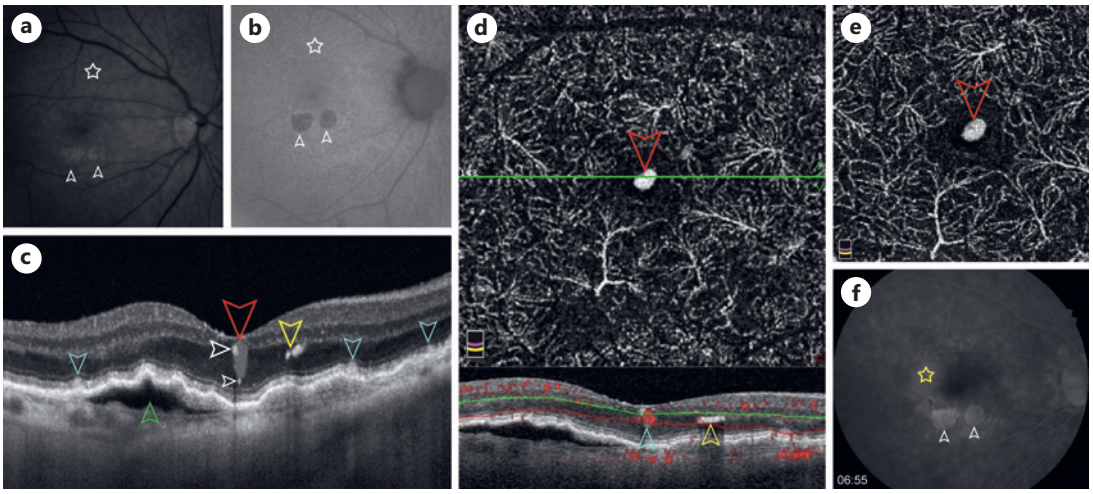

Fig. 1. Red-free fundus photograph (**a**) discloses RPE atrophic areas at the inferior macular region (white arrowheads), disrupted macular reflex, and reticular appearance (white star) at the paramacular and superior vascular arcade region of the retina in the right eye. Atrophic areas (white arrowheads) and reticular pattern (white star) are more prominent during autofluorescence (**b**). OCT (**c**) demonstrates a semi-reflective, oval-sharp lesion (red arrowhead) at umbo in the right eye. Two hyperreflective dots can be seen around the oval lesion (white arrowheads). Two more hyperreflective exudates are seen at HFL (yellow arrowhead). SDD are marked with blue stars. The double-layer sign is seen with serous fluid accumulation (green arrowhead) and irregularities above Bruch's membrane. The choroid is thin. A 3-mm *en face* OCTA deep capillary plexus slab (**d**) reveals an intense avascular hypersignal at umbo, indicating SSPiM (red arrowhead). Cross-sectional OCTA (**d**) shows that the intense hypersignal (blue arrowhead) is confined to the semi-reflective lesion at umbo. The hyperreflective hard exudates (yellow arrowhead) give almost no hypersignal (**d**). *En face* OCTA of a 2-mm deep capillary plexus slab (**e**) illustrates an intense hypersignal at umbo (red arrowhead) and well-preserved vortex pattern perifoveally. Late venous phase of the FA (**f**) shows window defects due to RPE atrophy (white arrowheads) and hyperfluorescence due to leakage of macular neovascularization (yellow star). In (**f**), no leakage at umbo in the right eye was seen during FA, which cannot reveal the SSPiM observed during OCTA in (**d**, **e**). FA, fluorescein angiography; HFL, Henle's fiber layer; OCT, optical coherence tomography; OCTA, optical coherence tomography angiography; RPE, retinal pigment epithelium; SDD, subretinal drusenoid deposits; SSPiM, suspended scattering particles in motion.

ultra-wide-field imaging, and OCTA retinal imaging techniques have improved our understanding of the nature and pathophysiology of RPD, as extensively reviewed by Spaide et al. [2].

In our patient, SSPiMs appeared in the same eye on two distinct occasions and at separate locations that were not reported previously (Fig. 1d, e; Fig. 3a, b, respectively). Initially, the presentation of SSPiMs was noticed during follow-up of ERPD under anti-VEGF treatment. However, the latter SSPiMs were seen 1 month after cataract surgery, which is the first report in the ophthalmic literature of SSPiMs noticed on two distinct occasions in the same eye. The topographic locations of SSPiMs were also different; the first one was at umbo, and the second was at the perifoveal location. Segmentation of OCTA showed that initial SSPiMs were in HFL at umbo (Fig. 1d), and the latter SSPiMs were in the deep capillary plexus in HFL (Fig. 3a, b). We noticed that the SSPiMs found at umbo during IVB treatment were not linked to any foveal capillaries (Fig. 1d, e); however, all perifoveal SSPiMs that developed after cataract surgery were connected to terminated vortex capillaries in the intermediate and deep capillary plexuses (Fig. 3b, c). Those capillaries were visualized flowing into dead space, representing SSPiM by OCTA (Fig. 3b, c). In addition, the late venous phase of FA disclosed petaloid perifoveal hyperfluorescence, indicating leakage after cataract surgery (Fig. 3e). OCTA

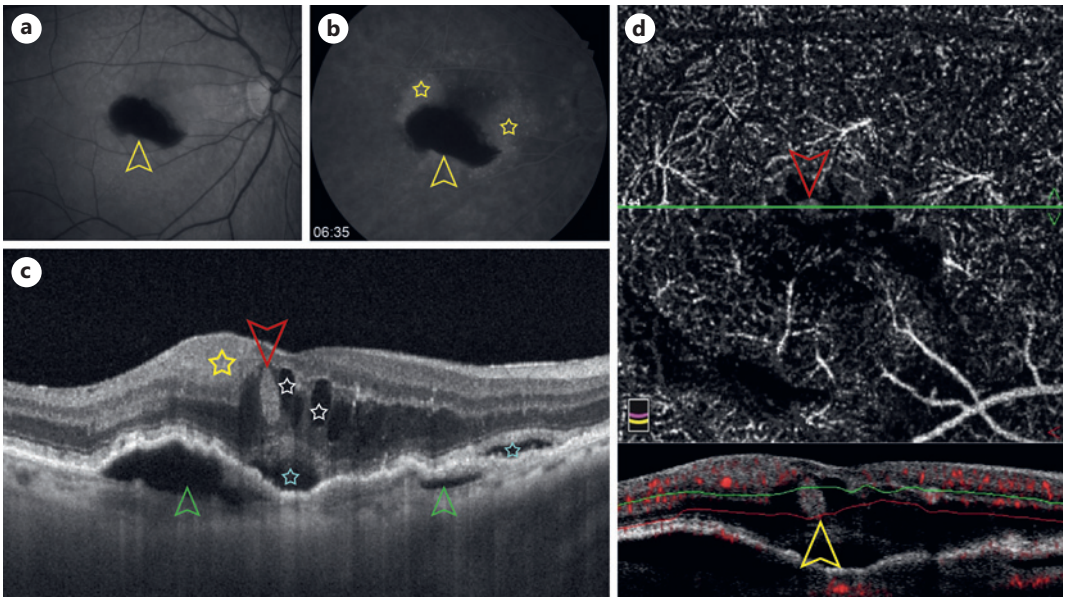

Fig. 2. A red-free fundus photograph (**a**) discloses a sharply demarcated HFL intraretinal hemorrhage (yellow arrowhead) at the macula in the right eye. Late venous phase of FA (**b**) shows blocked hypofluorescence (yellow arrowhead) at the macula and paramacular hyperfluorescence in the right eye (yellow stars). Punctate hyperfluorescence is also noticeable. OCT (**c**) discloses increased macular thickness due to HFL intraretinal hemorrhage (yellow star) and edema, an oval-shaped semi-reflective lesion at umbo (red arrowhead), exudative macular detachment/subretinal fluid (blue stars), intraretinal hyporeflective cysts (white stars), double-layer sign, and serous RPE detachments (green arrowheads). A 3-mm *en face* OCTA deep capillary plexus slab (**d**) reveals weak avascular hypersignal at umbo (red arrowhead). The perifoveal vortex pattern is disrupted because of intraretinal hemorrhage (**d**). The cross-sectional OCTA (**d**) shows a weak hypersignal (yellow arrowhead) in the oval-shaped lesion. FA, fluorescein angiography; HFL, Henle's fiber layer; OCT, optical coherence tomography; OCTA, optical coherence tomography angiography; RPE, retinal pigment epithelium.

showed that the appearance of SSPiMs was also petaloid (Fig. 3a–c), resembling cystoid macular edema (CME) after cataract surgery (Irvine-Gass syndrome). This is the first report of the petaloid appearance of SSPiMs after cataract surgery in the medical literature. We observed that the period between the appearance and resolution of both SSPiMs was 6 months in our patient with ERPD. The temporal change regarding the half-life of the SSPiMs has not been reported elsewhere.

Tso [10] reported that large extracellular spaces in the outer plexiform and inner nuclear layers (CME) in experimental (rhesus monkeys) talc retinopathy were reminiscent of Irvine-Gass syndrome and consistent with microinfarction of the retinal vessels due to talc microemboli. We could not find any disturbances in the circulation by OCTA indicating microemboli in the superficial, intermediate, and deep retinal capillary plexuses. The anatomic differences in macular circulation between human and monkey (cynomolgus macaques) eyes might explain this contradiction [11]. By OCTA, the retinal vessel densities in the superficial and deep layers of the fovea of healthy humans were found to be much higher than in monkeys [11].

Our study did not yield sufficient evidence as to why we observed different results on fluorescein staining in our patient between the SSPiM during anti-VEGF treatment and SSPiMs after cataract surgery. Furthermore, we could not exclude the possibility that segmentation artifacts led to misinterpretation of the connectivity between terminated vortex capillaries and SSPiMs or vice versa.

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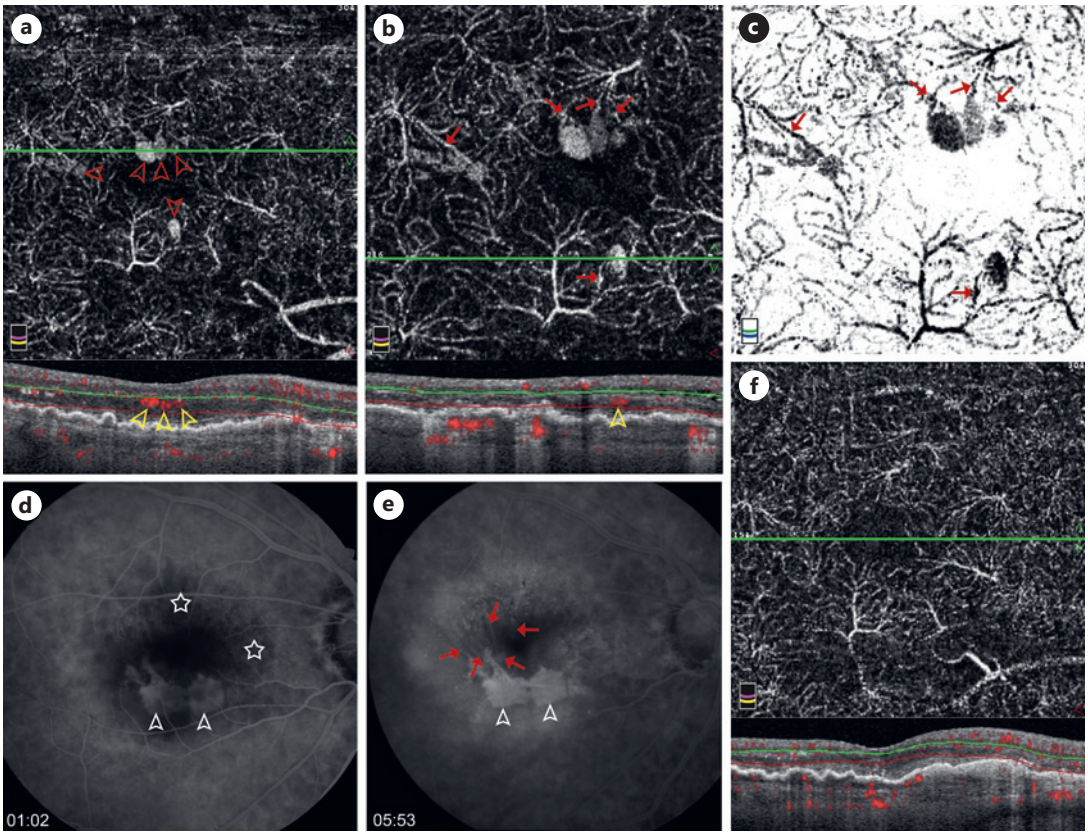

Fig. 3. A 3-mm *en face* OCTA deep capillary plexus slab (**a**) discloses several SSPiMs (red arrowheads) 1 month after cataract surgery at the perifoveal location in the right eye. The cross-sectional OCTA shows an intense discrete hypersignal (yellow arrowheads) (**a**). *En face* OCTA of a 2-mm deep capillary plexus slab (**b**) illustrates several SSPiMs perifoveally and a well-preserved vortex pattern. The SSPiMs are connected to the capillaries in the deep retinal vascular plexus (red arrows) (**b**). The cross-sectional OCTA (**b**) shows a hypersignal (yellow arrowhead) representing SSPiM at the oval-shaped lesion. **c** An inverted *en face* OCTA image of (**b**). The SSPiMs are connected to the capillaries in the deep retinal vascular plexus (red arrows) (**c**). Mid-venous phase of FA (**d**) shows window defects due to RPE atrophy (white arrowheads) and perimacular hypofluorescence (white stars). Late venous phase of FA (**e**) shows extensive paramacular hyperfluorescence, indicating leakage. Punctate hyperfluorescence and RPE atrophic areas (white arrowheads) are noticeable (**e**). Petaloid hyperfluorescence and striation (red arrows) are prominent perifoveally (**e**). Six months later, a 3-mm *en face* OCTA deep capillary plexus slab and the cross-sectional OCTA (**f**) showed that all perifoveal SSPiMs had disappeared. FA, fluorescein angiography; OCTA, optical coherence tomography angiography; RPE, retinal pigment epithelium; SSPiM, suspended scattering particles in motion.

Recently, SSPiMs have been reported in various exudative maculopathies, as revealed by OCTA [8]. SSPiMs were an extravascular hypersignal located at the edge or border of a vascular plexus at an avascular-vascular junction [8]. In our case, however, the initial presentation of SSPiMs during IVB treatment was not located at the edge or border of the vascular plexus (Fig. 1d, e), whereas the SSPiMs seen after cataract surgery manifested at the border of the vascular plexus at an avascular-vascular junction (Fig. 3a–c). Kashani et al. [8] stated that lipid aggregates, a key component of the suspended particles in SSPiMs, could generate hypersignals that are frequently located in the HFL rather than the inner nuclear layer. In a recent report, however, we indicated that the avascular hypersignals in the HFL and the subfoveal space could be attributed to altered lipoprotein turnover in a patient with exudative

cuticular drusen during anti-VEGF treatment [9]. Several investigators have pointed out that RPE is a polarized/bidirectional secretor of lipoproteins [2, 12]. Thus, in our patient with ERPD, lipoprotein turnover in the neural retina during the healing period after injection of IVB and after cataract surgery might have induced the development of SSPiMs in the HFL.

Conclusion

In conclusion, the SSPiMs detected by OCTA were not artifacts or hypersignals due to neovascularized vessels. They were a unique phase colloidal phenomenon generating pseudoflow and occurring during certain exudative diseases of the macula, including ERPD. The perifoveal vascular occurrence of SSPiMs after cataract surgery and the subclinical implications remain to be explored.

Acknowledgments

This manuscript does not include any non-author contributors to acknowledge.

Statement of Ethics

This study protocol was reviewed, and the need for approval was waived by the Bahçeşehir University School of Medicine Ethical Committee (approved on April 9, 2021), Istanbul. Written and signed informed consent was given by the patient to publish her case report, including the publication of images.

Conflict of Interest Statement

The author has no conflicts of interest to declare.

Funding Sources

The author did not receive any financial support from any public or private sources.

Author Contributions

Yusuf Durlu carried out the examination, interventions, and follow-up of the patient and wrote and reviewed the manuscript.

Data Availability Statement

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

References

1 Mimoun G, Soubrane G, Coscas G. Les drusen maculae's [Macular drusen]. J Fr Ophtalmol. 1990;13(10):511–30.

Case Rep Ophthalmol 2023;14:48–55
DOI: 10.1159/000528834

2 Spaide RF, Ooto S, Curcio CA. Subretinal drusenoid deposits AKA pseudodrusen. Surv Ophthalmol. 2018;63(6):782–815.
3 Zweifel SA, Spaide RF, Curcio CA, Malek G, Imamura Y. Reticular pseudodrusen are subretinal drusenoid deposits. Ophthalmology. 2010;117(2):303–12.e1.
4 Zhou Q, Daniel E, Maguire MG, Grunwald JE, Martin ER, Martin DF, et al. Pseudodrusen and incidence of late age-related macular degeneration in fellow eyes in the comparison of age-related macular degeneration treatments trials. Ophthalmology. 2016;123(7):1530–40.
5 Arnold JJ, Sarks SH, Killingsworth MC, Sarks JP. Reticular pseudodrusen. A risk factor in age-related maculopathy. Retina. 1995;15(3):183–91.
6 Querques G, Querques L, Forte R, Massamba N, Coscas F, Souied EH. Choroidal changes associated with reticular pseudodrusen. Invest Ophthalmol Vis Sci. 2012;53(3):1258–63.
7 de Carlo TE, Romano A, Waheed NK, Duker JS. A review of optical coherence tomography angiography (OCTA). Int J Retina Vitreous. 2015;151:5.
8 Kashani AH, Green KM, Kwon J, Chu Z, Zhang Q, Wang RK, et al. Suspended scattering particles in motion: a novel feature of OCT angiography in exudative maculopathies. Ophthalmol Retina. 2018;2(7):694–702.
9 Durlu YK. Response to treatment with anti-vascular endothelial growth factors in bilateral exudative cuticular drusen. Am J Ophthalmol Case Rep. 2021;22:10110.
10 Tso MO. Pathology of cystoid macular edema. Ophthalmology. 1982;89(8):902–15.
11 Peng J, Zhong L, Ma L, Jin J, Zheng Y, Jin C. Comparison of vascular parameters between normal cynomolgus macaques and healthy humans by optical coherence tomography angiography. BMC Ophthalmol. 2019;19(1):204.
12 Curcio CA, Messinger JD, Sloan KR, McGwin G, Medeiros NE, Spaide RF. Subretinal drusenoid deposits in non-neovascular age-related macular degeneration: morphology, prevalence, topography and biogenesis model. Retina. 2013;33(2):265–76.