Case Report

Non-Neovascular Pachychoroid Disease Mimicking Exudative Age-Related Macular Degeneration

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Abstract

Purpose: To describe a case of pachychoroid disease most compatible with central serous chorioretinopathy (CSC) presented with a large relapsing retinal pigment epithelial detachment (PED) associated with only a small amount of subretinal fluid (SRF) in the background of macular drusen in an elderly patient mimicking neovascular age-related macular degeneration (AMD).

Methods: This was a review of 32 months of the clinical course and findings on multimodal imaging including fundus photography, optical coherence tomography, fundus fluorescein angiography (FFA), indocyanine green angiography (ICGA), and optical coherence tomography angiography (OCTA).

Results: A large relapsing PED sometimes with small amount of SRF at its apex was found in the background of macular drusen in the right eye of a 63-year-old Thai woman. The relapses of the PED showed an apparent association with recent steroid exposure. Multimodal imaging demonstrated the characteristics of pachychoroid diseases with pachyvessels and choroidal hyperpermeability. The PED and SRF responded well to anti-vascular endothelial growth factor (anti-VEGF) therapy, especially aflibercept, but could also be spontaneously resolved without anti-VEGF. No evidence of choroidal neovascularization or polyps could be identified by serial FFA, ICGA, and OCTA even when the retinal pigment epithelium was completely flat with no obscuration by PED.

Conclusions: A large PED with little SRF could present signs of CSC. This clinical presentation could be confused with neovascular AMD, and multimodal retinal imaging was crucial to guide correct diagnosis and management.

Keywords: Age-related macular degeneration, Anti-vascular endothelial growth factors, Central serous chorioretinopathy, Pachychoroid, Pigment epithelial detachment

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INTRODUCTION

The pachychoroid disease spectrum (PDS) is a group of retinocchoroidal disorders that share common distinctive choroidal findings identified with multimodal retinal imaging. These choroidal characteristics include focal or diffuse choroidal thickening associated with dilated Haller’s layer vessels (termed “pachyvessels”) with thinning of the overlying inner choroid and choroidal hyperpermeability on indocyanine green angiography (ICGA). The PDS includes pachychoroid pigment epitheliopathy, central serous chorioretinopathy (CSC), pachychoroid neovasculopathy, polypoidal choroidal vasculopathy, focal choroidal excavation, and peripapillary pachychoroid syndrome.¹⁴

Retinal pigment epithelial detachment (PED) is a common finding not only in neovascular age-related macular degeneration (AMD) but also in PDS such as CSC. Sometimes,

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it could be difficult to confidently differentiate between vascularized and non-vascularized PED, especially in elderly patients with large serous PED associated with minimal subretinal fluid (SRF) in the background of macular drusen. Such patients were often assumed to have occult Type 1 neovascularization (NV) not detected by fundus angiography. We reported a unique case of relapsing non-vascularized large serous PED with minimal SRF as a presenting sign of CSC as opposed to neovascular AMD, confirmed by optical coherence tomography angiography (OCTA), fundus fluorescein angiography (FFA), and ICGA. This clinical presentation could be spontaneously resolved without anti-vascular endothelial growth factor (anti-VEGF) therapy.

CASE REPORT

A 63-year-old Thai female presented with blurry vision affecting the right eye for 1 month. Informed consent to use images for academic publication was obtained from the patient. Her underlying diseases included hypertension, dyslipidemia, and chronic bilateral sacroiliac joint pain. She had received 20 mg of triamcinolone injections into both of her sacroiliac joints twice at 4 months and 17 days before her visual symptom. Visual acuity was 20/50 in the right and 20/40 in the left eyes. Anterior segment examination was significant for mild-to-moderate nuclear sclerosis in both eyes. Fundus examination revealed multiple bilateral small to intermediate drusen in the temporal macula and along vascular arcades. A large serous PED of 4-disc diameter in size without hemorrhage was found in the right macula [Figure 1]. There appeared to be an adjacent small serous PED at the inferotemporal aspect of the large serous PED which coalesced into a single large serous PED during follow-up. Optical coherence tomography (OCT) (Spectralis®; Heidelberg, Germany) confirmed the presence of the large serous PED with a small pocket of SRF at the apex of the serous PED. Enhanced-depth imaging-OCT revealed dilated outer choroidal vessels with attenuation of inner choroid beneath the serous PED. Subfoveal choroidal thickness was 322 µm.

FFA (Spectralis®) showed hyperfluorescence pooling of the serous PED and some leakage into the SRF at the apex of the serous PED [Figure 2]. ICGA (Spectralis®) showed choroidal hyperpermeability surrounding the serous PED without any evidence of choroidal neovascularization (CNV) or polyps seen [Figure 3].

The patient was, however, treated with 1.25 mg of intravitreal bevacizumab injection, but the serous PED and SRF persisted. The treatment was then switched to 2 mg of intravitreal aflibercept injection twice monthly. The serous PED and SRF were dramatically resolved, and her vision improved to 20/30 [Figure 4]. The subfoveal choroidal thickness was 294 µm. Two months after the last aflibercept injection, a shallow serous PED recurred, and the patient was reevaluated. FFA and ICGA did not reveal any signs of CNV or polyps despite the fact that the obscuration by the shallow PED was minimal [Figure 5]. Nevertheless, due to the well

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**Figure 1:** Multimodal imaging of the right eye at the first presentation. (a) Infrared reflectance and optical coherence tomography (OCT) of the macula and (b) fundus photograph show a large pigment epithelial detachment (PED) at the macula with surrounding small and intermediate drusen. There was a small satellite PED which coalesced into a single large PED 6 days later. (c) Enhanced-depth imaging OCT scan through the foveal center shows a large PED with serous subretinal fluid at its apex.

**Figure 2:** Fluorescein angiography of the right eye shows pooling hyperfluorescence of the pigment epithelial detachment (PED). Hyperfluorescence was more intense at the inferotemporal area and gradually diffused through the residual area of the PED. There was some late dye leakage into subretinal fluid in the area of foveal avascular zone.
Kaseewat and Phasukkijwatana: Large relapsing pigment epithelial detachment in pachychoroid disease

Figure 3: Indocyanine green angiography (ICGA) of the right eye shows hypocyanscence blockage of the pigment epithelial detachment (PED). There was choroidal hyperpermeability surrounding the PED in the mid to the late phase of the ICGA. No evidence of choroidal neovascularization was identified.

responsiveness to aflibercept, the patient was treated again with 2 mg of aflibercept injection which resulted in a complete resolution of the serous PED 1 month later. OCTA (RTVue, Optovue, Fremont, California) was performed at this time when there was no PED, and it confirmed the absence of any abnormal choroidal neovascular membrane [Figure 6].

The disease had been in quiescence for 3 months before she reported blurry vision of her right eye again with a history of 8 mg of intravenous dexamethasone injection 7 days before presentation. The visual acuity was 20/40, and OCT showed a recurrence of the large serous PED with shallow SRF on the top [Figure 7]. She was observed for 1 month without improvement and was then treated with intravitreal aflibercept. The PED and SRF again completely disappeared 1 month after the treatment, and her vision was back to 20/25. Four months after the last intravitreal injection, a shallow PED recurred but this time was spontaneously resolved with observation. At the last follow-up visit (22 months after the last intravitreal injection), her vision remained stable, and OCT showed pachychoroid without further recurrences of PED or SRF [Figure 7].

DISCUSSION

We reported a unique case of a diagnosis dilemma of neovascular AMD versus a non-neovascular pachychoroid disease. With the clinical presentation of a large serous PED and SRF in a background of macular drusen in an elderly woman, neovascular AMD was high in the differential diagnosis. FFA and ICGA were performed to confirm the diagnosis, but no evidence of Type 1 NV or polyps could be identified. However, on FFA, it might be difficult to identify occult Type 1 NV in the presence of a large serous PED due to obscuration by fluorescein leakage and pooling of the PED itself. On ICGA, with less dye leakage compared with FFA, it could also be difficult to identify a tiny plaque of CNV, especially in the presence of hypocyanscence serous PED. A therapeutic trial with intravitreal anti-VEGF was performed with good clinical response, making the diagnosis of neovascular AMD even more likely. In this patient, on the other hand, there were also clinical characteristics of PDS, namely dilated large Haller’s layer vessels (pachyvessels) underlying the serous PED and choroidal hyperpermeability in the mid to the late phase of ICGA, which were not features of typical AMD. Interestingly, after anti-VEGF injections, the serous PED was completely flattened, and no irregularities of the retinal pigment epithelial (RPE) layer suspicious of occult Type 1 NV were identified. FFA and ICGA at this time when there was no obscuration by the serous PED did not reveal any evidence of Type 1 NV or polyps. OCTA also confirmed the absence of any Type 1 NV, leading to the diagnosis of a non-neovascular disease in PDS. The fellow eye also demonstrated dilated large Haller’s layer vessels and choroidal hyperpermeability consistent with the pachychoroid phenotype [Figure 8] which is typically bilateral.

PDS comprises several diseases that share common features of focal or diffuse choroidal thickening, pachyvessels with attenuation of the inner choroid, and choroidal hyperpermeability. The spectrum includes pachychoroid pigment epitheliopathy, CSC, pachychoroid neovasculopathy, polypoidal choroidal vasculopathy, focal choroidal excavation, and peripapillary pachychoroid syndrome. A case of relapsing
Our patient was, however, most likely compatible with CSC but with atypical presentation of serous PED more prominent than SRF. The choroidal hyperpermeability and extravascular hydrostatic pressure may cause accumulation of fluid under the RPE, resulting in serous PED and SRF. Interestingly, our patient showed that the choroidal hyperpermeability on ICGA was reduced when the serous PED was flattened as compared with baseline [Figures 3 and 5], supporting its role in the disease pathogenesis. The reason why the serous PED was more prominent than SRF in this patient compared with typical CSC is unknown, but it may depend on varying RPE-Bruch’s membrane adhesion force between individual patients. The association between steroid and recurrence of serous PED in this patient was apparent and also supported the diagnosis of CSC, for which steroid is a well-known risk factor. Our patient responded very well to aflibercept with regard to recurrences of the serous PED. Growing evidence has shown that PDS could be responsive to anti-VEGF in some cases, and aflibercept showed more efficacy than ranibizumab. Aflibercept may reduce choroidal hyperpermeability in PDS and was shown to cause reduction of choroidal thickness in pachychoroid neovasculopathy. Further studies are still needed to assess the efficacy and long-term safety of anti-VEGF against PDS. There is a small risk of RPE tear after anti-VEGF injection in cases of neovascular PED, especially when the PED is very high. The RPE tear can occur because of the contraction of

Figure 5: Multimodal imaging of the right eye at the first relapse of the pigment epithelial detachment (PED). (a) Fundus photograph, (b) infrared image, and (c) enhance-depth imaging optical coherence tomography show a relapse of shallow serous PED without subretinal fluid. (d) Fundus fluorescein angiography demonstrates the pooling of the PED beginning at the inferotemporal area. (e) Indocyanine green angiography shows hypocyanescence blockade of the PED. No abnormal hypercyanescence plaque of choroidal neovascularization was identified. The choroidal hyperpermeability was less intense than at the baseline visit.

Figure 6: Optical coherence tomography angiography when the pigment epithelial detachment (PED) was completely resolved (2 months after the fourth intravitreal injection). There was no sign of abnormal neovascularization in the choriocapillaris layer in both areas which used to be (a) the large PED and (b) the small satellite PED PED without SRF in pachychoroid pigment epitheliopathy has been described. Our patient was, however, most likely compatible with CSC but with atypical presentation of serous PED more prominent than SRF. The choroidal hyperpermeability and extravascular hydrostatic pressure may cause accumulation of fluid under the RPE, resulting in serous PED and SRF. Interestingly, our patient showed that the choroidal hyperpermeability on ICGA was reduced when the serous PED was flattened as compared with baseline [Figures 3 and 5], supporting its role in the disease pathogenesis. The reason why the serous PED was more prominent than SRF in this patient compared with typical CSC is unknown, but it may depend on varying RPE-Bruch’s membrane adhesion force between individual patients. The association between steroid and recurrence of serous PED in this patient was apparent and also supported the diagnosis of CSC, for which steroid is a well-known risk factor. Our patient responded very well to aflibercept with regard to recurrences of the serous PED. Growing evidence has shown that PDS could be responsive to anti-VEGF in some cases, and aflibercept showed more efficacy than ranibizumab. Aflibercept may reduce choroidal hyperpermeability in PDS and was shown to cause reduction of choroidal thickness in pachychoroid neovasculopathy. Further studies are still needed to assess the efficacy and long-term safety of anti-VEGF against PDS. There is a small risk of RPE tear after anti-VEGF injection in cases of neovascular PED, especially when the PED is very high. The RPE tear can occur because of the contraction of

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the neovascular component under the PED itself, which is potentially induced by anti-VEGF injection. However, in cases of large non-neovascular PED similar to the patient, whether the anti-VEGF would increase the risk of RPE tear is still unknown, and there are currently no standard treatments for this condition. On the other hand, it is known that anti-VEGF can decrease vascular permeability and may help to flatten the serous PED, as seen in this patient. However, larger studies are needed to validate the use of anti-VEGF in this specific condition.

In summary, this patient demonstrated a large relapsing serous PED with small SRF in non-neovascular PDS (likely CSC). The relapsing serous PED was associated with steroid use, could resolve spontaneously, and also responded very well to aflibercept. This clinical presentation in elderly patients with macular drusen might be confused with neovascular AMD. The choroidal thickness might look normal due to aging and the co-existence of dry AMD. Multimodal retinal imaging was crucial to reveal other clinical features of PDS in order to guide correct diagnosis and management.

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Conflicts of interest
There are no conflicts of interest.

REFERENCES
1. Phasukkijwatana N, Freund KB, Dolz-Marco R, Al-Sheikh M, Keane PA, Egan CA, et al. Peripapillary pachychoroid syndrome. Retina 2018;38:1652-67.
2. Dansingani KK, Balaratnasingam C, Klufas MA, Sarraf D, Freund KB. Optical coherence tomography angiography of shallow irregular pigment epithelial detachments in pachychoroid spectrum disease. Am J Ophthalmol 2015;160:1243-54.
3. Pang CE, Freund KB. Pachychoroid neovasculopathy. Retina 2015;35:1-9.
4. Warrow DJ, Hoang QV, Freund KB. Pachychoroid pigment epitheliopathy. Retina 2013;33:1659-72.
5. Akkaya S. Spectrum of pachychoroid diseases. Int Ophthalmol 2018;38:2239-46.
6. Zhang F, Qiu Y, Stewart JM. A case of relapsing retinal pigment epithelial detachment in peripapillary pachychoroid pigment epitheliopathy. Retin Cases Brief Rep 2018;12 Suppl 1:S110-13.
7. Bird AC, Marshall J. Retinal pigment epithelial detachments in the elderly. Trans Ophthalmol Soc U K 1986;105(Pt 6):674-82.
8. Hussain AA, Starita C, Hodgetts A, Marshall J. Macromolecular diffusion characteristics of ageing human Bruch’s membrane: Implications for age-related macular degeneration (AMD). Exp Eye Res 2010;90:703-10.
9. Jung B, Kim JY, Lee JH, Baek J, Lee K, Lee WK. Intravitreal aflibercept and ranibizumab for pachychoroid neovascularopathy. Sci Rep 2019;9:2055.
10. Okamoto M, Matsuura T, Ogata N. Choroidal thickness and choroidal blood flow after intravitreal bevacizumab injection in eyes with central serous chorioretinopathy. Ophthalmic Surg Lasers Imaging Retina 2015;46:25-32.

11. Kim DY, Joe SG, Yang HS, Lee JY, Kim JG, Yoon YH. Subfoveal choroidal thickness changes in treated idiopathic central serous chorioretinopathy and their association with recurrence. Retina 2015;35:1867-74.

12. Pitcher JD 3rd, Witkin AJ, DeCroos FC, Ho AC. A prospective pilot study of intravitreal aflibercept for the treatment of chronic central serous chorioretinopathy: The CONTAIN study. Br J Ophthalmol 2015;99:848-52.

13. Lim SJ, Roh MI, Kwon OW. Intravitreal bevacizumab injection for central serous chorioretinopathy. Retina 2010;30:100-6.

14. Hata M, Oishi A, Tsujikawa A, Yamashiro K, Miyake M, Ooto S, et al. Efficacy of intravitreal injection of aflibercept in neovascular age-related macular degeneration with or without choroidal vascular hyperpermeability. Invest Ophthalmol Vis Sci 2014;55:7874-80.

15. Koizumi H, Kano M, Yamamoto A, Saito M, Maruko I, Kawasaki R, et al. Short-term changes in choroidal thickness after aflibercept therapy for neovascular age-related macular degeneration. Am J Ophthalmol 2015;159:627-33.

16. Nagiel A, Freund KB, Spaide RF, Munch IC, Larsen M, Sarraf D. Mechanism of retinal pigment epithelium tear formation following intravitreal anti-vascular endothelial growth factor therapy revealed by spectral-domain optical coherence tomography. Am J Ophthalmol 2013;156:981-800.