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 retinochoroidal 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.[1-4]

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-neovascular 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

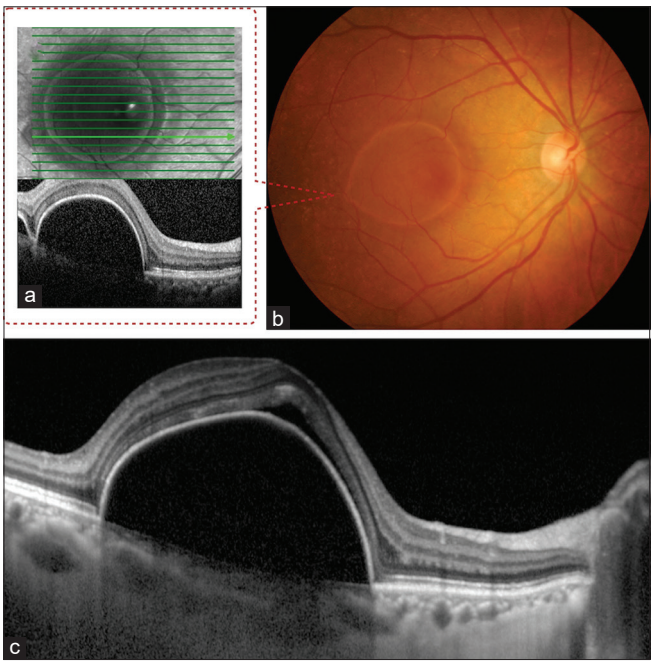

Figure 1: Multimodal imaging of the right eye at the first presentation. (a) Infrared reflectance and optical coherence tomography (OCT) of the macula and (b) fundus photograph show a large pigment epithelial detachment (PED) at the macula with surrounding small and intermediate drusen. There was a small 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

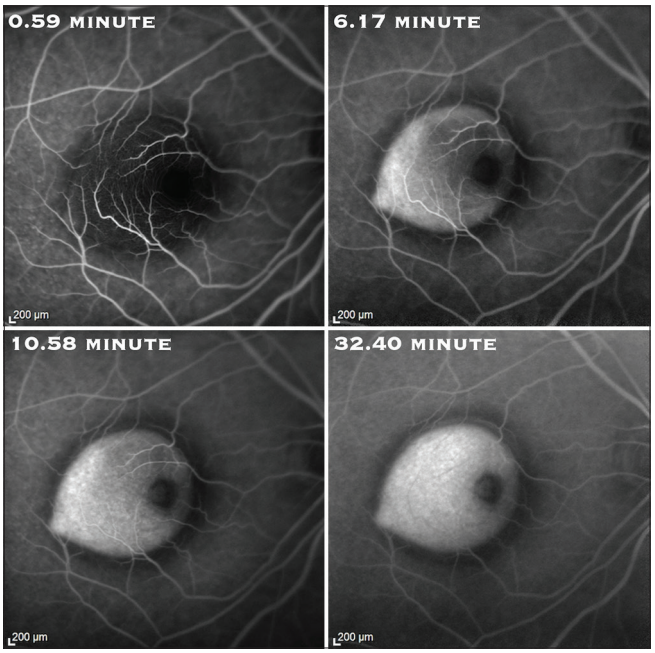

Figure 2: Fluorescein angiography of the right eye shows pooling hyperfluorescence of the pigment epithelial detachment (PED). Hyperfluorescence was more intense at the inferotemporal area and gradually diffused through the residual area of the PED. There was some late dye leakage into subretinal fluid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

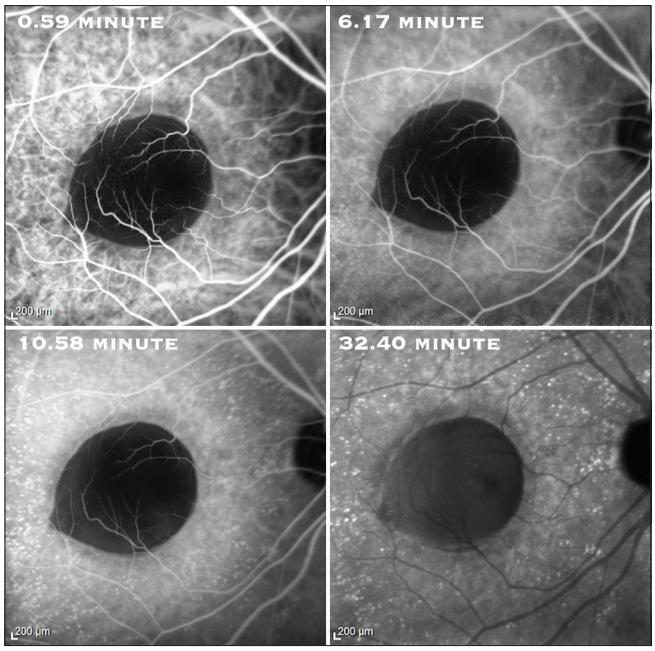

Figure 3: Indocyanine green angiography (ICGA) of the right eye shows hypocyanescence blockage of the pigment epithelial detachment (PED). There was choroidal hyperpermeability surrounding the PED in the mid to the late phase of the ICGA. No evidence of choroidal neovascularization was identified

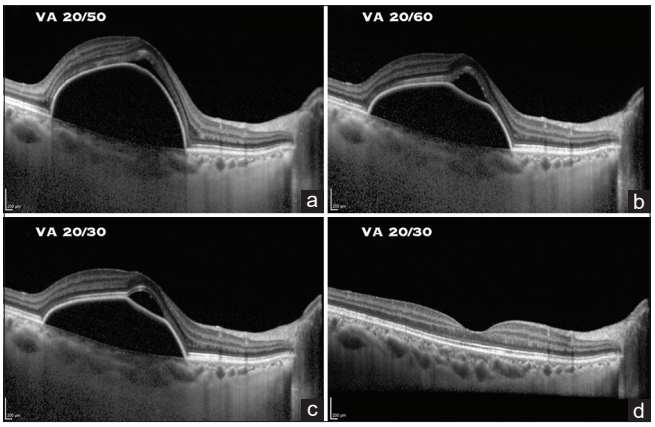

Figure 4: Evolution of the pigment epithelial detachment (PED) and subretinal fluid (SRF) of the patient. (a) Baseline enhance-depth imaging optical coherence tomography. (b) 1 month after the first intravitreal injection (bevacizumab), the PED was partially resolved, but SRF increased. (c) 1 month after the second injection (aflibercept), partial resolution of both PED and SRF is shown. (d) 1 month after the third injection (aflibercept), both PED and SRF were completely resolved. The patient's visual acuity improved to 20/30

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 hypocyanescence 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.[4,5] The spectrum includes pachychoroid pigment epitheliopathy, CSC, pachychoroid neovasculopathy, polypoidal choroidal vasculopathy, focal choroidal excavation, and peripapillary pachychoroid syndrome. A case of relapsing

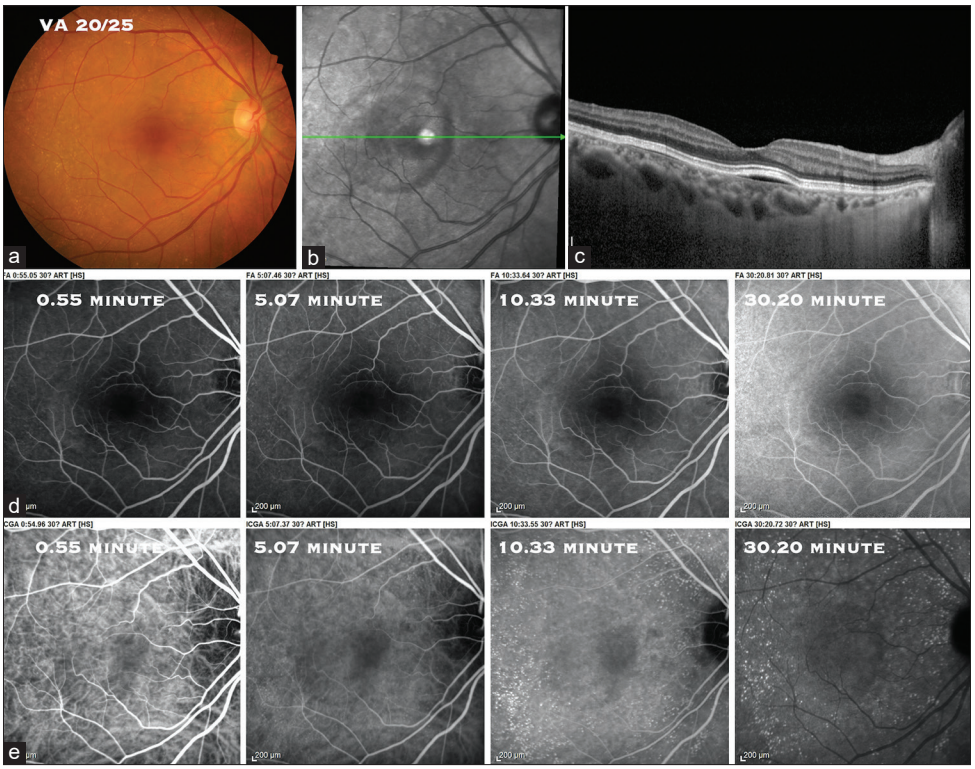

Figure 5: Multimodal imaging of the right eye at the first relapse of the pigment epithelial detachment (PED). (a) Fundus photograph, (b) infrared image, and (c) enhance-depth imaging optical coherence tomography show a relapse of shallow serous PED without subretinal fluid. (d) Fundus fluorescein angiography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

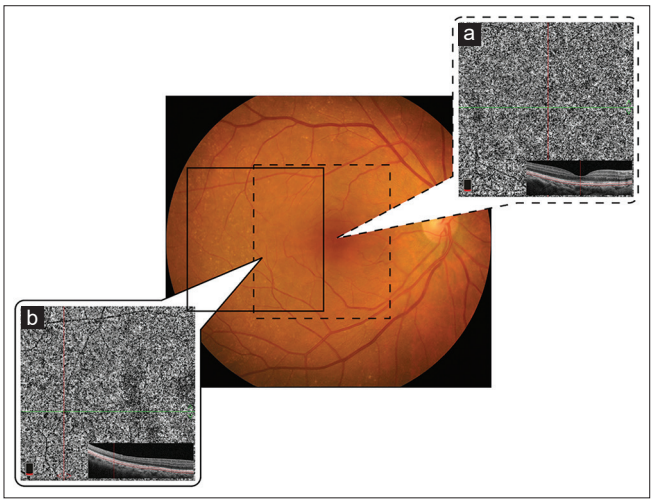

Figure 6: Optical coherence tomography angiography when the pigment epithelial detachment (PED) was completely resolved (2 months after the fourth intravitreal injection). There was no sign of abnormal neovascularization in the choriocapillaris layer in both areas which used to be (a) the large PED and (b) the small satellite PED

PED without SRF in pachychoroid pigment epitheliopathy has been described.[6] 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.[7,8] 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,[9-13] and aflibercept showed more efficacy than ranibizumab.[7] Aflibercept may reduce choroidal hyperpermeability in PDS and was shown to cause reduction of choroidal thickness in pachychoroid neovasculopathy.[9,14,15] 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

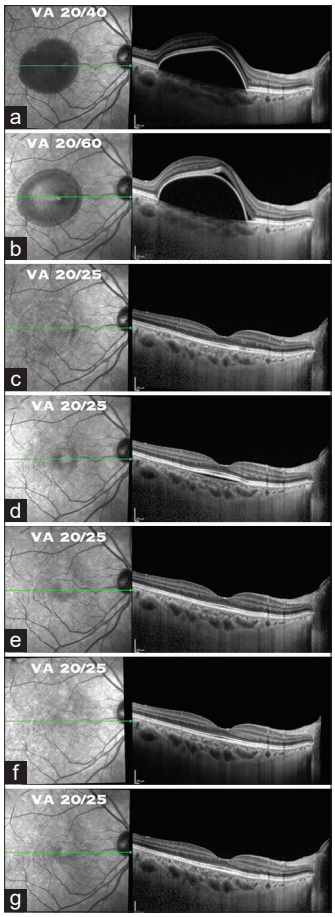

Figure 7: Enhanced-depth imaging optical coherence tomography shows relapses of the (PED). (a) 7 days after receiving 8 mg intravenous dexamethasone, the second relapse of the large PED is shown. (b) After 1 month of observation, subretinal fluid (SRF) developed. (c) After receiving the fifth intravitreal aflibercept injection, PED and SRF completely disappeared. (d) 4 months after the last injection, a shallow PED recurred but was spontaneously resolved. (e) 7 months, (f) 11 months, and (g) 22 months after the last injection, there were no further recurrences of the disease

the neovascular component under the PED itself, which is potentially induced by anti-VEGF injection.[16] 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 could be confused with neovascular AMD. The choroidal thickness might look normal due to aging and

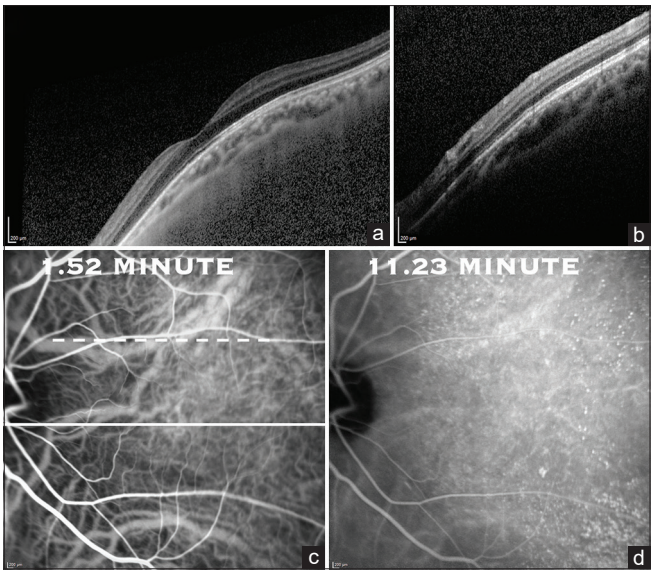

Figure 8: Enhanced-depth imaging optical coherence tomography of the fellow eye shows dilated Haller's layer vessels with thinning of the overlying inner choroid at (a) subfoveal area and (b) parafoveal area. Indocyanine green angiography shows dilated large choroidal vessels in (c) early phase and corresponding choroidal hyperpermeability in (d) mid to late phase. The solid line and the dash line in C represent the cross-section levels for A and B, respectively

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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Nil.

Conflicts of interest

There are no conflicts of interest.

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