Research Article

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# Swept Source Optical Coherence Tomography (En-Face) Imaging in Conjunction with (Retinal flow) Optical Coherence Angiography Map "Marking Out" Deep Capillary Plexus Ischemia in Paracentral Acute Middle Maculopathy

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## ABSTRACT

***Introduction:*** *PAMM, recently emerged retinal pathology involving preferentially deep retinal capillary system (ICP and DCP) where impaired blood flow occurs, and particularly anatomical and physiological watershed zone is affected (INL and OPL). Resultant ischemia is presented clinically with sudden drop of vision and manifested as band like hyperreflective lesions on SS OCT B scans. SS OCTA with Enface and Retinal flow maps have delineated ischemic lesions within middle retina and exhibited characteristic findings that may help in understanding the pathophysiology behind this entity.*

***Purpose:*** *To highlight PAMM diagnostic features on Optical Coherence Tomography Angiography and Enface, and to emphasize on their major role in detecting and assessing this condition.*

***Methods:*** *This is a retrospective study reviewing two clinical cases presented to our facility with sudden decrease in vision in one eye. DRI OCT Triton (Topcon Corporation, Tokyo, Japan) was employed. In addition to generating high quality conventional cross sectional B scan images, Enface C scans and three dimensional angiography images were obtained at different retinal levels. High-resolution color fundus imaging, Fluorescein Angiography (FA) and Fundus Auto fluorescence (FAF), and Enface in conjunction with OCTA were all used in the two cases. Detailed history, full comprehensive Eye exam was done, appropriate thorough systemic workup was performed; baseline blood tests (CBC, KFT, LFT, UA), coagulation profile (INR, APTT, D Dimer) with blood test for sickle cell (SC), and autoimmune profile.*

***Results:*** *In both cases, OCTA and Enface revealed multiple findings of PAMM during the acute phase of presentation. OCTA provided evidence of DCP ischemia by showing perfusion defects, or capillary dropout. Enface C scans visualized fern-like ischemic distribution at the level of DCP.*

***Discussion:*** *The use of OCTA in conjunction with Enface OCT has proved superior to other imaging modalities in identifying and diagnosing PAMM. It is anticipated that such imaging techniques may provide new insights for middle and deep retinal ischemic pathologies including PAMM which may have a constellation of imaging findings in the near future for its detection, diagnosis, classification, and perhaps management!*

## Keywords

Paracentral acute middle maculopathy (PAMM), Swept source optical coherence tomography (SS-OCT), OCT ANGIO, Enface OCT, Retinal flow map, fern like ischemia.

## Introduction

Paracentral Acute Middle Maculopathy PAMM was introduced in 2013 as a new variant of AMN at the time when AL Sarraf et al. described a spectral domain OCT (SD OCT) finding of middle

retinal layers ischemia at the level of the inner nuclear layer INL [1,2].

While it was described at the beginning as type 1 AMN, recently PAMM is more considered to be a separate entity, which preferentially involves intermediate and deep capillary plexuses (ICP/DCP) resulting in impaired blood flow. It may concomitantly present with other localized retinal vascular diseases, or may imply the presence of a systemic or extrinsic vascular abnormality. PAMM could also be idiopathic occurring in young healthy patients.

SD OCT imaging has played a gold standard role in establishing the diagnosis of PAMM, showing characteristic finding of placoid hyper reflective lesions at the level of the inner nuclear layer (INL), which were then descriptively labeled as PAMM.

Since the recent advent of sophisticated highly sensitive imaging techniques, visualization of deeper micro vascular flow is realized even at the level of DCP. Swept Source OCT (SS OCT) multimodal platform provides higher definition images as detective clues for DCP ischemia. As such, SS OCT Angiography high definition images delineate fern like ischemic distribution seen in PAMM.

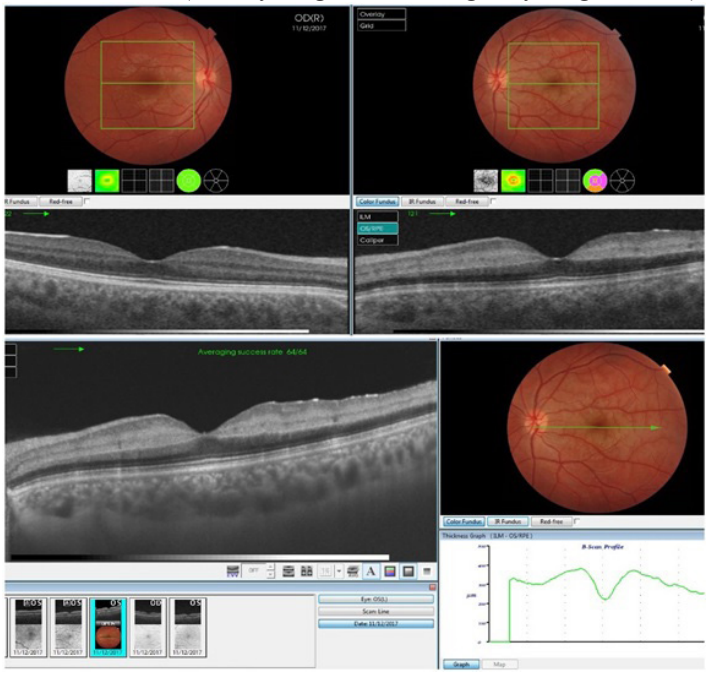
In our report, we describe two cases presenting with negative scotomas, and no fundoscopic abnormalities found on clinical examination. SS OCTA including Enface and Retinal Density Map modalities, have leaded the way to diagnose PAMM in these three cases. This implies the primary key part SS OCTA imaging plays in detecting and diagnosing PAMM. Furthermore, it may have a promising role in observing PAMM coarse while following patients, and possibly setting certain imaging indices in order to control management of these patients.

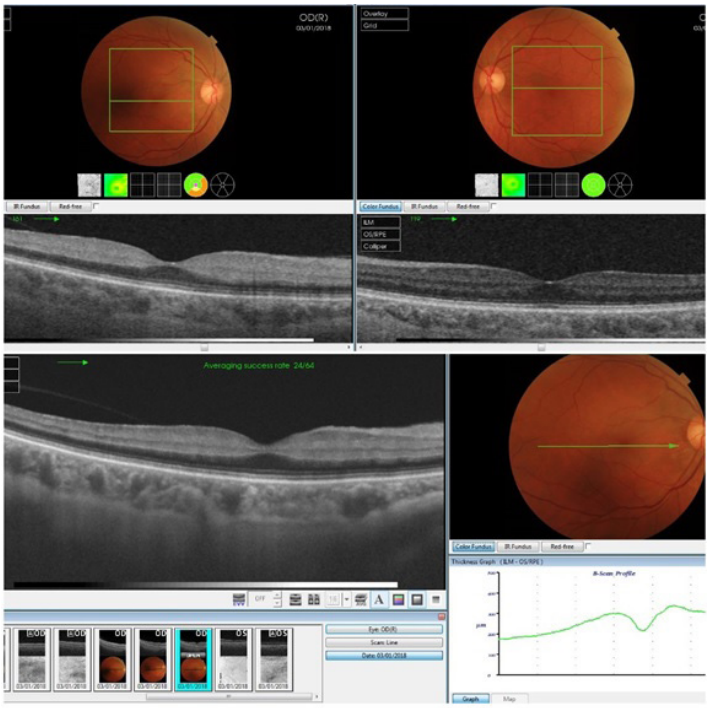
## Methods

This is a retrospective study reviewing two clinical cases presented to our facility with sudden decrease in vision in one eye. SS OCT multimodal imaging revealed PAMM lying behind the deterioration in vision in both cases. DRI OCT Triton (Topcon Corporation, Tokyo, Japan) was employed; In addition to generating high quality conventional cross sectional B scan images, Enface C scans and three dimensional angiography images were obtained at different levels. Through segmentation technique, SS OCT dissected the retina and delivered multiple coronal views at variant depths; showing firstly superficial retinal plexus (ILM_IPL), then deep retinal plexus (IPL_OPL), then avascular outer retina (OPL_BRM), and lastly penetrating to show choriocapillaris. Multi-modal color fundus imaging, Fluorescein Angiography (FA) and Fundus Auto fluorescence (FAF), and Enface in conjunction with OCTA were all used in the two cases. Detailed history was obtained, given special attention to medical conditions and systemic illnesses, which may predispose to retinal ischemia. Full thorough systemic workup was performed; baseline blood tests (CBC, KFT, LFT, UA), coagulation profile (INR, APTT, D Dimer) with blood test for sickle cell, and immunology/ Autoimmune profiles (ANA, RF, C ANCA, P-ANCA) were all tested in our two cases.

## Results

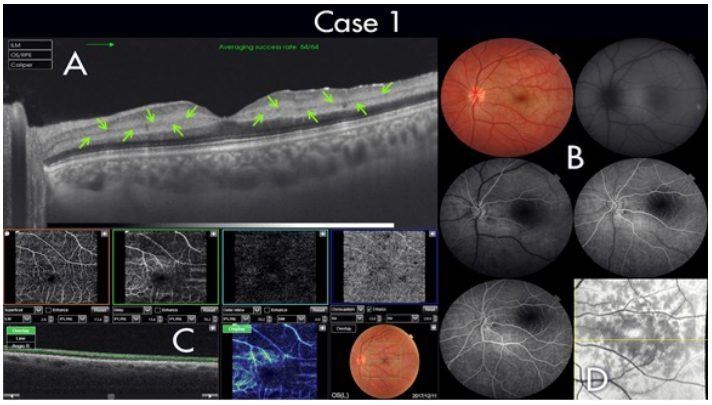
Deep Capillary plexus ischemia was clearly illustrated on SS OCTA and Enface imaging modalities in both of our cases. The conventional finding of PAMM viewed on two-dimensional B scans as middle retinal hyper reflective plaque like lesion was also detected in the two cases (Left Eye Figure 1A,B, Right Eye Figure 2A,B).



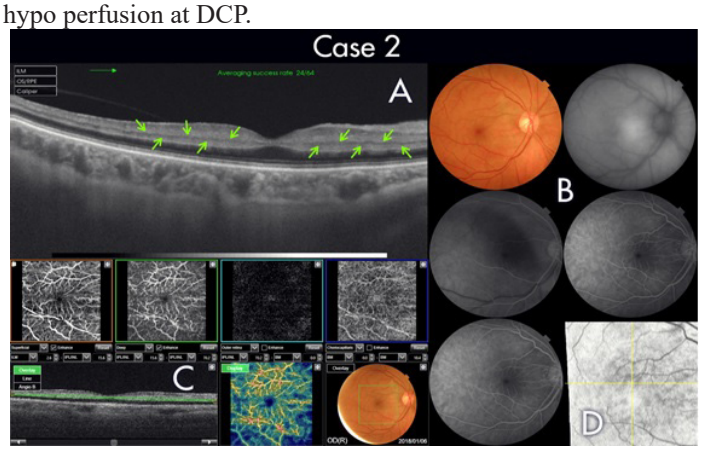


Our first case, 25 years old male patient medically free, had sudden deterioration in his left eye vision. Visual acuity on presentation was counting fingers at 3meter distance. Marked Relative Pupillary Afferent Defect (RAPD) was detected and fundoscopic exam

showed abnormal foveal reflex. SS OCT B scan: showed a hyper reflectivity of the inner plexiform layer (IPL), inner nuclear layer (INL) and OPL layer (figure 3A). FA images were normal (figure 3B). Angiography shows remarkable perifoveal capillary drop out within middle retinal layer correlating with perfusion density map which reveals significant decrease in capillary density at the same level (Figure 3C). Enface ads more proof to PAMM by delineating ischemic distribution in a fern like pattern of hyper reflective areas within DCP (Figure 3D).




Right eye is the affected eye in the second case of our series; 70 years old female patient known to have hypertension, presented with acute deterioration of left eye vision, best corrected visual acuity was 6/60. Fundoscopic exam showed abnormal foveal reflex whiting .SS-OCT B scan showed also a hyperreflectivity of the inner plexiform layer (IPL), inner nuclear layer (INL) and OPL layer. FA images were also normal. Segmented angiographic images elucidate ischemia and capillary drop out predominantly at the level of DCP but less severe than Case 1 (Figure 4C). Correspondingly, Enface highlights hyper reflective areas in a fern like distribution in the middle retina at similar depth of ischemic lesions demonstrated on B scans and OCTA (Figure 4D). It is worth to note that Enface fern like pattern in case number 1 (Figure 3D), was revealed to be denser and broader when compared to the other same pattern shown in case number 2 (Figure 4D). Alongside that, retinal perfusion map in the first case (Figure 3C) lines out areas of significant capillary loss and disruption of micro vascular flow. This would imply that the degree of ischemia was higher in case number 1 who had visual acuity (VA) of counting fingers. Clinical picture accordingly is related to the extent and severity of hypo perfusion at DCP.




## Discussion

The primary guide for PAMM was originally set by SD OCT that revealed band-like areas of hyperreflection in middle retina, which is known to embrace inner nuclear layer (INL) and outer plexiform layer (OPL) [3-5].

OCTA side by side with Enface imaging provide a more informative guide to localizing and clearly delineating PAMM lesions, defining their extents, and exploring its possible pathogentic mechanism [6].

Since the early description of PAMM in 2013, many case reports have provided considerable evidence pointing toward ischemic insult in retinal deep capillary system implicating this condition [7-10]. OCTA noninvasively provides high-resolution cuts exhibiting impaired blood flow in intricate capillaries feeding deeper retinal layers [11]. By so, it delivers investigative clues for ischemia lying beneath PAMM formation, whether in acute or chronic settings [12]. It can demonstrate capillary dropout acutely, then capillary ramification and pruning over time to mark out an old PAMM lesion.

Interestingly some acute cases may show normal angiographic findings without any structural changes. This still supports theory of ischemia as it has been suggested that an initial transient hypoperfusion event occurs [13], but the retina can autoregulate and control blood flow in deep capillaries. Subsequent reperfusion injury takes place, producing OCTA picture of attenuation and pruning of DCP on chronic setting [9], which correlates with INL atrophy detected on SS-OCT B scans [14,15]. In our case review, OCTA showed demarcated areas of capillary perfusion defect acutely. Evidences of old PAMM such as INL atrophy on B scans as well as capillary remodeling on OCTA are not shown as this review won't discuss chronic PAMM category, and imaging of the two cases was only performed in acute stetting.

Advanced capability of dissecting retinal layers, has enabled Enface OCT to accurately delineate ischemic areas at different retinal levels. It can assess microcirculation at level of DCP where complete occlusion or even slow sluggish flow can be detected. In relation, different captured ischemic lesions, exhibit variant morphological patterns on Enface cuts; such as globular 26, band-like, and Fern-like patterns [15]. While each pattern has a specific mechanism behind, all come under the same umbrella "theory of ischemia". Herein, the two cases showed typical fern-like distribution on Enface coronal sections in the absence of true occlusive event (i.e. CRAO, BRAO, or CRVO) as opposed to fern-like ischemic morphology previously described as a perivenular lesion [16-18], where CRVO has been frequently diagnosed [15,19].

Currently PAMM is appraised as a distinct entity from AMN, having different demographic background and more prevalence particularly among patients with systemic comorbidities, like Diabetes Mellitus, Hyperlipidemia [20], and Hypertension [14]. It has been associated with variant vascular retinopathies, such

as CRVO [15,16,18,21,22] CRAO, [4,6,23] CLRAO, [11,22] or BRAO [15], diabetic and hypertensive retinopathies. Chen et al. have reported novel spectrum of retinal vasculopathies. Such as sickle cell (SC) crisis [12,24], Purtscher's retinopathy [25], hypertensive retinopathy, and viral prodrome [5,14,25]. All aforementioned retinopathies were excluded in the two-presented cases of this series.

OCTA and Enface supported the theory of ischemic attribution to PAMM not only by showing disrupted flow in deep capillary system, but also by showing the preferential location of lesions within middle retinal layer (INL and OPL) in parafoveal area. INL receives blood supply from two sources: retinal vessels supply inner two thirds of INL and choroidal vasculature supplies outer one third, so this region is susceptible to any ischemic event. Additionally, Parafoveal macula in this middle vulnerable level has higher oxygen demands and limited supply in response. Limitations are attributed to increase retinal thickness and decrease capillary density for best optical penetrance to this particular area [26]. Observing PAMM in patients with SC has further emphasized that middle retina is a functional watershed zone. As we expect to find signs of ischemia in peripheral retina where capillary occlusive mechanism of SC manifests, but signs rather show up favorably in parafoveal macula of middle retinal layer [27].

Conventional FA fails to demonstrate blood flow at DCP layers and it doesn't detect any ischemic changes occurring in deep layers [28]. Most recited case reports in this review stressed the limited and uninformative role FA plays in PAMM diagnosis, except for its adjunct use to exclude the presence of vascular occlusion finding in Superficial Capillary plexus (SCP).

SS OCT multimodal imaging can be applied to monitor PAMM course upon patients follow up process. Some imaging angiographic features can be used to assess the degree of ischemia over a period of time, capillary density [14,23,29]. Foveal Avascular Zone distortion and degree of capillary remodeling and pruning at DCP that correlates with atrophy destined for INL band like lesions demonstrated acutely on B scan. Analyzing such features and plotting related data on measurement scale might help in predicting the vision outcome of PAMM. Most reported patients who continued to have negative scotomas, were found to have deep capillary ramification and pruning on OCTA after a while.

In the setting of constant increase in PAMM cases encountered nowadays, better understanding of this entity is warranted. The use of OCTA in conjunction with Enface OCT has proved superior to other imaging modalities in identifying PAMM; OCTA penetrates deep layers and delivers 3-dimensional visualization of Retina with Enface enabling vascular network visualization layer-by-layer. It is anticipated that such imaging techniques may provide new insights for middle and deep retinal ischemic pathologies including PAMM which may have a constellation of imaging findings in the near future for its detection, diagnosis, classification, and perhaps management!

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