Optical coherence tomography angiography in comparison with other multimodal imaging techniques in punctate inner choroidopathy

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ABSTRACT

Aims To characterise punctate lesions and choroidal neovascularisation (CNV) in eyes with punctate inner choroidopathy (PIC) using current standard multimodal imaging techniques and optical coherence tomography angiography (OCTA).

Methods In our prospective, single-centre study, 20 individuals with PIC underwent imaging with spectral-domain optical coherence tomography (SD-OCT), fluorescein angiography (FA), indocyanine green angiography, fundus autofluorescence, fundus colour photography and OCTA.

Results Thirty-two eyes of 20 patients were affected. Eight (20%) eyes revealed typical punctate lesions, while 24 (60%) eyes had confirmed CNV on SD-OCT and FA in addition to punctate lesions. Of these 24 eyes with CNV, a reoccurrence of active CNV was detected in 5 (21%) eyes, a residual fluid in 3 (13%) eyes, while 16 (67%) eyes were defined as being stable. On OCTA, CNV was classified as having 'lacy wheel', 'pruned large-trunk' and 'dead tree aspect' vessel shapes with or without areas of non-perfusion. The disease activity was dependent on several predictors in the regression analysis such as intraretinal fluid (p=0.0014), CNV type (p=0.0199), leakage (p<0.0001) and hypoperfusion/non-perfusion (p<0.0001) on OCTA.

Conclusion OCTA offers additional valuable insight into the current standard multimodal imaging techniques used for characterisation of PIC. This imaging technique can be a useful tool for analysis of disease activity.

INTRODUCTION

Punctate inner choroidopathy (PIC) is a subtype of multifocal choroiditis (MFC) and a rare form of posterior uveitis of unknown aetiology. Some authors propose that there is a familiar predisposition to autoimmune/inflammatory disease[1] while others suggest that it may be part of entities known as white dot syndromes.[2] Young myopic women are commonly affected and the disease is characterised by the presence of multiple, small, round, well-defined, yellowish-white punctate lesions, in the absence of signs of intraocular inflammation.[3] The most common complication is the development of choroidal neovascularisation (CNV)[4] which has been reported in up to 69%–75%.[5 6]

The current standard imaging modalities for characterisation of PIC are spectral-domain optical coherence tomography (SD-OCT), fluorescein angiography (FA), indocyanine green angiography (ICGA) and fundus autofluorescence (FAF).[7 8]

A new application of OCT technology, OCT angiography (OCTA), is a non-invasive method that allows for visualisation of retinal and choroidal vasculature. This is achieved through a process of high-density OCT volume scans and multisampling to identify motion associated with blood flow. In contrast to standard OCT, OCTA analyses not only the intensity of the reflected light but also the temporal changes in the reflection caused by erythrocytes flowing through vessels. These changes in the OCT signal are detected by repeatedly capturing OCT images at each point on the retina and allow for the creation of an image contrast between the perfused vessels and the static surrounding tissues. In contrast to FA or ICGA imaging, which requires a contrast agent to visualise the perfusion of retinal and choroidal vessels in two-dimensional images, the OCTA module allows for a three-dimensional view of distinct retinal and choroidal vessel plexuses without injecting dye. In addition, while OCTA imaging cannot display static or very slow flow phenomena, it may be able to non-invasively detect subtle microvascular abnormalities, which are not detectable with FA, ICGA and FAF imaging.

In this study, we evaluated a cohort of 20 patients using OCTA imaging in combination with other currently available multimodal imaging approaches in order to describe retinal changes associated with PIC. The addition of OCTA imaging to current clinical imaging standards may enhance our understanding of the pathophysiology of PIC, perhaps enabling clinicians to detect disease activity with more certainty.

METHODS

This study was performed in accordance with the Declaration of Helsinki. Written informed consent was obtained from each participating patient before imaging.

Forty eyes of 20 patients with PIC were examined between April and December 2016. The diagnosis of PIC was based on classically accepted clinical findings: appearance of multiple chorioretinal lesions localised in the posterior pole, myopia and absence of intraocular inflammation.

On the study day, all relevant patient demographics and clinical characteristics of the patients were documented. These data included visual acuity (VA) in Logarithm of Minimum Angle of Resolution (logMAR), slit-lamp findings and indirect ophthalmoscopy. The current immunosuppressive

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treatments as well as history of intravitreal antivascular endothelial growth factor (anti-VEGF) injections were recorded.

Fundus photography was performed using a fundus camera (Zeiss FF 450+) to document lesions on the posterior pole.

SD-OCT was performed to assess lesion characteristics—subretinal or intraretinal fluid, subretinal hyper-reflective material and retinal pigment epithelium (RPE) atrophy.

FA, ICGA, FAF and SD-OCT were performed simultaneously on the SPECTRALIS (Heidelberg Engineering, Heidelberg, Germany). Active CNV was identified as an area presenting with uniform, early hyperfluorescent vasculature that showed extensive leakage in the intermediate and late phases. Inactive CNV was defined as an area presenting with fluorescein staining or as a window effect due to RPE defect and scar tissue.

FAF was performed with BluePeak–Blue Laser (BAF) and infrared reflectance (IR) by SPECTRALIS (Heidelberg Engineering, Heidelberg, Germany).

OCTA images were acquired using a prototype SPECTRALIS OCT device (SPECTRALIS, Heidelberg Engineering, Heidelberg, Germany) with an A-scan rate of 70 000/s. For this study, a 15°×10° scan angle protocol was used to acquire a total of 261 B-scans resulting in images with an axial resolution of approximately 4 µm, within B-scan resolution of approximately 11 µm (6.99 µm/pixel), and between B-scan resolution of also approximately 11 µm. The standard OCTA viewing module 6.6.0.1 and its associated automatic segmentation of the retinal layers was applied to derive the en face slabs for each vascular plexus. However, the presentation of lesions and neovascular complex were best visualised after manual segmentation adjustments were made.

Statistical analysis

All data were analysed using GraphPad Prism 7 (GraphPad Software, La Jolla, California, USA). Regression analysis and X^2 test were used. A significant p value was defined as $p \leq 0.05$.

RESULTS

Study population

Forty eyes (20 patients) with PIC were examined at our Department of Ophthalmology. Eighteen patients were women (90%, 18/20) with a mean age of 45±10 years (range, 26–64). All patient demographics are presented in table 1.

A total of 32 eyes (80%) were affected and showed the typical presence of PIC lesions. Twenty-four of 40 eyes (60%) revealed a secondary CNV, of which 16 of 24 eyes (67%) had received several intravitreal ant-VEGF inhibitor injections previously. One eye had been treated with intravitreal triamcinolone. Four eyes of the 24 CNV eyes (17%) had sustained photodynamic therapy.

Table 1 Patients' demographics

			CNV / PIC lesion (x)		Myopia		VA (logMAR)		IVI			
Patient	Age, years	Sex	R	L	R	L	R	L	R	L	Current systemic therapies	Previous therapies
#1	43	F	CNV	CNV	–6	– 6	0.1	1.3	1x A 3x B 6x R	1x B	Prednisolone 5 mg	MMF, prednisolone, R/L PDT
#2	57	F	CNV	CNV	– 9	– 7	0.1	0.4	2x R	3x R	–	L PDT
#3	64	F	CNV	x	– 11	– 6	0.7	0.2	–	----	MMF, prednisolone 5 mg	–
#4	34	F	–	CNV	– 4	– 5	0	0.1	–	1x T 2x R	–	–
#5	35	F	–	CNV	– 4	– 3	0	0.7	–	8x B 6x R	MMF	CSA, MTX, prednisolone L PDT
#6	46	M	–	CNV	– 1	– 1	0	0.1	–	1x B 2x R	–	–
#7	44	F	x	x	– 6	– 6	0.2	0.2	–	–	Prednisolone 5 mg	–
#8	44	F	CNV	CNV	– 10	– 9	0.3	1.3	12x R	–	MMF	CSA, MTX
#9	36	F	x	–	– 3	– 3	0.9	0.1	–	–	Prednisolone 10 mg	–
#10	54	F	CNV	CNV	– 7	– 8	0.2	1.8	4x B 5x A 17x R	–	Adalimumab, prednisolone 7.5 mg	CSA, MMF, MTX
#11	48	F	CNV	CNV	– 7	– 7	0.2	1.8	1x R	–	Prednisolone 5 mg	–
#12	50	F	CNV	CNV	– 12	– 14	0	0.2	2x R 3x A	–	Prednisolone 5 mg	–
#13	56	F	–	CNV	–9	– 9	0	0.3	–	3x R 4x B	–	CSA, MTX
#14	37	F	–	CNV	– 4	– 4	0	0	–	4x R	–	–
#15	52	F	CNV	CNV	– 9	– 10	0.1	1.3	–	–	CSA	MTX, prednisolone
#16	26	F	–	CNV	–6	–7	0	0.7	–	5x R	Adalimumab, MTX	Azathioprine, CSA
#17	64	F	CNV	x	–10	–3	1.8	0	–	–	–	–
#18	31	F	x	x	–7	–7	0	0	–	–	–	Azathioprine, CSA
#19	39	M	CNV	x	–5	–5	0.1	0	6x R	–	–	Prednisolone
#20	48	F	CNV	–	–5	–4	0	0	5x B	–	–	–

A, aflibercept; B, bevazicumab; CNV, choroidal neovascularisation; CSA, ciclosporin A; DR, diabetic retinopathy; IVI, intravitreal injection; logMAR, logarithm of the minimum angle of resolution; MMF, mycophenolat mofetil; MTX, methotrexate; PIC, punctate inner choroidopathy, PDT, photodynamic therapy; R, ranibizumab; VA, visual acuity, x, PIC lesions.

Table 2 Standard imaging features

	PIC lesions n=8 eyes (20%)	CNV n=24 eyes (60%)
SD-OCT		
Intraretinal fluid	0 (0)	8 (33)
Punched out lesions	1 (13)	
RPE elevation	3 (38)	24 (60)
Subretinal hyper-reflective material:	0 (0)	
Above RPE		*15 (63)*
With disrupted RPE		11 (46)
With intact RPE		4 (17)
Below RPE		*5 (21)*
With disrupted RPE		4 (17)
With intact RPE		1 (4)
Above and below RPE		*4 (17)*
FA (n = 22)*		
Leakage	0 (0)	5 (23)
Staining	4 (50)	6 (27)
Window defect	3 (38)	11 (50)
ICGA (n = 22) *		
Hypofluorescence (late phase)	7 (88)	22 (100)
Isofluorescence (late phase)	2 (25)	0 (0)
FAF		
Hypofluorescence	8 (100)	22 (92)

*No fluorescein and ICGA in one patient.
CNV, choroidal neovascularisation; FA, fluorescence angiography; FAF, fundus autofluorescence; ICGA, indocyanine green angiography; PIC, punctate inner choroidopathy; RPE, retinal pigment epithelium; SD-OCT, spectral-domain optical coherence tomography.

Eleven of 20 patients (55%) were on systemic immunosuppressive treatments. On the study day, VA ranged from 0 to 1.8 logMAR and all eyes showed myopia (−1.5 to −15.0 dpt).

Assessment of punctate lesions

Eight eyes of 40 (20%) revealed only white or yellow, multiple, small (100–300 µm in diameter) round lesions through the posterior pole, partly confluent without CNV. None of these eyes showed intraretinal fluid in SD-OCT or leakage on FA. Typically, lesions of all effected eyes showed staining areas 4/8 (50%) or window defects 3/8 (38%) on FA and hypofluorescent areas in early, intermediate and late phases of ICGA. In two of eight eyes (25%), some lesions presented as isofluorescent in the late phase of ICGA. In FAF, all lesions were detected as hypofluorescent spots (table 2).

On OCTA, all lesions revealed areas of non-perfusion in the choriocapillaris. Additionally, in all eyes other areas of non-perfusion were observed which were not detected with the other imaging modalities. In the outer retina layer, the lesions displayed a collection of capillaries with crippled whitening (figure 1, table 3).

Assessment of choroidal neovascularisation

Twenty-four of 32 affected eyes (75%) had a clinical course complicated by CNV. On SD-OCT examination, 15/24 eyes (63%) revealed subretinal hyper-reflective material above RPE, of which 11/24 eyes (46%) showed a disrupted RPE. Hyper-reflective material below RPE was detected in 5/24 eyes (21%), of which 4/24 eyes (17%) presented with disrupted RPE. In total,

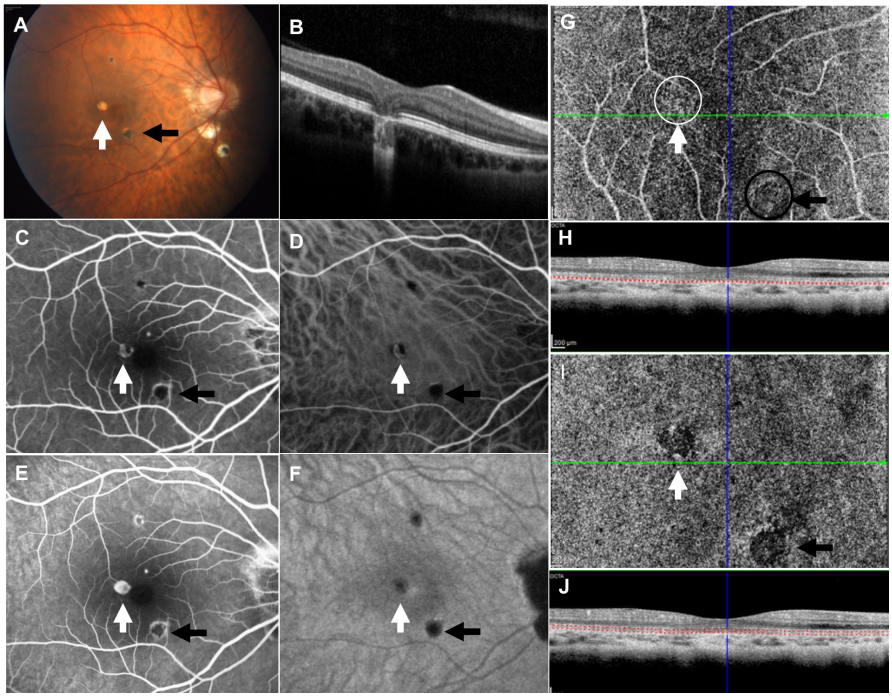

Figure 1 Fundus photography, SD-OCT, FA, ICGA and OCTA images of patient #18. (A) Fundus picture showing a whitish punctate lesion (white arrow) and a pigmented dark lesion (black arrow) at the posterior pole. (B) Corresponding SD-OCT, (C) intermediate and (D) late-phase FA images showing fluorescein staining of the whitish lesion (white arrow) and filling defect with a hypofluorescent circle and a hyperfluorescent rim (black arrow). (E) Intermediate and (F) late-phase ICGA images showing corresponding hypofluorescent round areas whereby the whitish lesion becomes more isofluorescent in the late phase, caused by partial thickness stromal inflammatory lesion. (G) The corresponding OCTA showing a collection of crippled whitening in the outer retina layer of the whitish lesion (white arrow and white circle) while the pigmented lesion (black arrow and black circle) revealing no accumulation of blood cells. (I) The choriocapillaris in OCTA showing circular, punched out, non-perfused areas whereby the whitish lesion showing a blurred rim. (H,J) Corresponding B-scan images. FA, fluorescein angiography; ICGA, indocyanine green angiography; OCTA, optical coherence tomography angiography; SD-OCT, spectral-domain optical coherence tomography.

Table 3 Optical coherence tomography angiography

	PIC lesions n=8 eyes (%)	CNV n=23 eyes (%)*
SCP		
Abnormalities of capillary network†	1 (13)	12 (52)
Capillary non-perfusion/hypoperfusion		0 (0)
Intraretinal cystoid spaces		3 (13)
DCP		
Abnormalities of capillary network†	1 (13)	12 (52)
Capillary non-perfusion/hypoperfusion		2 (9)
Intraretinal cystoid spaces		5 (22)
Outer retina		
Collection of crippled whitening	8 (100)	
Capillary hypoperfusion		
Without vessels		2 (9)
One filamentous vessel		1 (4)
Lacy wheel shape		7 (30)
With capillary non-perfusion		4 (17)
Without capillary non-perfusion		3 (13)
Pruned large-trunk vessels		4 (17)
With capillary non-perfusion		2 (9)
Without capillary non-perfusion		2 (9)
Dead tree aspect		8 (35)
With capillary non-perfusion		0 (0)
Without capillary non-perfusion		8 (35)
Choriocapillaris		
Capillary non-perfusion/hypoperfusion	8 (100)	22 (96)

*In two eyes OCTA could not be performed due to macular scar.
†Capillaries abnormalities include dilatation, anastomotic connection and areas of rarefied capillaries.
CNV, choroidal neovascularisation; DCP, deep capillary plexus; OCTA, optical coherence tomography angiography; PIC, punctate inner choroidopathy; SCP, superficial capillary plexus.

5/22 eyes (23%) showed macular leakage, while 6/22 eyes (27%) presented with staining and 11/22 eyes (50%) with window defects on FA. ICGA imaging showed hypofluorescence in the late phase on all CNV-affected eyes. RPE defect on FAF was found in 22/24 eyes (92%) (table 2).

Abnormalities of capillary network detected on OCTA included dilatation, anastomotic connection and areas of rarefied capillaries in superficial capillary plexus (SCP) and deep capillary plexus (DCP) in 12/22 eyes (55%). Areas of capillary non-perfusion/hypoperfusion were detected in 2/22 eyes (9%) within the DCP, which were not seen in the SCP. Intraretinal cystoid spaces were found in 3/22 eyes (14%) within the SCP and in 5/22 (23%) within the DCP. Eyes with CNV presented with different shapes which were classified as 'lacy wheel' vessels in 7/22 eyes (32%), 'pruned large-trunk' vessels in 4/22 eyes (18%), and 'dead tree aspect' small and large vessels in 8/22 eyes (36%) (figure 2).[9 10] Areas with vessels surrounded by non-perfusion were classified as non-perfused areas without vessels. More details are shown in table 3.

Classification of disease activity of choroidal neovascularisation

Five of 24 eyes (21%) showed evidence of recurrent activity of CNV. In most of these eyes, 4/5 (80%), either intraretinal fluid on SD-OCT or macular leakage on FA was seen. In one eye, no intraretinal fluid was detected on SD-OCT, but macular leakage on FA was seen. In another patient intraretinal fluid on SD-OCT was detected, but FA could not be performed due to dye allergy. On OCTA, CNV was shaped as 'lacy wheel' in three of these five eyes (60%). In one case, the affected eye showed one filamentous vessel with great, surrounded, sickle-shape non-perfused area (figure 3).

Three of 24 eyes (13%) revealed residues of intraretinal fluid. Two of these three eyes (67%) showed intraretinal fluid on SD-OCT examination and in one of these three eyes (33%) macular leakage was found on FA. Sixteen of 24 (67%) eyes without CNV activity presented with staining or window defect on FA, while only 2/16 eyes (13%) showed minimal intraretinal fluid cysts on SD-OCT. Hyper-reflective material was observed above and below the RPE in inactive eyes, while eyes with recurrence or residues of fluid showed hyper-reflective material above the RPE in all cases. The 'dead tree aspect' vessel shape was mainly observed in 9/16 eyes (60%) on OCTA. More details are shown in table 4.

Statistical analysis

Grading of disease activity was dependent on several predictors in the regression analysis such as (1) intraretinal fluid ($p=0.0014$), (2) CNV type ($p=0.0199$) on SD-OCT, (3) leakage ($p<0.0001$) on FA and (4) hypoperfusion/non-perfusion in the outer retina ($p<0.0001$) on OCTA. There was a slight positive

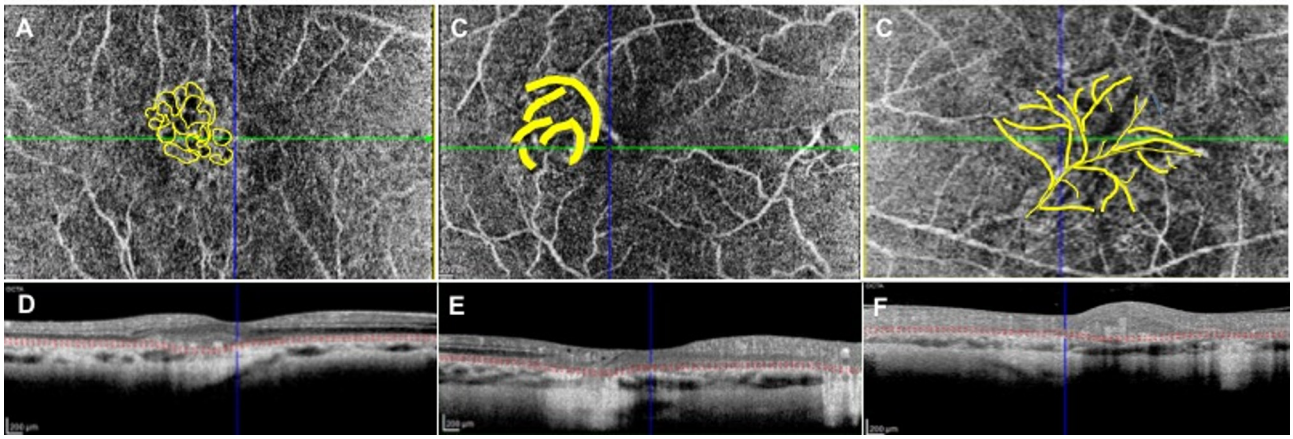

Figure 2 Images of optical coherence tomography angiography (OCTA) of different vessel shapes (yellowish marked). (A) 'Lacy wheel' vessel of patient #3, (B) 'pruned large-trunk' vessels of patient #1 and (C) 'dead tree aspect' small and large vessels of patient #4. OCTA, optical coherence tomography angiography.

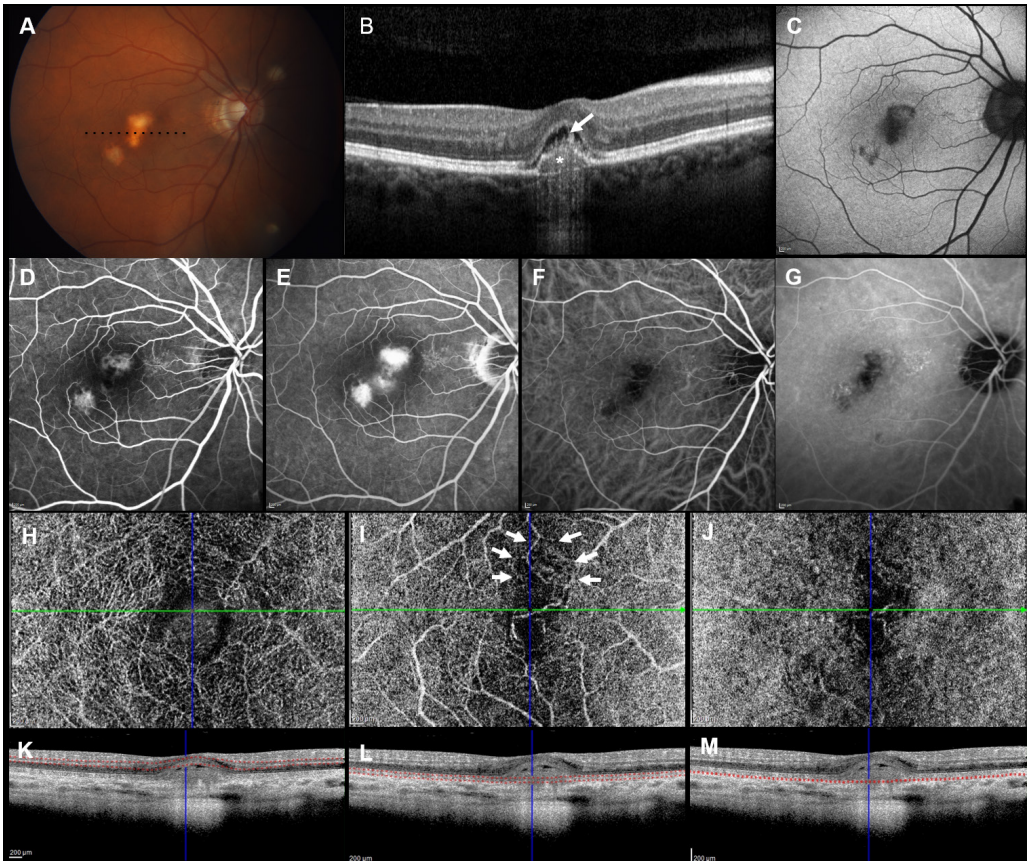

Figure 3 Images of fundus photography, SD-OCT, FA, ICGA, FAF and OCTA of patient #20. (A) Fundus picture reveals a subfoveal choroidal neovascularisation (dashed lines). (B) SD-OCT showing a fibrovascular membrane (asterisk) above RPE with disruption of RPE and subretinal collection of fluid (white arrow). (C) The FAF detects the RPE defects. (D) intermediate and (E) late phase of FA; fluoresceine hyperfluorescence with leakage is visible. (F) Intermediate and (G) late phase of ICGA showing corresponding hypofluorescent round areas. (H) The corresponding OCTA showing sickle-shape non-perfused areas in the superficial capillary layer. One filamentous vessel with surrounded non-perfused area is revealed in the deep capillary layer (I) and in the outer retina (white arrows) **(J).** (K,L,M) Corresponding B-scan. This eye was classified into active, recurrent state. FA, fluorescein angiography; FAF, fundus autofluorescence; ICGA, indocyanine green angiography; OCTA, optical coherence tomography angiography; RPE, retinal pigment epithelium; SD-OCT, spectral-domain optical coherence tomography

correlation between vessel shape and disease activity (p=0.075). More hypoperfused/non-perfused areas were detected on OCTA in 'lacy wheel shape' vessels than in 'pruned large-trunk' vessels and 'dead tree aspect' vessels (X^2 test: p=0.04). And more hypoperfused/non-perfused areas were seen in cases of recurrence (X^2 test: p=0.0001).

DISCUSSION

In this study, we characterised punctate inflammatory lesions and CNV in 20 patients with PIC using OCTA, and standard multimodal imaging techniques.

Funduscopic features of PIC are isolated inflammatory lesions which occur at the level of the outer retina, RPE and choriocapillaris.[3] It can often be difficult to distinguish CNV from isolated punctate inflammatory lesions. Channa *et al* found that most lesions (89%) revealed involvement of the RPE.[11] In our cohort, a total of eight eyes (40%) showed punctate lesions, of which seven (88%) were involved the RPE, such as RPE elevation overlying an intact Bruch's membrane. No leakage was observed for any of these eyes on FA, while 50% of these eyes showed staining and 38% eyes a window defect on FA, suggesting that these lesions are inactive. In this study, eyes with punctate lesions did not present with a surrounding hyper-fluorescent halo on FAF, which has been proposed as a sign of disease activity.[8] But all eyes presented with hypofluorescent atrophic areas on FAF.

On OCTA, all eyes with punctate lesions revealed capillaries with crippled whitening, which may be indicative of erythrocyte accumulation in this area. Moreover, areas of non-perfusion/hypoperfusion in the choriocapillaris were detected, which normally would not have been seen on standard imaging modalities. A recent study investigated MFC using OCTA, suggesting that OCTA imaging shows lack of flow in the outer retina and the choriocapillaris for inactive lesions. In active lesions, OCTA imaging indicated the presence of a small highly organised dense high-flow neovascular network in the outer retina.[12]

We also characterised CNV lesions using OCTA and standard multimodal imaging techniques. The risk of CNV development is the most common and visual-threatening complication of patients with PIC and its prevalence significantly varies between studies. Similar to results of this study, Gerstenblith *et al* reported that 69% of 77 patients with PIC were diagnosed with CNV.[5] In our study, 60% of PIC eyes had a clinical course complicated by CNV. We classified CNVs based on three disease activity grades 'recurrence', 'residual fluid' and 'stable'. In addition, we described the CNV type, because several publications postulated that inflammatory CNV are usually of classic CNV type 2.[7 13–15]

Table 4 Classification of disease activity

Clinical assessment n=eyes (%)	Recurrence n=5 (21)	Residual fluid n=3 (13)	Stable n=16 (67)
SD-OCT			
Intraretinal fluid	4 (80)	2 (67)	2 (13)
Hyper-reflective material			
Above RPE	5 (100)	3 (100)	7 (44)
Below RPE			5 (31)
Above and below RPE			4 (25)
FA*			
Leakage	4 (80)	1 (33)	
Staining			7 (44)
Window defect		2 (67)	9 (56)
OCTA†			
Hypoperfusion			
No vessels			2 (13)
One filamentous vessel	1 (20)		
Lacy wheel shape	3 (60)	2 (67)	2 (13)
Pruned large-trunk vessel	1 (20)	1 (33)	2 (13)
Dead tree aspect			9 (60)

*No FA in one patient.
†No OCTA in one eye.
FA, fluorescence angiography; OCTA, optical coherence tomography angiography; SD-OCT, spectral-domain OCT.

In our cohort, 63% of eyes revealed subretinal hyper-reflective material above the RPE of which 46% had a disrupted RPE. In 21% of eyes, hyper-reflective material was detected below RPE while 17% of eyes presented with both types. Interestingly, eyes with disease activity on SD-OCT revealed hyper-reflective material above the RPE compared with stable eyes, which showed hyper-reflective material below the RPE. Eyes with macular scaring presented with both types of RPE disruptions.

OCTA imaging offered the opportunity to characterise the morphology of CNV types, in detail. Kuehlwein *et al* analysed type 1 neovascular membranes in age-related macular degeneration on OCTA. In their study, 72% of eyes presented with vessels radiating in branching patterns ('medusa' or 'seafan' pattern) from the large main central trunk/feeder vessels.[16] Based on the study of Coscas *et al*, we identified and stratified different CNV patterns/shapes.[9] 'Lacy wheel shape', 'pruned large-trunk vessels' or just hypoperfusion with one vessel formation were represented in active diseases, while most stable eyes presented with 'dead tree aspect' vessels. Moreover, 'lacy wheel shape' and 'pruned large-trunk' vessels were found above the RPE, whereas 'dead tree aspect' vessels were observed below the RPE. A recently published study by Astroz *et al* looked only for subretinal or intraretinal fluid on FA and OCT in patients with MFC, prior to OCTA analysis. The authors did not observe a statistically significant difference in terms of morphological features such as collaterals, peripheral arcades and dark halo between active and inactive CNVs on OCTA.[12] Similar to our results, Zahid *et al* reported that sub-RPE lesions did not reveal neovascular flow on OCTA. The authors further suggest that the development of CNV in MFC is intrinsically linked to the integrity of the RPE.[17] This group also mentioned that the understanding of the pathophysiology of MFC is difficult due to different treatment strategies. The benefit of OCTA in characterising punctate and CNV lesions could be a useful tool for monitoring and quantifying the response of CNV to treatment.[2 18 19] To our knowledge, there are currently only two published studies which include patients with PIC characterised on OCTA. One is a case series which includes only 7 patients with PIC and the other was a case report.[2] Therefore, further studies are necessary to characterise patients with PIC and to evaluate long-term changes of vasculature observed on OCTA imaging, particularly as related to treatment.

This study provides important information about the morphology of isolated punctate lesions and CNV in patients with PIC. It is the largest cohort of eyes with PIC and OCTA imaging currently reported in the literature. However, the study has several limitations. We reported data from single time points, the sample size is limited and there is a lack of overall inequality of the individuals regrading to previous treatment types and their onset of PIC. Furthermore, while OCTA imaging continues to have limitations, the OCTA images used in this study may have been prone to even more considering that the software and hardware used were both prototypes. For this reason, the OCTA images may present with more than typical projection artefacts, motion artefacts, segmentations errors and poor signal strength. Our imaging was also limited to the macular region and, therefore, isolated punctate lesions outside this area were not characterised. OCTA imaging has since evolved significantly, and the OCTA imaging capabilities of the Spectralis have been significantly improved, perhaps mitigating many of these limitations.

In conclusion, our findings suggest that OCTA is a useful imaging modality to complement the existing standard multimodal imaging techniques in order to delineate isolated punctate lesions and CNV vessel shapes in patients with PIC.

Contributors DP: conception and design, analysis and interpretation; overall responsibility. DP, SW and UP: data collection. SW, UP and AMJ: review.

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Patient consent Obtained.

Ethics approval Ethic comité Charité.

Provenance and peer review Not commissioned; externally peer reviewed.

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