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CORRESPONDENCE

Comment on: 'Paracentral acute middle maculopathy and acute macular neuroretinopathy following SARS-CoV-2 infection'

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TO THE EDITOR:

We read with interest Virgo et al.'s article which reported one case each of paracentral acute middle maculopathy (PAMM) and typical acute macular neuroretinopathy (AMN) following Covid-19 infection [1]. We would like to report two symptomatic patients with bilateral findings of AMN following Covid-19 infection and one patient who developed unilateral AMN 3 weeks following Covid-19 vaccination (Pfizer-BioNTech vaccine). All these cases were serologically positive for Covid-19 antibody.

CASE 1

A 59-year-old male with type 2 diabetes mellitus presented with bilateral sudden onset of blurry vision, preceded by typical Covid-19 symptoms 2 weeks prior. On examination, his corrected visual acuity (CVA) was 6/9 in both eyes. Ocular examination was unremarkable. Optical coherence tomography (OCT) revealed bilateral hyper-reflective bands in the outer plexiform layer (OPL) associated with loss of volume in the outer nuclear layer (ONL) and disruption to the ellipsoid zone, appearance suggestive of AMN (Fig. 1a, b). At 6 weeks follow-up, the blurry vision had resolved subjectively but OCT appearance remained unchanged.

CASE 2

A 24-year-old, fit and well female patient reported 2-week history of paracentral scotomas in both eyes, preceded by typical Covid-19 symptoms 1 week before onset. CVA was 6/6 in both eyes. Examination revealed perifoveal dark gray patches. OCT changes were similar to Case 1 (Fig. 1c, d). A diagnosis of AMN was made. Unfortunately, her symptoms did not improve and OCT findings were unchanged 4 months later.

CASE 3

A 54-year-old male with well-controlled type 2 diabetes mellitus who was a low myope, presented with sudden onset of photopsias and a small scotoma in his left eye, 3 weeks after the first dose of Covid-19 vaccination (Pfizer-BioNTech). CVA was 6/6 in both eyes. Fundal examination demonstrated an orange–brown oval-shaped lesion supero-temporal to the fovea with no other retinal pathology. OCT revealed a hyper-reflective band in the OPL and disruption of the interdigitation/ellipsoid zone, consistent with AMN (Fig. 1e). At 2 months follow-up,

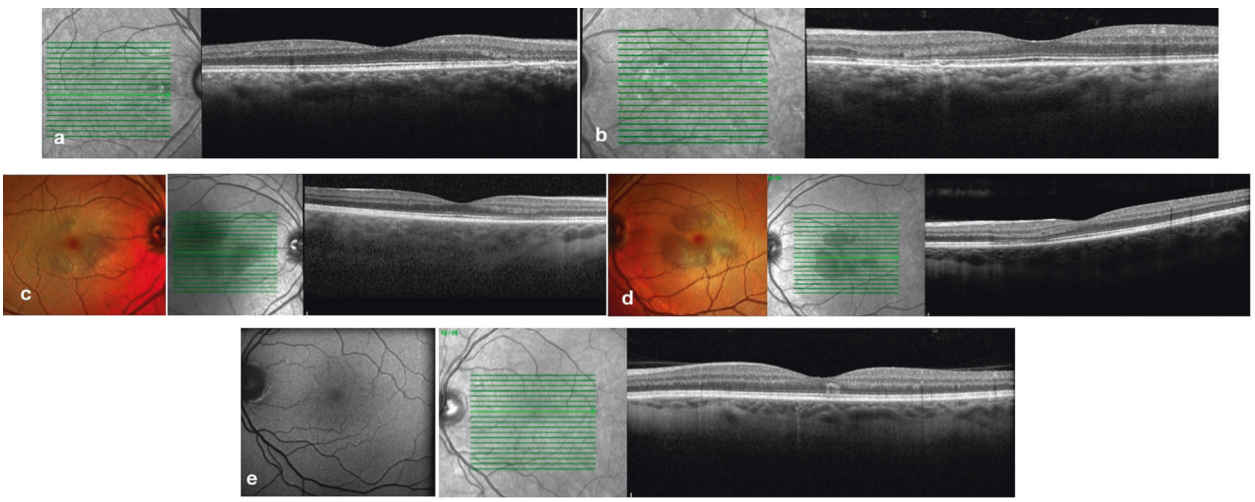

Fig. 1 Fundoscopic and Optical Coherence Tomography findings in patients with Covid-19-related AMN. a, **b** Case 1. Optical coherence tomography (OCT): bilateral hyper-reflective bands in the outer plexiform layer (OPL) associated with loss of volume in the outer nuclear layer (ONL) and disruption to the ellipsoid zone in right eye (RE) and left eye (LE), respectively, **c**, **d** Case 2. Fundus photograph shows RPE changes. Infrared fundus photography reveals dark gray perifoveal lesions and OCT scans show thickening of the OPL and volume loss in the ONL nasal to the fovea associated with disruption of the interdigitation zone in RE and LE, respectively, **e**: Case 3. LE Fundus autofluorescence appears normal while OCT demonstrates hyper-reflective band at the level of OPL.

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Table 1. AMN/PAMM associated with Covid-19.

Author	Journal - date of publication	No of cases	Age sex	Presenting symptoms	VA	Other findings	Diagnosis
Diafas et al.	Eye - 06/2021	3	59/M	Bilateral decreased VA	6/9	RPE changes	Typical AMN
			24/F	Bilateral paracentral scotoma	6/6 (BE)	Parafoveal RPE changes	Typical AMN
			54/M	LE Paracentral scotoma/spot & photopsia	6/6	Orange-brown atrophic oval-shaped area in the macula	Typical AMN
Giacuzzo et al. [4]	Acta Ophthalmol - 05/2021	1	23/F	Bilateral paracentral scotoma & photopsia, LE dyschromatopsia	6/6 (BE)	Bilateral hyporeflective petaloid-shaped lesion around the fovea shown on NIR	Typical AMN
Preti et al. [5]	Retin Cases Brief Rep - 05/2021	1	70/M	LE paracentral scotoma	6/30	Inferonasal parafoveal lesion	Typical AMN
Aidar et al. [6]	Am J Case Rep - 04/2021	1	71/F	LE decreased VA	6/19	Foveal pigment mobilization Hypofluorescent fovea surrounded by irregular hyperfluorescent defects on FFA	Typical AMN
Sim et al. [7]	Br J Ophthalmol - 03/2021	11	N/A	No symptoms	Normal	2/11 patients showed CWS & microhaemorrhages	Other
Turedi et al. [8]	Eur J Ophthalmol - 02/2021	1	54/M	RE vision loss	CF (30 cm)	-	CRAO & PAMM
Paddy et al. [9]	BMJ Case Rep - 02/2021	1	19/F	Bilateral acute-onset scotoma	6/12 RE 6/38 LE	CWS	PAMM
Zamani et al. [10]	J Ophthalmic Inflamm Infect - 01/2021	1	35/F	RE paracentral scotoma & photopsia	6/6	Roth spots	AML & Typical AMN
Komro et al. [11]	Ophthalmol Case Rep - 01/2021	1	34/M	RE acute paracentral scotoma	Normal	Dark oval lesion inferonasal to the fovea shown on NIR	Typical AMN
Gascon et al. [12]	Ocul Immunol Inflamm - 11/2020	1	53/M	LE paracentral scotoma, Dyschromatopsia, Decreased VA	6/19	Deep retinal haemmorrhages, Roth spots	Typical AMN & PAMM
Zago Filho et al. [13]	Ocular Immunol Inflamm - 11/2020	1	57/F	Bilateral conjunctival hyperemia	6/7.5 RE 6/6 LE	Vitritis, yellowish macular lesion, hyperfluorescence on FFA	Other
Virgo et al. [1]	Eye - 07/2020	2	37/F	LE paracentral scotoma	Normal	Fundus normal	PAMM
			32/M	RE paracentral scotoma	Normal	Fundus Normal	Typical AMN
Marinho et al. [14]	Lancet - 05/2020	12	N/A	No symptoms	Normal	4/12 patients showed CWS & Microhaemorrhages	Other

M male, *F* female, *VA* visual acuity, *RPE* retinal pigment epithelium, *AMN* acute macular neuroretinopathy, *RE* right eye, *LE* left eye, *BE* both eyes, *NIR* near infrared, *FFA* fundus fluorescence angiography, *CWS* cotton wool spots, *PAMM* paracentral acute middle maculopathy, *CF* counting fingers, *CRAO* central retinal artery occlusion, *AML* acute myeloid leukemia.

patient remained symptomatic but macular OCT showed complete resolution of the hyper-reflective band.

DISCUSSION

All of our patients presented with different severity of symptoms but retinal findings were consistent with the diagnosis of typical AMN [2], two following serologically proven Covid-19 infection, and one following Covid-19 vaccination. There have been several reports in the literature documenting AMN/PAMM in patients infected with Covid-19 (Table 1) but to the best of our knowledge there has been no other reports of this condition following Covid-19 vaccination. It did appear that the OCT changes in Case 3 following Covid-19 vaccination were less severe and demonstrated complete resolution, compared to Case 1 and Case 2. Further post-vaccination reports are needed before any relationship can be implicated to vaccination.

While the pathophysiology of AMN is not clear, a microvascular etiology seems to be implicated [2]. Although a true association between AMN/PAMM and Covid-19 infection remains unclear, microangiopathy and microvascular occlusion have been described in patients infected by Covid-19 [3]. Further studies are required to understand the link between AMN and COVID-19. Reporting vigilance should apply to cases of AMN/PAMM after Covid-19 vaccination.

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AUTHOR CONTRIBUTIONS

All authors contributed to the study conception and design. Patient's examination, diagnosis and treatment were performed by Dr Nima Ghadiri, Prof Ian Pearce and Dr Shi Zhuan Tan. The original draft of the manuscript was written by Dr Asterios Diafas. Dr Diafas also conducted a thorough literature search. Dr Nicholas Beare contributed to data collection and presentation. Dr Shi Zhuan Tan and Dr Savita Madhusudhan supervised research activity planning and execution. All authors read, commented, and approved the final version of the manuscript.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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