OPTICAL COHERENCE TOMOGRAPHY ANGIOGRAPHY-CONFIRMED PARACENTRAL ACUTE MIDDLE MACULOPATHY ASSOCIATED WITH SARS-COV-2 INFECTION

Running title: PAMM and COVID-19

Rajesh DESHMUKH1 FRCS, Antony RAHARJA2 MBBS, Farzana RAHMAN1 FRCOPht and Harry PETRUSHKIN1 FRCOPht

1Moorfields Eye Hospital, London, UK
2Guy’s and St Thomas’ NHS Foundation Trust, London, UK
*Equally contributing co-first author

Corresponding author: Rajesh Deshmukh, Moorfield Eye Hospital, London, UK
+44 7800 756704, Rajesh.Deshmukh@nhs.net

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A 56-year-old Caucasian woman presented to the emergency department with a three-week history of acute painless sudden-onset paracentral visual field defect in her left eye associated with a new-onset ipsilateral headache.

Her past medical history includes a three-year history of type 2 diabetes mellitus, on single-agent therapy with metformin 1g twice daily. Her blood pressure was 135/78 mmHg on 8mg perindopril. There was no personal or family history of eye pathologies. She regularly attended the Diabetic Eye Screening Programme with no previous history of diabetic retinopathy (R0) or macular oedema (M0).

On the basis of her visual loss and headache, she was started on daily 60mg oral prednisolone by the medical team for presumed giant cell arteritis and admitted for further investigation and ophthalmology input. Her visual acuity was 6/6 in both eyes, with normal colour vision and no relative afferent pupillary defect. She demonstrated left paracentral visual field scotoma (supplementary fig 1). Ophthalmic examination of the left eye revealed parafoveal retinal whitening with no evidence of intraocular inflammation. Optical coherence tomography (OCT) showed corresponding hyper-reflective bands at the level of the outer plexiform layer (OPL) and inner nuclear layer (INL) in the left eye (Figure 1A and B, yellow arrows). Fundus autofluorescence showed parafoveal hypoautofluorescence. OCT angiography (OCT-A) demonstrated corresponding ischaemia within the superficial and deep retinal plexi (Figure 1C and 1D respectively). Fundus fluorescein and indocyanine green angiography were normal. Blood tests including ESR, anti-cardiolipin antibody, lupus anticoagulant and anti-β2
glycoprotein I were normal. She was tested positive for SARS-CoV-2 on reverse-
transcriptase polymerase chain reaction test of nasopharyngeal swab taken on
admission, but had not been unwell with fever, cough, dyspnoea, malaise or anosmia.
Magnetic resonance imaging of the brain and orbit including venography was normal.
Carotid ultrasound showed bilateral mild atheroma plagues at carotid bulb and
internal carotids but blood flow on Doppler was not impaired.

Given the findings from ophthalmic investigations and the absence of another
identifiable cause, her visual defect was attributed to SARS-CoV-2 infection related
PAMM. Her symptoms remained unchanged after 1 week and prednisolone was then
discontinued as giant cell arteritis was deemed unlikely. Her symptom remained stable
with persistent visual field defect at 3 and 12 months.

To our knowledge, this is the first case of OCT-A proven retinal ischaemia associated
with SARS-CoV-2 infection. Previous case series of 12 visually asymptomatic
labatory-confirmed SARS-CoV-2 individuals reported inner retinal hyperreflective
bands in despite normal OCT-A.(1) Concerns about these findings have raised in
another article.(2) Another case series by Virgo et al reported PAMM in two patients
presenting with new paracentral scotoma weeks following SARS-CoV-2 infection but
did not utilise OCT-A to assess retinal vasculature.(3) Our case report adds to the
currently limited literature supporting the association between SARS-CoV-2 and
PAMM. In particular, the use of OCT-A confirms the retinal findings to be true
pathological finding of an ischaemic nature. This may be due to capillary non-perfusion
and focal ischaemia induced by SARS-CoV-2-related hypercoagulable state.(4) The localised retinal capillary ischaemia at the level of superficial and deep plexi presents as hyper-reflective bands at the outer plexiform and inner nuclear layers, characteristic of PAMM.(5) Additionally, the absence of intraocular signs of inflammation and non-response to high dose steroids in this case made inflammatory, vasculitic or postinfectious autoimmune aetiology less likely. Larger studies are required to ascertain this association and pathophysiology underlying PAMM in SARS-CoV-2 infection.
Ethics statement: This study has been evaluated by the Research Management Committee of Moorfields Eye Hospital (reference number CaRS_17). Ethics approval was deemed not required for this study, and patient’s written approval was obtained for this case report.
REFERENCES:


**Figure Legends:**

**Figure 1:** Optical coherence tomography (OCT) of the left eye showing hyperreflective bands at the outer plexiform layer and inner nuclear layer (A and B). OCT angiography showing superficial (C) and deep (D) retinal plexi.
**Supplementary Figure 1:** Scotoma charting on Amsler grid, at reading distance of approximately 35cm, demonstrating left paracentral visual field scotoma.
Statement of Authorship

1. Category 1:
   a) Conception and design
      RD, AR
   b) Acquisition of data
      RD, AR
   c) Analysis and interpretation of data
      RD, AR, FR, HP

2. Category 2:
   a) Drafting the manuscript
      RD, AR
   b) Revising it for intellectual content
      RD, AR, FR, HP

3. Category 3:
   a) Final approval of the completed manuscript
      RD, AR, FR, HP