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Acute posterior multifocal placoid pigment epitheliopathy following COVID-19 infection☆

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ABSTRACT

Purpose: To report a case of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) following COVID-19 infection.

Observations: A 17-year-old female developed central scotomas and photopsias two weeks after SARS-CoV-2 diagnosis with polymerase chain reaction studies. She presented with poor visual acuity of 3/60 on the Feinbloom eye chart in the left eye. Dilated examination and multi-modal retinal imaging were consistent with the diagnosis of APMPPE, with noteworthy subretinal fluid. The patient was treated with an oral prednisone taper starting at 60mg with rapid resolution in subretinal fluid and improvement of visual acuity. Five weeks after presentation, visual acuity improved to 20/20 OU with complete resolution of the creamy white choroidal lesions and subretinal fluid.

Conclusion: There is a growing body of literature reporting the ocular manifestations of COVID-19. Rarely inflammation of the retina or choroid have been associated with the infection. To the best of our knowledge, there are no prior reports that describe the clinical course or visual outcome in a patient with APMPEE associated with recent COVID-19 infection. Accordingly, we are not aware of any other reports that describe the treatment of APMPEE associated with COVID-19 with corticosteroids. The mechanism linking COVID-19 infection to inflammatory ocular disorders in unclear and likely multi-factorial.

1. Introduction

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), the novel coronavirus responsible for a global pandemic since December 2019, primarily affects the respiratory system but has been associated with extra-pulmonary manifestations. Systemic effects of coronavirus disease 2019 (COVID-19) are likely a result of endothelial disruption, complement activation, and generalized inflammation leading to a procoagulant state and microvascular damage.[1] It is estimated that 11.3% of patients have ocular manifestations of COVID-19 with conjunctivitis comprising the majority of ocular disease (88.8%).[2,3] A small but growing number of publications demonstrate vitreoretinal involvement of COVID-19. A recent review confirmed the majority of retinal findings in COVID-19 patients were from microvascular changes at all levels of the retina including cotton wool spots, flame-shaped hemorrhages, retinal vein occlusions, paracentral acute middle maculopathy (PAMM), and acute macular neuroretinopathy (AMN).[4–6] Rarely, inflammation involving the retina or the choroid, can be seen.[6–11]

We present a case of acute posterior multifocal placoid pigment epitheliopathy (APMPPE) that occurred 2 weeks after COVID-19 infection.

2. Case report

A 17-year-old healthy Caucasian female presented with 3 days of a central scotoma and photopsias. Prior medical and ocular history were unremarkable. Two weeks preceding visual symptoms, she experienced fever, cough, shortness of breath, myalgias and subsequently tested positive for SARS-CoV2 by polymerase chain reaction (PCR) testing.

A complete ophthalmological exam was performed. Her best corrected visual acuity (BCVA) was 20/20–2 in the right eye (OD) and 3/60 on the Feinbloom eye chart in the left eye (OS). Anterior segment

☆ All authors attest that they meet the current ICMJE criteria for Authorship.

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Abbreviations

ACE-2	angiotensin-converting enzyme 2 receptor
AMN	acute macular neuroretinopathy
APMPPE	acute posterior multifocal placoid pigment epitheliopathy
BCVA	best corrected visual acuity
CBC	complete blood count
COVID-19	coronavirus disease 2019
EZ	ellipsoid zone
FA	fluorescein angiography
FTA-ABS	fluorescent treponemal antibody test absorption test
IRF	intraretinal fluid
MRI	magnetic resonance imaging
mRNA	messenger ribonucleic acid
OCT	Optical Coherence Tomography
OCT-A	OCT-Angiography
OD	right eye
OS	left eye
OU	both eyes
PAMM	paracentral acute middle maculopathy
PCR	polymerase chain reaction
SARS-CoV-2	severe acute respiratory coronavirus-2
TMPRSS	transmembrane serine protease

biomicroscopy, pupillary reflexes and intraocular pressure were normal in both eyes (OU). Dilated fundus exam and fundus imaging revealed a flat choroidal nevus in the right eye and 1+ vitreous cell in the left eye with multiple large yellow-white placoid lesions within the posterior pole and a blunted foveal reflex (Fig. 1). Optical Coherence Tomography (OCT) scans were normal in the right eye and demonstrated disruption of the ellipsoid zone (EZ) with marked subretinal fluid in the nasal macula as well as intraretinal fluid (IRF) extending into the fovea (Fig. 2). Fluorescein Angiography (FA) demonstrated early hypofluorescence (blockage) corresponding to the placoid lesion with late hyperfluorescence (staining) in the left eye. Indocyanine Green Angiography (ICG) showed a temporal focus of hypocyanescence of the right eye and diffuse patchy hypocyanescence of the central macula of the left eye. Laboratory evaluation demonstrated negative QuantiFERON-TB gold, non-reactive fluorescent treponemal antibody test absorption test (FTA-ABS), and complete blood count (CBC) was within normal limits. The constellation of clinical findings and imaging were consistent with acute posterior multifocal placoid pigment epitheliopathy. Magnetic resonance imaging (MRI) with and without contrast was performed and was negative for cerebral vasculitis. The patient was treated with an oral prednisone taper starting at 60 mg daily with subsequent improvement in subretinal fluid and visual acuity. Five weeks after presentation, visual acuity improved to 20/20 OU with complete resolution of the creamy white choroidal lesions and subretinal fluid (Fig. 2).

3. Discussion

There is a growing body of research reporting ocular manifestations of COVID-19. Most of the current literature encompasses common findings including conjunctivitis, chemosis, and dynamic vascular changes such as AMN and PAMM. Rarely, inflammation of the retina or choroid have been associated with infection.

We report a case of macular dysfunction two weeks after PCR confirmed COVID-19 infection. Clinical course and multi-modal imaging correlate well with previous descriptions of APMPPE, albeit with quite noteworthy SRF as compared to most cases of APMPPE. Subretinal fluid is an unusual finding, but its rapid resolution is consistent with prior literature.[12,13] To the best of our knowledge, this is the second reported case of APMPPE following COVID-19 infection, but the first to describe the full clinical course and visual outcome.[11] Olguín-Manríquez et al. reported unilateral APMPPE six weeks after presumed COVID-19 infection as diagnosed by positive SARS-CoV-2 IgG antibody testing, but did not discuss treatment or report the final visual acuity. Similarly, there are reports of bilateral ampiginous and serpiginous choroiditis following COVID-19 infection. In both cases, there was evidence of chronic, inactive punched out retinal lesions indicating COVID-19 infection may serve as an immunologic trigger for the development or reactivation of ocular disease in susceptible hosts. Our case did not have evidence of prior retinal disease.[9,14]

The exact pathogenesis of APMPPE is controversial. When Gass first described APMPPE in 1968, he attributed the placoid lesions to direct inflammation of the retinal pigment epithelium (RPE).[15] Evidence from multi-modal imaging and OCT-Angiography (OCT-A) studies suggest a focal choroidal vasculitis and choriocapillaris hypoperfusion precede the characteristic placoid lesions.[16–20] In addition, the systemic associations of the disease suggest an underlying vasculitis. A viral prodrome has been reported in up to one-third of cases with prior studies showing an association with mumps, Coxsackievirus B, and Adenovirus type 5 titers.[16,21–23] APMPPE has also been found to occur following influenza, varicella, hepatitis B and recently COVID-19 messenger ribonucleic acid (mRNA) vaccinations.[24–28]

The mechanism linking COVID-19 infection to inflammatory ocular disorders in unclear. One theory is COVID-19 injures tissue via direct infection. The SARS-CoV-2 coronavirus has been demonstrated to gain cell entry via the angiotensin-converting enzyme 2 receptor (ACE-2) in the presence of transmembrane serine protease (TMPRSS). ACE-2

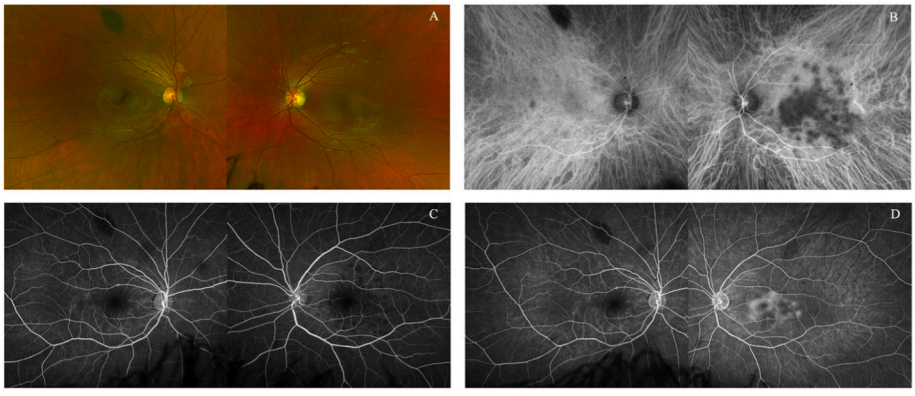

Fig. 1. Multi-modal retinal imaging in a patient with APMPPE following COVID-19 infection. A: wide-field color fundus photos of the right and left eye. The right eye is unremarkable in A, C, and D. A: The left eye demonstrates subtle yellow-white placoid lesions within the posterior pole. B: Late phase indocyanine green (ICG) angiography reveals a single focus of patchy hypocyanescence of the right eye and large areas of patchy hypocyanescence and choroidal perfusion defects of the left eye. C: Early phase fluorescein angiography (FA) demonstrates hypofluorescent blocking of the lesions. D: Subsequent late phase FA shows hyperfluorescent staining classic for APMPPE. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

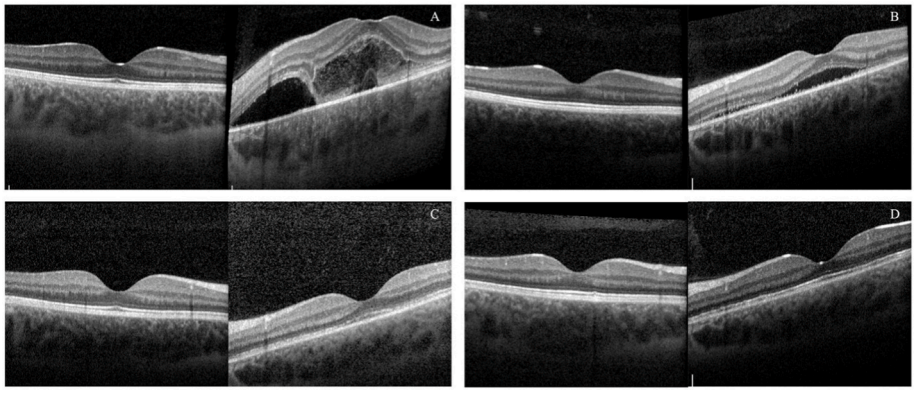

Fig. 2. Serial Optical Coherence Tomography scans of the right and left eye. Right eye is unremarkable in A-D. A: B-scan OCT foveal scans demonstrate significant subretinal and intraretinal fluid within and nasal to the fovea. There is marked disruption of the outer retinal architecture and a thickened choroid. B: One week after diagnosis and initiation of prednisone therapy, OCT shows interval improvement but residual subretinal fluid and choroidal thickness. There continues to be disorganization of the outer retinal layers. C: Three weeks after diagnosis and treatment there, OCT reveals resolution of subretinal fluid and scattered focal irregularities of the ellipsoid zone and external limiting membrane. D: OCT at five weeks shows normal retinal architecture with persistent focal irregularities of the ellipsoid zone.

receptors are expressed in the retinal ganglion cell layer, inner plexiform layer, inner nuclear layers, and photoreceptor outer segments.[5] TMPRSS is also expressed in retinal neuronal cells, vascular and perivascular cells, and Müller glia.[29] Indeed, SARS-CoV-2 RNA has been confirmed by PCR in retina biopsies of deceased patients.[30] Additionally, COVID-19 infection, either by direct infection or molecular mimicry, may trigger a vascular hyperinflammation and endothelial damage leading to a thromboembolic event and reduced choroidal perfusion.[5]

Regardless of the mechanism, there appears to be a component of choroidal inflammation. There is no consensus data on the use of corticosteroids in patients who present with APMPPE as there are no prospective randomized controlled trials. However, corticosteroids or immunosuppressive therapy have been advocated to expedite recovery and decrease chorioretinal scarring.[31] Given the severity of visual deficit and recent COVID-19 infection, our patient was treated with a taper of oral prednisone with a good visual outcome. Tom et al. report a case of bilateral ampiginous choroiditis following COVID-19 infection who maintained visual acuity of 20/20 in both eyes after 3-months of a prednisone taper and maintenance on azathioprine. A case report by Atas et al. demonstrated complete visual recovery in a patient with APMPPE following COVID-19 vaccination without steroid therapy.[24] To the best of our knowledge there are no prior reports that describe the clinical course or visual outcome in a patient with APMPPE associated with recent COVID-19 infection. Accordingly, we are not aware of any other reports that describe the treatment of APMPPE associated with COVID-19 with corticosteroids.

4. Conclusion

We report a case of APMPPE associated with recent SARS-CoV-2 infection with complete visual recovery. A consensus understanding of incidence, pathophysiology, and management is still needed.

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Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

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