



# Case Report: Acute Macular Neuroretinopathy Which Led to COVID-19 Infection Diagnosis

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## Abstract

We present a case of Acute Macular Neuroretinopathy (AMN), which led to the coronavirus disease of 2019 (COVID-19) infection diagnosis. A 27-year-old female patient with flu-like symptoms later proven to be COVID-19 infection presented with acute-onset bilateral gray-like paracentral scotomas. Fundus examination showed a hypopigmented, wedge-like lesion on the superior temporal juxtafoveal area in the right eye, while no significant finding was found in the left eye. Infrared reflectance images demonstrated bilateral hyporeflective lesions in the parafoveal regions of the macula. Spectral-domain optical coherence tomography scans over the corresponding areas detected focal hyperreflectivity in the outer nuclear layer with disruption in the ellipsoid zone and retinal pigment epithelium layers. Based on these findings, the AMN diagnosis was considered. The COVID-19 infection diagnosis was confirmed by a polymerase chain reaction test. COVID-19 disease may cause retinal vascular complications such as AMN. AMN, which shares common viral prodromal symptoms with COVID-19 infection, may be a presenting sign of COVID-19 infection.

**Keywords:** Acute macular neuroretinopathy, coronavirus, COVID, COVID-19, SARS-CoV-2

## Introduction

Acute macular neuroretinopathy (AMN) is a rare condition of unknown etiology that most commonly affects young to middle-aged white females (1). Several associations or risk factors have been identified in patients with AMN. The most commonly reported associations are recent nonspecific flu-like illness or fever, oral contraceptive use, exposure to either epinephrine or ephedrine and antecedent trauma (1,2). This disease can be variable presentation. Most typically, it presents with the acute onset of one or multiple paracentral scotomas that affect one or both eyes. Symptoms differ in frequency and persistence. The etiology and pathogenesis of the disease remain unclear (1). Full resolution of scotomas

has never been reported. Some scotomas partially resolve; some do not resolve at all. However, there are no reports of this disease-causing meaningful vision loss. There is no proven treatment for the condition (1).

Only a handful of cases of coronavirus disease in 2019 (COVID-19) and AMN association were recently reported in the literature (3-7). In this paper, we report a case of AMN that led to COVID-19 infection diagnosis.

## Case Report

A 27-year-old female patient presented with an acute onset of bilateral, grey-like paracentral scotomata and a 3-day history of COVID-19 susceptible symptoms, including fever and nasal discharge. No previous remarkable history of ocular

**How to cite this article:** Guleser UY, Chehab Z, Kesim C, Hasanreisoglu M. Case Report: Acute Macular Neuroretinopathy Which Led to COVID-19 Infection Diagnosis. *Beyoglu Eye J* 2023; 8(4): 293-296.

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**Submitted Date:** February 21, 2023 **Revised Date:** March 08, 2023 **Accepted Date:** June 01, 2023 **Available Online Date:** December 01, 2023

*Beyoglu Eye Training and Research Hospital - Available online at [www.beyoglueye.com](http://www.beyoglueye.com)*

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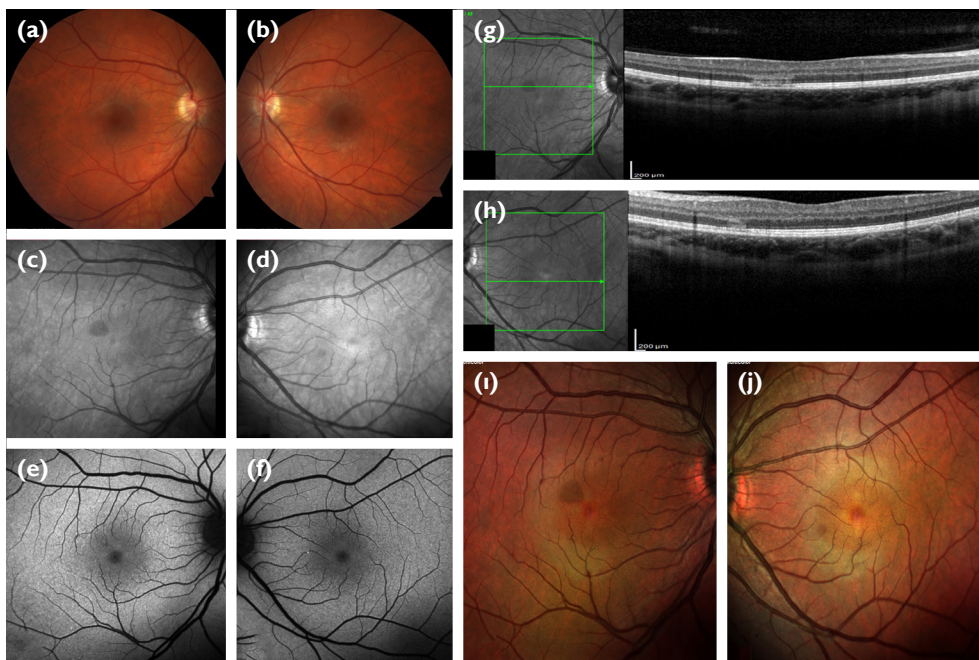


or systemic disease was present. The best-corrected visual acuity was 20/20 on the Snellen chart for both eyes. The patient was able to draw two paracentral scotomata that she had been experiencing over a blank sheet of white paper. A biomicroscopic examination was found normal, with no sign of anterior chamber or vitreous inflammation. Fundus examination revealed a hypopigmented, wedge-like lesion on the superior temporal juxtafoveal area in the right eye (RE) (Fig. 1a), while no significant finding was found in the left eye (LE) (Fig. 1b). Infrared reflectance images revealed bilateral hyporeflective, well-circumscribed lesions in parafoveal regions of the macula (Figs. 1c and d). Spectral domain optical coherence tomography (SD-OCT) (Heidelberg Spectralis HRA + OCT MultiColor, Germany) scans over the corresponding area detected focal hyperreflectivity in the outer nuclear layer (ONL) with disruption on the ellipsoid zone (EZ) and retinal pigment epithelium layers (Figs. 1g and h). Fundus autofluorescence imaging at presentation showed subtle macular hypoautofluorescence on the lesion area in RE and no significant finding in LE (Figs. 1e and f). Multicolor imaging showed a hyporeflective parafoveal wedge-like

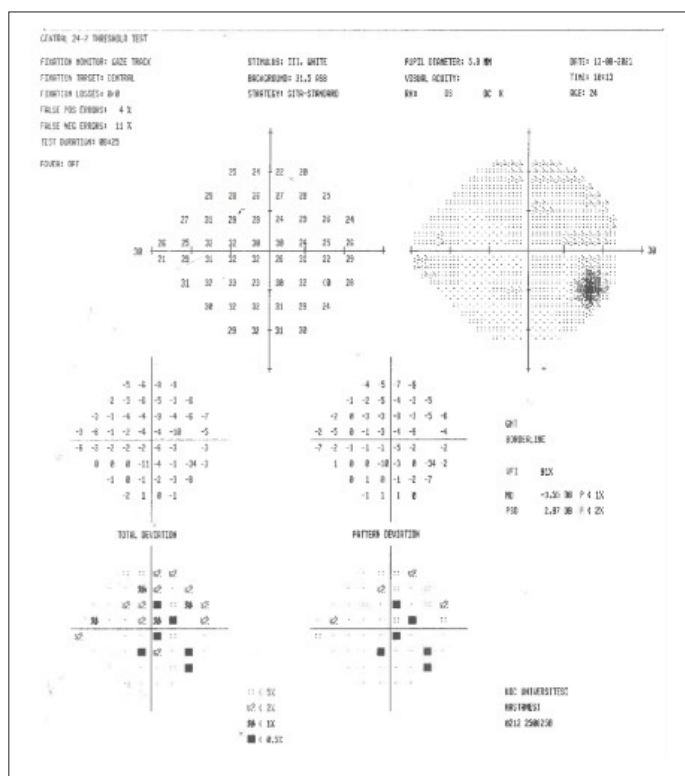
lesion in RE corresponding to the lesion area and a small parafoveal well-circumscribed lesion in LE corresponding to the lesion area (Figs. 1i and j). Humphrey visual field 24-2 testing confirmed bilateral paracentral scotomata (Figs. 2 and 3). Fluorescein angiography was recommended for the patient. However, the patient refused due to anxiety about the intravenous access procedure. Based on the present findings, the patient was diagnosed with acute macular neuroretinitis and referred to infectious disease clinics for further evaluation. The patient was confirmed to have a COVID-19 infection following an oral and nasal swab test for polymerase chain reaction. She was treated conservatively. At her follow-up 1 month later, her symptoms improved, and her SD-OCT showed focal thinning in the ONL and disruption in the EZ where the lesions were present.

## Discussion

AMN is a rare retinal disorder whose pathogenesis remains unknown. A vascular theory has been proposed based on the nature of the precipitating factors and the anatomical localization of pathology. It is currently thought to be a result



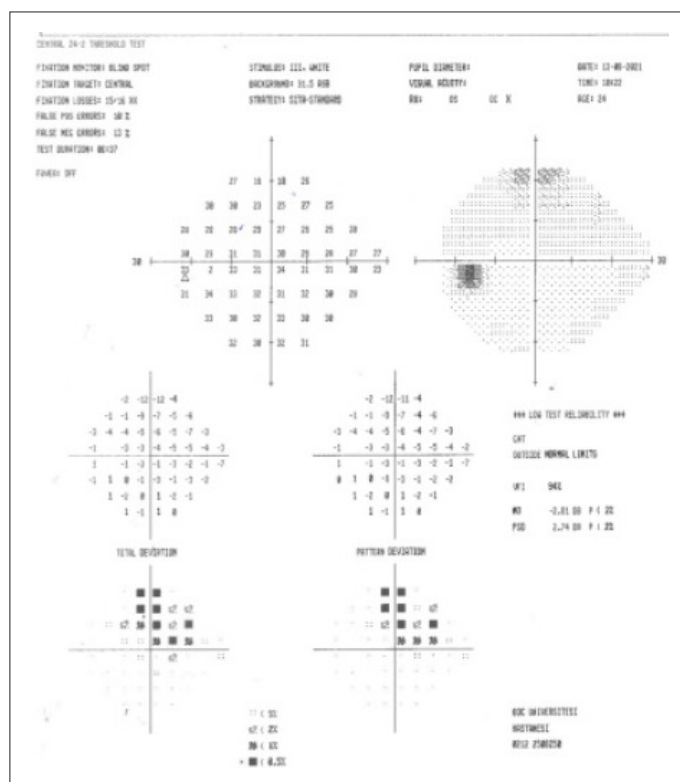
**Figure 1.** Multimodal imaging of both eyes. **(a)** Color fundus photograph (CFP) of RE showing hypopigmented, wedge-like lesion on the superior temporal juxtafoveal area **(b)** CFP of LE showing no apparent pathology. **(c and d)** Infrared (IR) reflectance images revealed hyporeflective, well-circumscribed parafoveal lesion corresponding to the lesion area in RE **(c)** and LE **(d)**. **(e and f)** Fundus autofluorescence (FAF) of right **(f)** showed subtle macular hypoautofluorescence in the lesion area, and FAF of LE **(e)** showed no significant finding. **(g and h)** Spectral-domain optical coherence tomography (OCT) RE **(g)** and LE **(h)** showing focal hyperreflectivity in the outer nuclear layer (ONL) with disruption on ellipsoid zone and retinal pigment epithelium (RPE) layers. **(i)** Multicolor imaging of RE showing hyporeflective circumscribed wedge-like lesion on the superior temporal juxtafoveal area **(j)** Multicolor fundus imaging of LE showing hyporeflective small wedge-like lesion on the inferior nasal juxtafoveal area.



**Figure 2.** Paracentral scotomata in the visual field for the right eye.

of ischemia of the deep capillary plexuses and may theoretically be seen in any patient with retinal vascular disease or systemic vasculopathic risk factors (8). COVID-19 is caused by a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that was first documented in Wuhan, China. This ribonucleic acid (RNA) virus has been known to cause a proinflammatory and hypercoagulable state that leads to multiple systemic complications, including respiratory failure, myocardial infarction, deep venous thromboembolism, and cerebrovascular events with profound morbidity and mortality (9).

Angiotensin converting enzyme-2 (ACE2), an essential cell membrane enzyme, is the main receptor for SARS-CoV-2 entry into the cell (10,11). Beside lung type II alveolar cells, ACE2 is mainly found in arterial and venous endothelial cells and arterial smooth muscle cells in most organs (12). ACE2 has been found in the human retina as well as ACE, the homologous enzyme of ACE2, which has been reported to be present in the choroid and different cell types of the retina, such as Muller cells and retinal vessel endothelial cells (13). Therefore, SARS-CoV-2 may be implicated in causing AMN as there are receptors for the virus associated with the retinal tissues. It was also reported that SARS-CoV-2 viral RNA was detected in the retina of deceased COVID-19 patients (14). The infection with the virus may cause a hypercoagulable state and result in ischemia of the deep capillary plexuses, which precipitates in AMN.



**Figure 3.** Paracentral scotomata in the visual field for left eye despite high fixation losses.

Many case reports are now emerging in the literature that link cases of AMN with COVID-19 patients (3-7). In a recent retrospective observational study done by Azar et al., (15) they noticed a significant increase in the incidence of AMN admitted to hospitals during the COVID-19 pandemic in 2019-2020. Masjedi et al. (6) 2021 reported a case of a 29-year-old woman with a chief complaint of experiencing acute-onset paracentral visual field defect 2 weeks after being diagnosed with COVID-19. SD-OCT demonstrated the disruption of the inner segment/outer segment junction in the LE. Our patient had the visual symptoms at an earlier onset from the course of the disease within a few days, and she had them bilaterally in both eyes with similar SD-OCT findings. Gascon et al. (3) presented a case of possible combined AMN and paracentral acute middle maculopathy (PAMM) findings in a male patient with COVID-19 infection. The patient had unilateral decreased visual acuity, a paracentral scotoma, many deep retinal hemorrhages, Roth spots, and subretinal fluid. However, it can be thought that the presence of multiple retinal hemorrhages, subretinal fluid, and Roth spots may be due to unilateral diffuse retinal vascular involvement rather than AMN or PAMM. David and Fivgas (5) 2021 reported a case of a 22-year-old female with bilateral scotomas concurrent with a mildly symptomatic COVID-19 infection. She had normal visual acuity, bilateral reddish-brown petaloid retinal

lesions that were hyporeflexive on near-infrared optical coherence tomography, and associated hypoperfusion of the deep vascular plexus on OCT-angiography (OCT-A) consistent with bilateral AMN. Our patient had a similar clinical presentation. However, their patient was using oral contraceptive medication, which is also a risk factor for AMN. Our patient was not using any sort of medication. In the previously presented cases, AMN was determined in a patient with a recent diagnosis of COVID-19 infection. In our patient, the first presentation was visual symptoms without a COVID-19 diagnosis. Considering the accompanying flu-like symptoms to the visual symptoms, how rare AMN is, and its incidence increasing after the COVID pandemic, we thought that the underlying cause might be the COVID-19 infection. Finally, in the current case, the ocular examination and diagnosis of AMN led to the diagnosis of COVID-19 infection, which in turn led to the social isolation of the patient and the prevention of further dissemination of the virus.

## Conclusion

In conclusion, our case report adds to the literature that the hypercoagulable state associated with COVID-19 disease may cause retinal vascular complications such as AMN. On the other hand, both sharing the same common viral prodromal symptoms, AMN may be a presenting sign of COVID-19 infection. This association should be kept in mind when evaluating patients with decreased visual acuity with suspected ophthalmic disease.

## Disclosures

**Informed consent:** Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – M.H.; Design – M.H.; Supervision – M.H.; Data collection and/or processing – Z.C., Ü.Y.G.; Analysis and/or interpretation – C.K.; Literature search – Ü.Y.G.; Writing – Z.C., Ü.Y.G.; Critical reviews – M.H., C.K.

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