



A Case of Concurrent Acute Macular Neuroretinopathy and Paracentral Acute Middle Maculopathy Following Pfizer-BioNTech COVID-19 Vaccination

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Abstract

We present a 65-year-old woman who developed sudden and severe vision loss in her left eye one day after the administration of the second dose of COVID vaccine. The best corrected visual acuity in this eye was 1/10. Diffuse paracentral acute middle maculopathy was detected on spectral domain optical coherence tomography (OCT). OCT angiography images revealed concurrent vascular flow defects consistent with acute macular neuroretinopathy in the deep retinal capillary plexus and choriocapillaris layers. At the end of the six-month follow-up, there was no improvement in visual acuity, and atrophy and thinning developed in all layers of the retina.

Keywords: Acute macular neuroretinopathy, optical coherence tomography angiography, paracentral acute middle maculopathy, Pfizer-BioNTech COVID-19 vaccine, spectral domain optical coherence tomography

Introduction

Since December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which caused the coronavirus disease (COVID-19) pandemic, has caused many deaths and serious morbidity worldwide. In the last months of 2020, the US Food and Drug Administration (FDA) issued emergency use permits for some vaccines, and accelerated vaccine campaigns were launched in many countries. Following the widespread administration of COVID-19 vaccines produced using different technologies, reports also emerged of various vaccine-related systemic and ocular adverse effects.^{1,2,3,4}

There are a few cases in the literature related to the retinal complications of vaccines. Among these, cases of acute macular neuroretinopathy (AMN), paracentral acute middle maculopathy (PAMM), and retinal artery and vein occlusions are most common, and most occurred after the administration of inactivated virus and adenovirus-vector COVID-19 vaccines, with fewer cases observed in association with messenger RNA (mRNA) vaccines.^{1,2,3,4,5,6,7,8}

First described as a variant of AMN (type I AMN) by Sarraf et al.⁹ in 2013, PAMM is a retinal finding characterized by sudden-onset paracentral scotomas and a focal or diffuse hyperreflective band-like lesion in the inner nuclear layer (INL) and inner plexiform layer (IPL) above the outer plexiform layer (OPL) on spectral domain optical coherence tomography (SD-OCT). Although it may be idiopathic, it has often been reported to develop secondary to retinal vascular diseases such as diabetic and hypertensive retinopathy, retinal artery and vein occlusion, or a systemic disease, and ischemia in the middle and/or deep retinal capillary plexus has been implicated in its pathogenesis.^{9,10,11,12}

Cite this article as: Menteş J, Nalçacı S, Değirmenci C. A Case of Concurrent Acute Macular Neuroretinopathy and Paracentral Acute Middle Maculopathy Following Pfizer-BioNTech COVID-19 Vaccination. *Turk J Ophthalmol* 2023;53:186-191

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Received: 02.09.2022 Accepted: 23.02.2023

DOI: 10.4274/tjo.galenos.2023.65118

To the best of our knowledge, this article is the first published report of a case of AMN and concomitant PAMM presenting with sudden and severe vision loss and in one eye immediately after Pfizer-BioNTech COVID-19 vaccination, with multimodal imaging features including optical coherence tomography angiography (OCTA).

Case Report

A 65-year-old female medical doctor presented with complaints of sudden-onset central vision loss and blotchy vision in her left eye starting 4 hours earlier. The patient reported receiving a second dose of the Pfizer-BioNTech vaccine the day before, the first dose of Pfizer-BioNTech vaccine 3 months before this vaccine, and two Synovac vaccines 6 and 8 months earlier. She had a history of drug-controlled diabetes mellitus, stage 1 hypertension, stage 1 chronic kidney disease, alcohol drinking habit, and low water intake.

Her best corrected visual acuity (BCVA) was 10/10 in the right eye and 1/10 in the left eye (with head movement), and intraocular pressure (IOP) was 12 mmHg in both eyes. On slit-lamp examination, the anterior segment and fundus of both eyes appeared normal.

On infrared (IR) imaging of the left eye, there was a lobular-appearing hyporeflective lesion in the parafoveal area that covered the entire macula (Figure 1A). Short-wavelength (488 nm) blue fundus autofluorescence (FAF) imaging also revealed lobular, markedly hypoautofluorescent areas in the left eye corresponding to the lesion area in IR images (Figure 1B). On fluorescein angiography (FA), all phases and filling times were normal in the left eye (Figure 1C, D). On SD-OCT of the left eye, a diffuse band of hyperreflectivity and thickening in the INL and IPL above the OPL was detected in the parafoveal area and was more pronounced on the nasal side. A band of hyporeflectivity and granular appearance were also detected just below these areas in the outer nuclear layer (ONL), external limiting membrane (ELM), and ellipsoid zone (EZ). In the INL, 1-2 small intraretinal cysts were observed (Figure 1E). In the en face OCTA images, the foveal avascular zone in the left eye was noted to be irregular and slightly enlarged (Figure 1F) and there were concurrent marked vascular flow defects in the deep retinal capillary plexus and choriocapillaris (Figure 2A, B). The areas of flow defect were consistent with the lesion areas seen in IR and FAF. In addition, there was a marked decrease in vascular density and increased retinal thickness in the deep retinal capillary plexus in the parafoveal region on OCTA (Figure 2C).

Although IR, FAF, FA, OCT, and en face OCTA imaging in the right eye (Figure 3A, B, C, D, E, F) were completely normal, small vascular flow defects were observed in the deep retinal capillary plexus on OCTA, while no flow defects were detected in the choriocapillaris and vascular density was found to be normal in the deep retinal layers (Figure 4A, B, C).

The presumed diagnosis for the left eye was diffuse PAMM with microvascular obstructions in the capillary beds of the deep retinal layers and choriocapillaris associated with the

Pfizer-BioNTech vaccine. Treatment was initiated with an IOP-lowering agent (timolol-dorzolamide combination eye drops twice daily; Tomec drops, Abdi İbrahim Pharmaceuticals, Istanbul, Turkey), an antiaggregant (acetylsalicylic acid 100 mg/day; Coraspin tablet, Bayer Türk Chemical Co., Istanbul, Turkey), a vasodilator (pentoxifylline 400 mg twice daily; Trental tablet, Sanofi Health Products Ltd. Sti., Istanbul, Turkey), a corticosteroid (prednisolone 32 mg/day; Prednol tablet, Mustafa Nevzat Pharmaceuticals, Istanbul, Turkey), and vitamin C (500 mg/day), and ample fluid consumption was recommended. Consultations with the infectious diseases, cardiology, hematology, nephrology, and genetics units, thrombophilia panel, hemogram and D-dimer tests, and carotid Doppler ultrasonography were requested as etiological studies. As a result of all examinations, it was determined that the patient's comorbidities were under control and she had no genetic predisposition to thrombophilia.

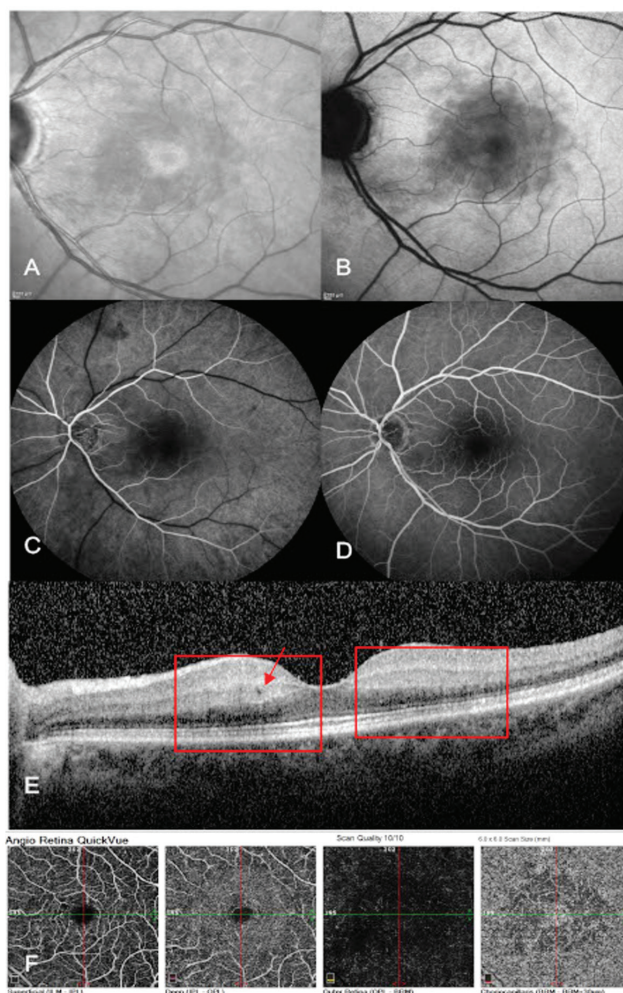


Figure 1. Left eye, initial examination. A) Infrared photography; B) fundus autofluorescence; C,D) fluorescein angiography, early and late phase; E) spectral domain optical coherence tomography showing diffuse hyperreflectivity and thickening of the inner plexiform and inner nuclear layers and hyporeflectivity and granular appearance in the outer retinal layers (red square) with a cyst in the inner nuclear layer (red arrow); F) en face optical coherence tomography angiography

The patient was followed up weekly at first and later at 15-day and 30-day intervals for 6 months.

At 6-month follow-up, BCVA was still 1/10 in the left eye, IR and FAF images were normal, collateral vessels had formed in the optic nerve head, and FA demonstrated filling of these vessels in the arterial phase, with no leakage (Figure 5A-D). In the SD-OCT examination, in addition to atrophy and thinning in all retinal layers, the hyporeflective and granular appearance in the ELM and EZ persisted in the parafoveal area (Figure 5E). On OCTA imaging, the flow defects in the choriocapillaris had resolved while those in the deep retinal capillary plexus persisted (Figure 5F, 6A, B, C).

Discussion

To the best of our knowledge, this article is the first published report of a case of AMN presenting with sudden and severe vision loss and concomitant diffuse PAMM with vascular flow defects in the deep retinal capillary plexus in one eye immediately after receiving the Pfizer-BioNTech recombinant mRNA COVID-19 vaccine, with a description of multimodal imaging features including OCTA.

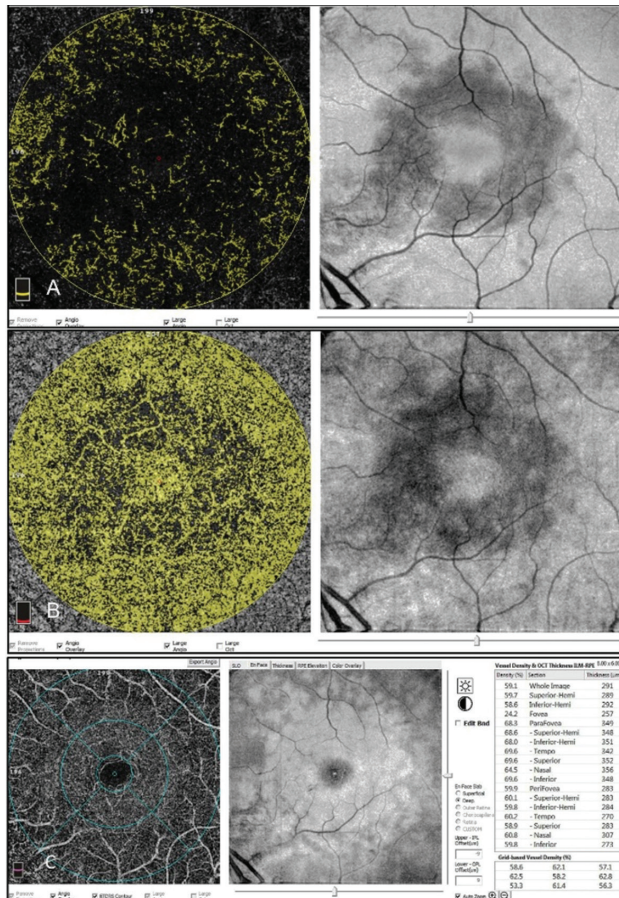


Figure 2. Left eye, optical coherence tomography angiography at initial examination. A) deep retinal capillary plexus vascular flow defects; B) choriocapillaris vascular flow defects; C) deep retinal capillary plexus vascular density changes

Although many instances of PAMM and AMN after receiving inactivated virus and adenovirus-vector COVID-19 vaccines have been documented in the literature, only one case of PAMM and two cases of AMN after the Pfizer-BioNTech COVID-19 vaccine have been described.¹⁻⁸ There is no report of AMN and PAMM developing concomitantly in the same eye. In a case of PAMM described by Ishibishi et al.,⁶ complaints occurred on day 7 after the second dose of Pfizer-BioNTech vaccine, visual acuity was perfect, the lesion was focal, and OCTA imaging was not performed. Similarly, AMN cases reported in association with the Pfizer-BioNTech vaccine appeared on days 2 and 8 after the second dose of vaccine, visual acuities were well preserved, and lesions were focal.^{1,6}

Although PAMM and AMN are regarded as two distinct clinical entities both characterized by sudden-onset paracentral

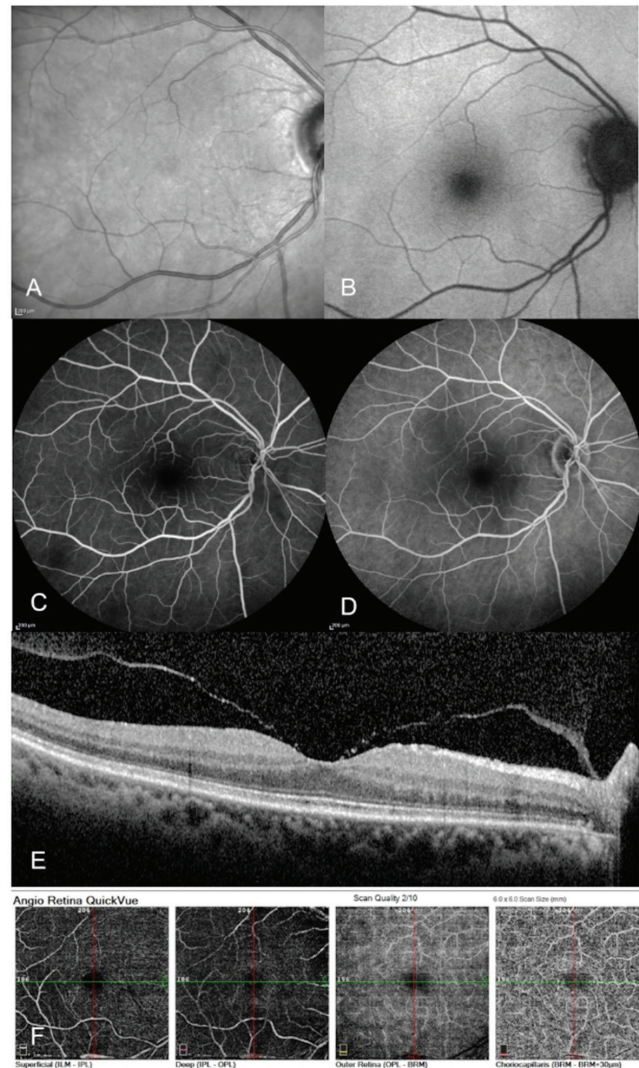


Figure 3. Right eye, initial examination. A) infrared photography; B) fundus autofluorescence; C,D) fluorescein angiography, early and late phase; E) spectral domain optical coherence tomography; F) en face optical coherence tomography angiography

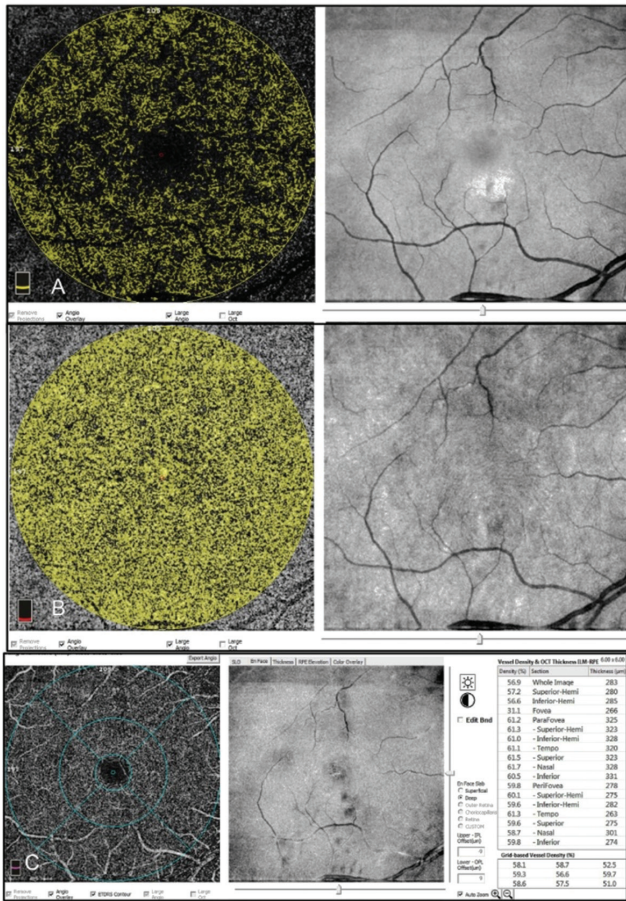


Figure 4. Right eye, optical coherence tomography angiography at initial examination. A) deep retinal capillary plexus vascular flow; B) choriocapillaris vascular flow; C) deep retinal capillary plexus vascular density

scotomas and hyporeflective paracentral lesions on IR imaging, Sarraf et al.⁹ reported in 2013 that there were actually two variants of AMN, PAMM being one of them, and they named PAMM “type I AMN.” They named the other variant, in which only the outer retinal layers (i.e., the ONL and EZ) are affected, type II AMN. To date, a case of AMN and PAMM occurring simultaneously in the same eye has not been described in the literature. Therefore, we think that our case could be defined as a new variant, type III AMN (combined AMN), in addition to the type I and II AMN variants defined by Sarraf et al.⁹

Our case was accompanied by sudden and severe vision loss, and SD-OCT imaging demonstrated PAMM as a diffuse hyperreflective band appearing on both sides of the central macula. In the literature, it has been emphasized that if PAMM is diffuse, it may be a symptom of latent or reperfused central retinal artery occlusion (CRAO).^{10,12,13} However, the absence of signs consistent with CRAO on fundus examination or SD-OCT imaging, the normality of arterial filling time as well as all phases and the peripheral retina on FA, and the presence of vascular flow defects in the choriocapillaris, which has a different circulatory supply, were data that led us away from a diagnosis of latent or reperfused CRAO in our case.

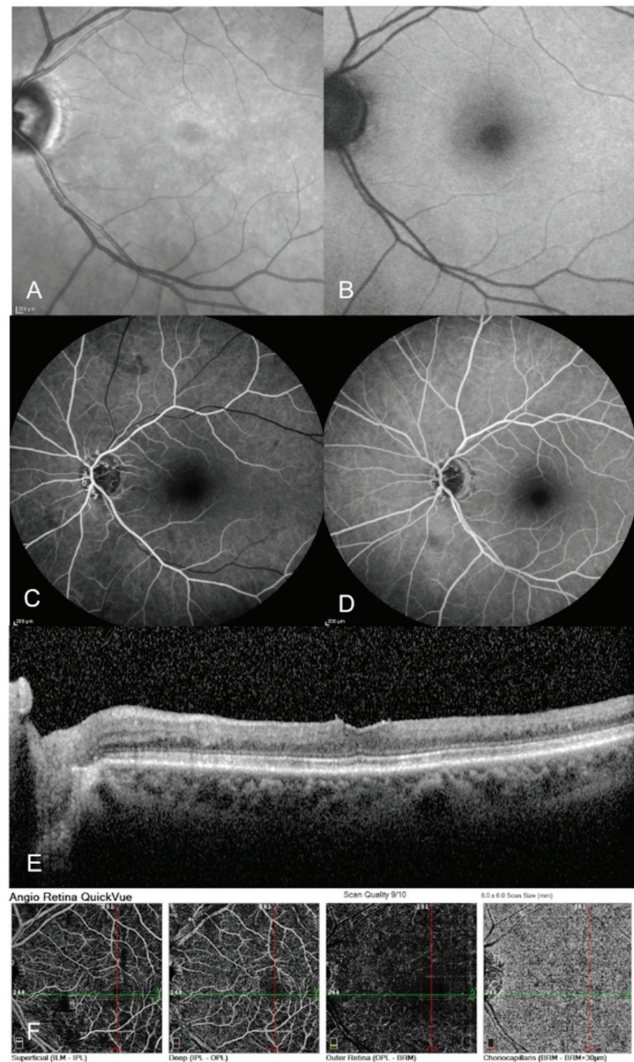


Figure 5. Left eye, 6 months later. A) infrared photography; B) fundus autofluorescence; C,D) fluorescein angiography, early and late phase; E) spectral domain optical coherence tomography; F) en face optical coherence tomography angiography

The SD-OCT images of our patient showed a hyporeflective and granular appearance in the outer retinal layers in the parafoveal region just below the PAMM lesions. Sarraf et al.⁹ reported that in PAMM (i.e., type I AMN), hyperreflectivity in the middle layers may be associated with a corresponding finding in the outer retinal layers, which they attributed to a shadowing effect. However, in our patient’s 6-month SD-OCT images, the PAMM-related hyperreflectivity had resolved and the entire retina was atrophic and thinned, but the hyporeflective and granular appearance in the outer retinal layers persisted. This cannot be explained by the shadowing effect, thus leading us to believe the appearance of the outer retinal layers was a sign of disease involvement in these layers.

OCTA is a new, non-invasive, and reproducible imaging technique that enables evaluation of the vascular structures of the

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