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Acute macular neuroretinopathy following Pfizer-BioNTech COVID-19 vaccination

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ABSTRACT

Purpose: To describe a case of acute macular neuroretinopathy (AMN) in a patient immediately following administration of the Pfizer-BioNTech COVID-19 vaccine.

Observations: The patient complained of paracentral scotoma supported by paracentral visual field loss on multiple Humphrey visual fields that corresponded to outer retinal pathology on optical coherence tomography. The patient's symptoms resolved without treatment.

Conclusions and Importance: We conclude that the clinical testing demonstrated findings consistent with AMN. AMN may be an exceedingly rare adverse ocular effect of a novel vaccine and likely only in the setting of multiple other risk factors. Despite this, we strongly recommend vaccination against COVID-19.

1. Introduction

Since December 2019, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the cause of the coronavirus disease 2019 (COVID-19) pandemic, has led to excessive mortality and morbidity. Since late 2020, an accelerated distribution of vaccine has begun, with several vaccines granted emergency use authorization by the U.S. Food and Drug Administration (FDA). We describe a case of acute macular neuroretinopathy (AMN) in a patient immediately following administration of the Pfizer-BioNTech COVID-19 vaccine. This patient had no previous known ophthalmic medical history. Clinical testing demonstrated visual field and optical coherence tomography (OCT) findings consistent with AMN. This case brings awareness to the potential ocular side effects of a novel vaccine.

2. Case report

A previously healthy 20-year-old female college student presented for photopsias and scotomata in both eyes 48 hours after receiving her second dose of the Pfizer-BioNTech COVID-19 vaccine. The patient stated that 12–24 hours after receiving her second dose of the vaccine, she developed myalgias, headache, and bilateral anterior cervical and supraclavicular lymphadenopathy. Symptoms evolved to include difficulty swallowing. She presented to a walk-in clinic and was treated empirically with 60mg oral prednisone and 50mg diphenhydramine. While her generalized symptoms subsequently improved, she developed paracentral "black spots" and shimmering lights several hours later prompting presentation to the emergency department. Her medical history was only significant for use of etonogestrel/ethinyl estradiol 0.12–0.015 mg/24 hr vaginal ring for birth control. She was examined by the ophthalmology consult service. Snellen visual acuity was measured at 20/20 in both eyes. There was no relative afferent pupillary defect or dyschromatopsia. Intraocular pressure was physiologic and slit-lamp and dilated fundus examinations were unrevealing. She had no focal neurological deficits and was discharged.

In the ophthalmology clinic, six days after receiving the vaccine, the patient described persistent bilateral paracentral scotomata. Her visual acuity remained 20/20 in both eyes. Both eyes were white and quiet and there was no evidence of anterior chamber or vitreous inflammation. Dilated fundus examination was unrevealing, with no hemorrhages, retinal vascular sheathing, retinal or choroidal lesions, and normal appearance of the optic nerve head. A Humphrey Visual Field 10–2 confirmed the presence of bilateral paracentral scotomata (Fig. 1). Optical coherence tomography (OCT) demonstrated corresponding parafoveal foci of outer nuclear layer hyperreflectivity with granularity of the underlying ellipsoid (Fig. 2). One week later, repeat visual field testing (10–2) showed stable bilateral paracentral scotomata and scanning laser ophthalmoscopy revealed hyporeflective foci typical for acute macular neuroretinopathy (AMN) (Figs. 1 and 2). She returned the following week with complete resolution of scotomata and headache.

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3. Discussion

AMN is an uncommon retinal vascular disorder that predominantly affects young, non-Latino white women. AMN is thought to result from ischemia to the deep retinal capillary plexus due to viral, immunologic, and hypercoagulable etiologies.[1] Patients typically present with para-central scotomata, photopsias, and mild vision loss. Visual acuity is 20/40 or better acuity in 80.8% of cases.[1] The findings may be bilateral in as many as 54.4% of patients and scotomata are usually permanent. On fundus examination, there may be characteristic wedge-shaped retinal lesions that are described as petaloid, oval, or teardrop in shape. The lesions are often red-brownish or orange in color and may be better appreciated with near-infrared reflectance imaging.

This disorder has been associated with flu-like illness, fever, and oral contraceptive use. Rarer associations include exposure to epinephrine or ephedrine, antecedent trauma, shock, intravenous contrast media, pre-eclampsia, post-partum hypotension, and caffeine consumption. Cases of AMN immediately following influenza vaccines have been

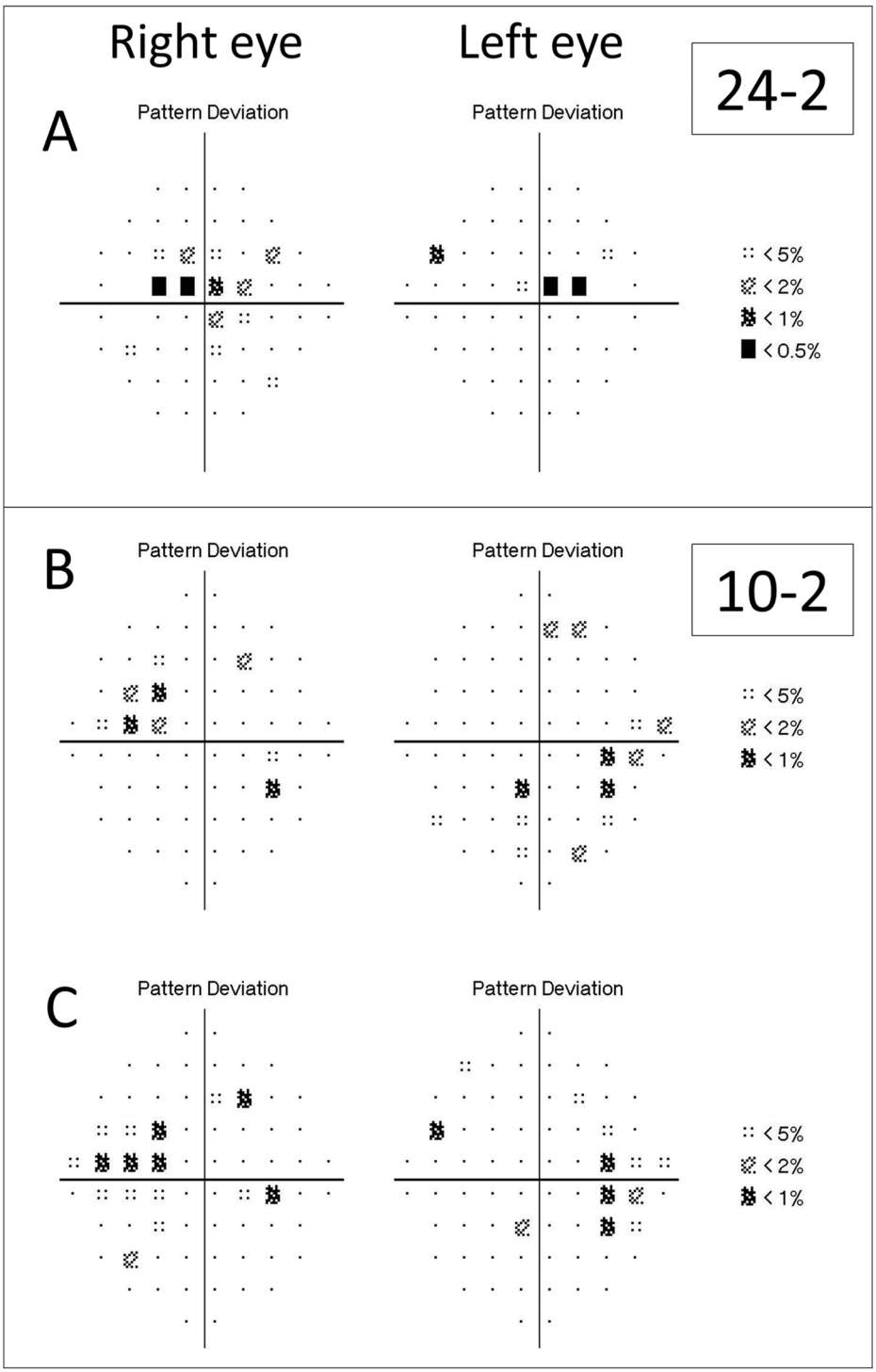

Fig. 1. Series of Humphrey Visual Fields. A series of Humphrey Visual Fields of the right and left eyes done on post-vaccination day 6 (A–B) and day 13 (C). Humphrey Visual Field 24–2 with good reliability and central depression (A). Humphrey Visual Field 10–2 with good reliability showing bitemporal depressed points worse in the right eye (B) and stable on repeat exam one week later (C).

reported.[2,3] However, to our knowledge this is the first known case of acute macular neuroretinopathy following vaccination with the Pfizer-BioNTech COVID-19 vaccine. And while our patient harbored several risk factors for AMN, including her age, sex, race, and her use of hormonal contraception, the temporal association of her symptoms with her vaccination and her systemic immunological symptoms point toward an association. It is also possible that the vaccine may have only triggered the episode of acute macular necrosis due to the patient's underlying risk factors, especially given her reaction is not common with the vaccination.

The Pfizer-BioNTech COVID-19 vaccine is a mRNA vaccine. It is found to be 95% effective 28 days after the first dose. The phase III trial evaluated 170 confirmed cases of COVID-19, 162 of which were observed in the placebo group. There were 10 severe cases, nine of which were in the placebo group.[4] Others have postulated that the immunogenicity of COVID-19 vaccines could potentially induce ophthalmic antibody-dependent enhancement with ocular adverse effects.[5] As of this date, the Vaccine Adverse Event Reporting System (VAERS) has 285 instances of visual adverse events including vision blurred (178), visual impairment (91), visual field defect (15), and abnormal visual tracking test (1).[6]

4. Conclusions

Given the millions of doses of the Pfizer-BioNTech COVID-19 vaccine that have already been given to date, it is likely that this patient's adverse reaction is rare. In addition, the effect was transient and we are unsure they are causative given this patient's underlying risk factors. While additional reports are needed to confirm the association, this case adds to the knowledge of immunologic sequelae after COVID-19 vaccination, as well as vaccinations more broadly. Despite this finding, we strongly recommend vaccination against COVID-19.

Patient consent

The patient provided consent to use her de-identified images and clinical history for education and publication.

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Declaration of conflicts of interest

The authors have no disclosures to report.

Authorship

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

Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Author agreement statement

The submission, or parts of it, is not currently submitted elsewhere for publication. All coauthors and acknowledged parties have read and approved the final revised manuscript.

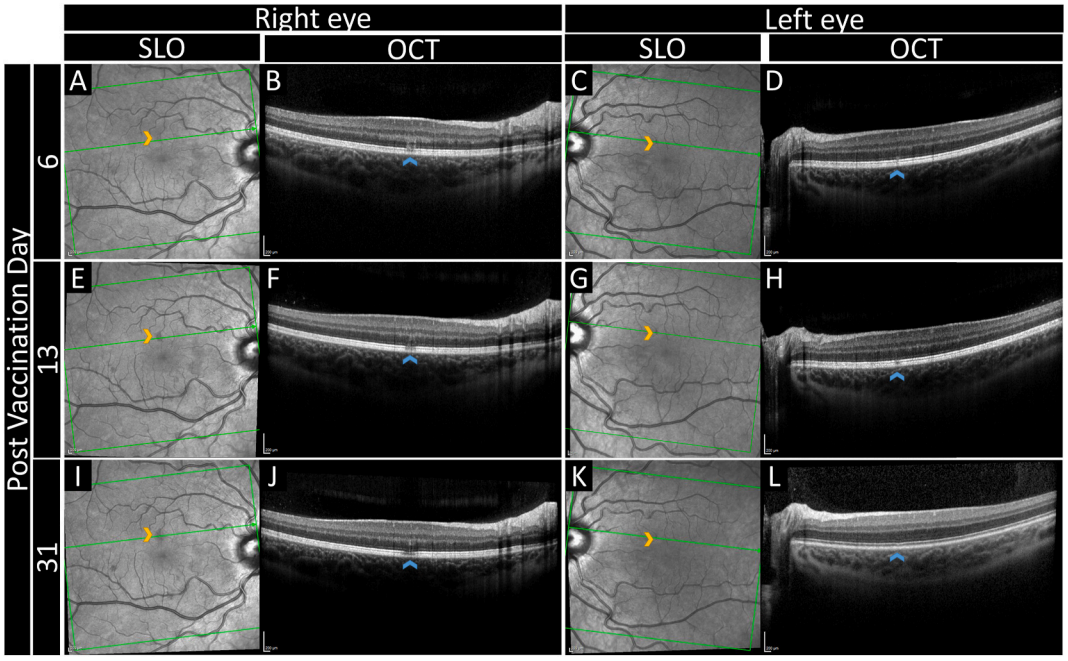

Fig. 2. Series of Optical Coherence Tomography. Near-infrared scanning laser ophthalmoscope (SLO) fundus image and Optical Coherence Tomography (OCT) of the right and left eye on post-vaccination day 6, 13, and 31. There are triangular dark lesions (yellow chevron) in the superior macula with corresponding bilateral focal ellipsoid zone loss (blue chevron) worse in the right eye. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Author's contributions

Daniel A. Valenzuela and Kenneth Taubenslag performed literature review and writing of the manuscript. Sylvia Groth and Sapna Gangaputra obtained pertinent clinical data and clinical images as well as editing of the manuscript.

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