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Case report

Acute macular neuroretinopathy (AMN) following COVID-19 vaccination

Daniela Drüke[a,*], Uwe Pleyer[b], Hans Hoerauf[a], Nicolas Feltgen[a], Sebastian Bemme[a]

[a] University Medical Center Goettingen, Department of Ophthalmology, Robert-Koch-Straße 40, 37075, Göttingen, Germany
[b] Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Department of Ophthalmology, Campus Virchow, Charité, 13353, Berlin, Germany

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ABSTRACT

Purpose: To describe a case of acute macular neuroretinopathy (AMN) in a 23-year-old Caucasian female after a COVID-19 vaccination (Vaxzevira).

Observations: Our patient perceived visual symptoms in both eyes one day after COVID-19 vaccination. Hypo-reflective petalloid shaped perifoveal lesions appeared in infrared reflectance (IR) imaging, and Spectral domain-optical coherence tomography (SD-OCT) revealed structural alterations of outer retinal layers that resulted in persistent disruption of the ellipsoid zone (EZ) and the interdigitation zone (IZ).

Conclusions and importance: We report a novel association between AMN and COVID-19 vaccination. In addition to a febrile infection and oral contraception, previous vaccination should also be considered a potential risk factor for AMN.

1. Introduction

COVID-19 is a global pandemic that has affected over 120 million people around the world,[1] and viral mutants are potentially causing incidence levels to rise even faster. Twelve vaccines have so far been approved by national regulatory authorities,[2] and more than 500 million COVID-19 vaccination doses have been administered worldwide.[3]

COVID-19 Vaccine Vaxzevria© (previously COVID-19 Vaccine AstraZeneca, AZD1222) is based on an adenovirus vector encoding the SARS-CoV-2 S glycoprotein.[4] According to the product information, common adverse reactions to COVID-19 Vaccine Vaxzevria include pain at the injection site, headache, myalgia, fatigue, malaise, fever, chills, arthralgia and nausea.[4] Recently, very rare cases of cerebral venous sinus thrombosis (CVST) and disseminated intravascular coagulation (DIC) have been reported in patients mostly under 55 years of age after vaccination.[5] A causal relation with the vaccine, however, could not be proven.[5] To our knowledge, ocular side effects of COVID-19 vaccines have not been described so far.

2. Case report

A 23-year-old Caucasian female presented with a one-day history of dark paracentral spots in both eyes. One day before symptom onset, she had received a COVID-19 vaccine (Vaxzevria©, AstraZeneca). She also reported a headache and cervical pain on the first day after vaccination, fever was denied. Her medical history was significant for juvenile idiopathic arthritis (JIA) and associated recurrent iritis. Systemic treatment consisted of methotrexate 10 mg weekly and sulfasalazine 2000 mg daily, and she had been applying topical steroids once a day into her right eye since having presented with an anterior chamber inflammation six weeks earlier. She had reported joint swelling in her left knee, for which she had been injected with an intraarticular steroid three weeks before her vaccination. Except for oral contraception, she was taking no other medications.

On examination, visual acuity was 20/20 in both eyes without correction. Amsler grid and microperimetry showed paracentral scotoma (Fig. 1 A and 3A). Except for a superficial punctate keratitis, each eye's anterior segment exam was unremarkable. Fundus examination revealed a normal optic disc, and juvenile reflexes of the macula in both eyes. Fundus photography indicated a subtle brownish rimmed lesion parafoveal in the right eye and a bigger blurred lesion nasal to the macula in the left eye (Fig. 1 B).

Infrared reflectance (IR) imaging showed two distinct hyporeflective lesions located parafoveal superior-nasally in the left eye and a smaller grayish area inferior-nasally of the macula in the right eye (Fig. 1C). Spectral domain-optical coherence tomography (SD-OCT) showed corresponding hyperreflective lesions of the outer retina with a thickened outer plexiform layer (OPL), a thinning of the outer nuclear layer (ONL)

* Corresponding author. Robert-Koch-Straße 40, 37075, Göttingen, Germany.
E-mail address: Daniela.drueke@med.uni-goettingen.de (D. Drüke).

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and a disruption of the external limiting membrane (ELM), the ellipsoid zone (EZ) and the interdigitation zone (IZ) (Fig. 1D). Optical coherence tomography angiography (OCTA) revealed no reduced flow in the superficial and deep capillary plexus (Fig. 2 A and B). However, we noted a subtle flow void in the choriocapillaris (Fig. 2C).

We diagnosed AMN and started 40 mg prednisolone daily for one week followed by a dose of 20 mg for another week. After initial improvement, the patient reported consistent scotomas over the subsequent weeks. Within a period of 15 weeks, however, structural alterations of the outer retina appeared regressive on SD-OCT (Fig. 3B–E) accompanied by decreasing scotomas on microperimetry (Fig. 3 A, F).

3. Discussion

AMN is a rare disorder of the outer retinal layers characterized by a sudden paracentral scotoma in one or both eyes.[6,7] On ophthalmoscopy, lesions are typically brown reddish, wedge shaped, and fade over time while scotomas persist.[7,8] Infrared reflectance images typically show petalloid-shaped hyporeflective lesions located around the fovea[8] corresponding to structural alterations at the level of the EZ and IZ (interdigitation zone) on SD-OCT cross-sections, which we also observed in both eyes of our patient. AMN typically affects young women during their reproductive years and it is most commonly associated to non-specific flu-like illness or fever.[9] Although the pathophysiological mechanism is still under investigation, reports of AMN-preceding viral infections including influenza,[10] Dengue fever,[11] cytomegalovirus (CMV)[12] and COVID-19[13–15] led to the assumption of a viral or immune-mediated etiology. Other Risk factors include oral contraceptives, caffeine intake, vasoconstrictive agents, epinephrine, ephedrine, hypotension, headache, anemia, thrombocytopenia and immunotherapy.[6,7,9,16–18] Acute symptom onset and circulatory risk factors, however, suggested a vascular pathomechanism. Recently, improved visualization of the retinal and choroidal microvasculature by OCTA showed areas of flow void at the level of the deep capillary plexus and inner choroid within AMN lesions.[19–21]

Due to the coincidence of time between vaccination and onset of symptoms, AMN is here highly suspected to be an immune-mediated reaction after COVID-19 vaccination. Furthermore, AMN has already been described as a potential adverse effect after immunization. Until now, two cases of AMN have been reported following influenza vaccination.[21,22] The underlying pathomechanism remains unsolved. There is no evidence for a direct link between Vaxzevria vaccination and reduced blood flow or increased thrombus formation within the inner choroidal vasculature. The prednisolone treatment in our patient might have contributed to the initial improvement of the scotomas since it has recently been described to improve capillary and choroidal blood void in AMN.[23]

Nevertheless, oral contraception, JIA, and immunomodulatory therapy represent important risk factors, which possibly contributed to the manifestation of AMN in our patient. A potential association of AMN to the previously occurred arthritis exacerbation cannot be completely excluded. Sulfasalazin and Methotrexate (MTX) as immunosuppressive drugs could potentially decrease the immunologic reaction after vaccination. However, the recurrent exacerbations of the rheumatic disease with arthritis episodes in our patient indicated an insufficient immunosuppressive effect in this case. To our knowledge, there are no reported cases of AMN associated with juvenile idiopathic arthritis and as we detected no reactivated anterior uveitis, a direct link to our patient's underlying rheumatologic disease seemed unlikely. However, the timepoint of vaccination should be chosen carefully. While immune therapy is not considered a contraindication for vaccination[4,24,25], immunization might rather be postponed during ongoing inflammation.

COVID-19 vaccinations only started recently and there are no reports of associated ocular complications, yet. In our patient, we are assuming an immune-mediated reaction that has been described after influenza vaccination.

4. Conclusion

To our knowledge, this is the first report of AMN following a COVID-19 vaccination. AMN might present a rare but severe post-immunization complication due to possibly persisting scotomas in the long-term course. Considering the enormous number of individuals receiving COVID-19 immunization at present, the history of previous vaccination should be included in the anamnesis of AMN patients.

Moreover, a previous exacerbation of an underlying rheumatologic disease might increase the risk for adverse events. Thus, COVID-19 vaccination might rather be postponed in the presence of ongoing inflammation.

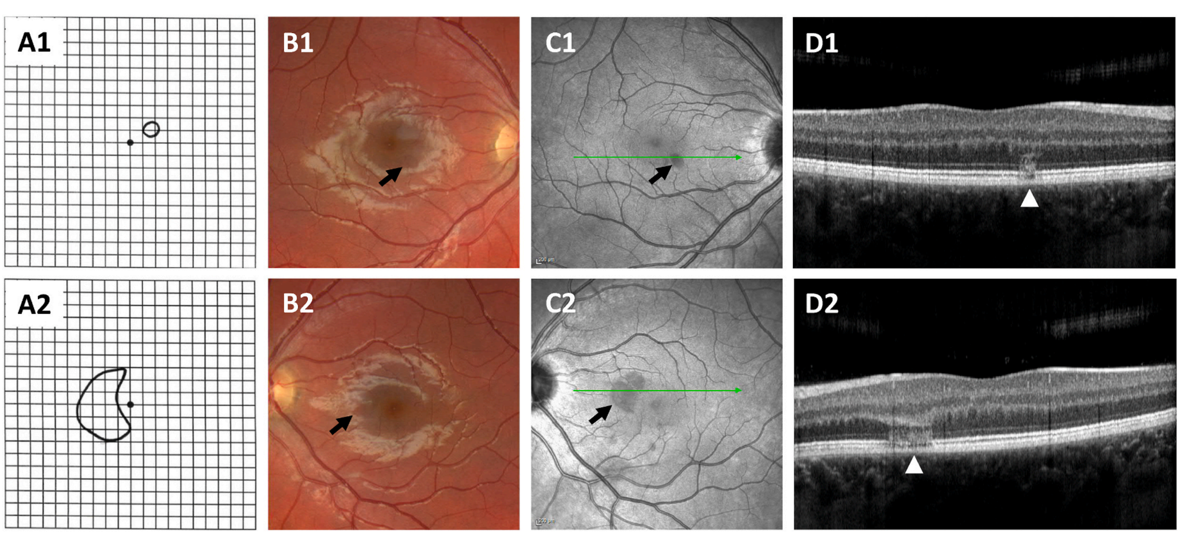

Fig. 1. Amsler grids on the day of presentation revealed a small round scotoma temporally-superior located in the right eye (A1) and an extended crescent-shaped scotoma temporally located in the left eye (A2). Fundus photographs showed only subtle brownish lesions nasal to the fovea in both eyes (B1 and 2, black arrows). Infrared reflectance (IR) imaging revealed distinct grayish lesions (C1 and 2) correlating with the scotomas as well as with the hyperreflective changes visible on spectral domain-optical coherence tomography (SD-OCT) cross sections in the outer nuclear layer (D1 and 2).

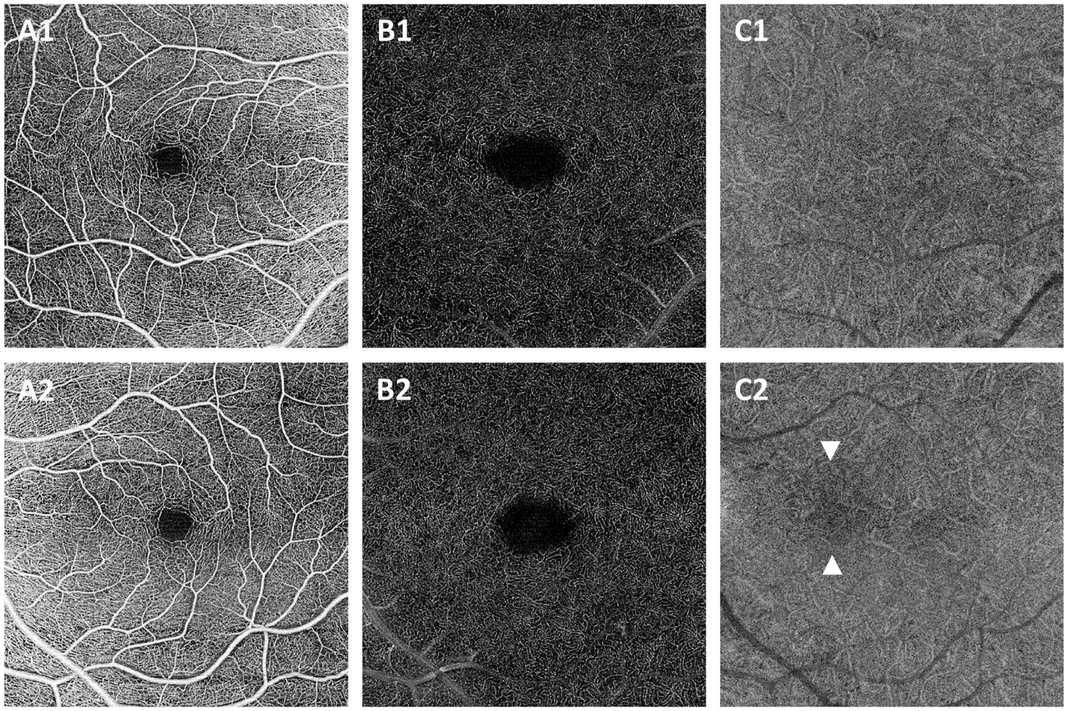

Fig. 2. Optical coherence tomography angiography (OCT-A) of the right (A1-C) and the left eye (A2-C2). En-face images of the superficial (A) and deep capillary (B) plexus showed no flow voids. However, a subtle flow reduction was visible within the choriocapillaris of the left eye (C2, arrowheads).

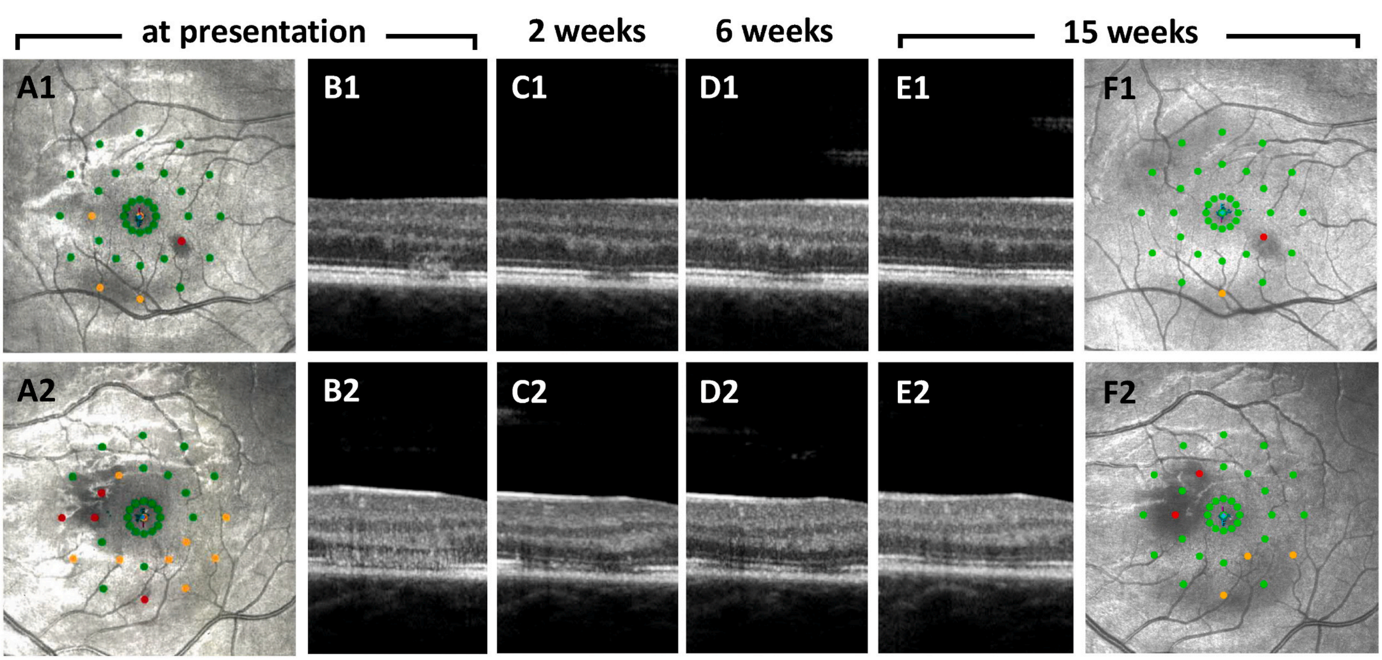

Fig. 3. Time course of the scotomas on microperimetry (A and F) and of the retinal lesions on SD-OCT scans (B–E). At presentation, the lesion showed a thickened outer plexiform layer (OPL) and hyperreflective blurred layer between retinal pigment epithelium (RPE) and outer nuclear layer (ONL). External limiting membrane (ELM), ellipsoid zone (EZ) and interdigitation zone (IZ) cannot be differentiated. After 2 and 6 weeks, the hyperreflective layer gradually faded and ELM was again definable. After 15 weeks, the EZ and IZ showed persistent disruption. The scotomas appeared regressive but persistent in both eyes.

Patient consent

No patient consent was obtained as this report does not contain any patient identifying information.

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Authorship

All authors attest that they meet the current ICMJE criteria for

Authorship.

Declaration of competing interest

The authors declare that there is no conflict of interest.

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