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Acute idiopathic maculopathy after COVID-19 vaccination

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ABSTRACT

Purpose: We report a case of acute idiopathic maculopathy (AIM) that developed after COVID-19 vaccination. *Observations*: A 54-year-old woman complained of a sudden decrease of visual acuity in her right eye one day after receiving a second COVID-19 vaccination (Pfizer). Fundus photograph showed a circular yellow lesion at the fovea in right eye. Optical coherence tomography revealed the thickening of retinal pigment epithelium and the presence of subretinal fluid. Three months after the initial visit, the BCVA and the fundus images had favorable recovery in the right eye.

Conclusions and Importance: We describe a case of AIM after receiving COVID-19 vaccination. These findings may be a helpful in understanding the pathogenesis of AIM.

1. Introduction

Acute idiopathic maculopathy (AIM) is a rare macular disease with a sudden onset, unilateral central vision reduction following a flu-like illness.^{1–4} AIM is an inflammatory process involving the outer retina and retinal pigment epithelium (RPE) in the macular area with subretinal fluid. Most patients report a spontaneous recovery within several weeks to months with favorable recovery of the visual acuity. We report a case of AIM that developed after a COVID-19 vaccination.

2. Case report

A 54-year-old woman complained of a sudden decrease of visual acuity in her right eye one day after receiving a second COVID-19 vaccination (Pfizer). Her medical history was unremarkable. Three days after the onset of the symptoms, her best-corrected visual acuity (BCVA) was 20/40 in the right eye and 20/20 in the left eye. Slit-lamp biomicroscopy showed that the anterior segment was normal. Ophthalmoscopy showed a circular yellow lesion at the fovea (Fig. 1, Top). Optical coherence tomography (OCT) revealed the thickening of retinal pigment epithelium (RPE) and the presence of subretinal fluid (Fig. 1, Bottom). Fluorescein angiography showed a central hypofluor-escence which corresponded to a transmission defect (Fig. 2, Top). Indocyanine green angiographic images show a central hypofluor-escence from a filling defect of the choriocapillaris and a blockage by the

RPE thickening (Fig. 2, Bottom).

Two weeks after the initial visit, her BCVA decreased to 20/100 in the right eye. The RPE thickening was almost resolved and subretinal fluid was not present in the OCT images (Fig. 3, Top). The OCT images also showed an absence of the RPE band and the ellipsoid zone of the photoreceptors. The external limiting membrane at the fovea was intact.

The patient was prescribed topical 0.1% betamethasone, and three months after the initial visit, the BCVA had improved to 20/20 in the right eye. The OCT images showed a recovery of the ellipsoid zone but the RPE band at the fovea was still absent (Fig. 3, Bottom).

3. Discussion

An ongoing COVID-19 pandemic has been declared by the World Health Organization, and a vaccine for prevention of COVID-19 infection was anxiously awaited. Then, a vaccine was developed in less than one year. Many vaccine doses have been administered worldwide. However, ocular adverse events have been reported after receiving the COVID-19 vaccine.^{5–7} Pichi and associates reported seven patients who presented with ocular complaints following a COVID-19 vaccination in Abu Dhabi.⁵ One patient was diagnosed with episcleritis, 2 with anterior scleritis, 2 with acute macular neuroretinopathy, 1 with paracentral acute middle maculopathy, and 1 with subretinal fluid. However, to the best of our knowledge, no cases of AIM associated with COVID-19 vaccination have been reported. The pathogenesis of AIM remains largely unresolved although the involvement of coxsackievirus, zika

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Fig. 1. Fundus photograph and optical coherence tomographic image at the initial visit. Fundus photograph shows a circular yellow lesion at the fovea (Top). Optical coherence tomographic image shows a dome-shaped RPE band and subretinal fluid (Bottom). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

virus, and yellow fever virus has been hypothesized.^{8–11} Recently, Venkatesh and associates reported a case of AIM following COVID-19 infection, that is the first report of AIM associated with COVID-19 infection.¹² Indeed, the association of AIM with virus and prodromal flu-like illness, suggests that this disease mechanism may result from a direct viral infection of the RPE cells or an immune-mediated damage of the RPE cells.

In our case, the outer retinal and RPE anatomic changes with subretinal fluid and disrupted ellipsoid zone of the photoreceptors following the recovery of the anatomic changes and the visual acuity are consistent with AIM.^{1–4,8–11} However, the thickening of the RPE and persistent RPE defect were more severe than that reported for AIMs.^{1-4,8-11} With the Pfizer vaccines,¹³ the mRNA for a spike protein is encapsulated in lipid nanoparticles which are endocytosed into muscle cells. The mRNA is translated into a spike protein in the host cells. Then, the mRNA vaccination results in the production of high levels of antibodies for the spike protein. Recently, the immunohistochemistry study for human ocular specimens revealed that a staining with spike protein was found in the RPE whereas no signal was detected in the sensory retina.¹⁴ The molecular mimicry between a spike protein and a component of the RPE cells may lead to the activation of the host immune response. Our case of AIM developed after receiving a second COVID-19 vaccination. It is possible that the host immune response was augmented when the patient received the second vaccination, since the immune system was likely primed from the first vaccination. Then, the primed immune system may react with a robust response leading to this maculopathy event. Thus, the pathogenesis in this case may be strongly associated with an immune-mediated damage of the RPE cells.

4. Conclusions

In conclusion, the findings in this case may be a helpful in understanding the pathogenesis of AIM.

Patient consent

Consent to publish this case report has been obtained from the patient in writing.

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Authorship

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

Declaration of competing interest

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Fig. 2. Fluorescein angiographic images and indocyanine green angiographic images at the initial visit. Fluorescein angiographic images show a central hypofluorescence surrounded by hyperfluorescence which is due to a transmission defect (Top right, early phase; Top left, late phase). Indocyanine green angiographic images show a central hypofluorescence from a filling defect of the choriocapillaris and a blockage by the RPE thickening (Bottom right, early phase; Bottom left, late phase).



Fig. 3. Fundus photograph, fundus autofluorescence, and OCT images during follow-up period. Two weeks after the initial visit (Top), fundus photograph shows a circular yellow lesion surrounded by blurry outline (arrow). Fundus autofluorescence shows a central hypoautofluorescence with surrounding hyperautofluorescence (arrow). OCT image shows an absence of RPE band and ellipsoid zone of the photoreceptors (arrowhead). Three months after the initial visit (Bottom), the perifoveal blurry outline and hyperautofluorescence disappear. The OCT image shows a recovery of the ellipsoid zone (arrowhead), and a persistent absence of the RPE band (arrow) at the fovea. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

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References

- Yannuzzi LA, Jampol LM, Rabb MF, Sorenson JA, Beyrer C, Wilcox Jr LM. Unilateral acute idiopathic maculopathy. Arch Ophthalmol. 1991;109(10):1411–1416. https:// doi.org/10.1001/archopht.1991.01080100091049.
- Freund KB, Yannuzzi LA, Barile GR, Spaide RF, Milewski SA, Guyer DR. The expanding clinical spectrum of unilateral acute idiopathic maculopathy. Arch Ophthalmol. 1996;114(5):555–559. https://doi.org/10.1001/ archopht.1996.01100130547007.
- Gupta A, Rogers S, Matthews BN. Unilateral acute idiopathic maculopathy. Br J Ophthalmol. 2009;93(8):1073–1074. https://doi.org/10.1136/bjo.2008.140335.
- Hashimoto Y, Saito W, Saito M, et al. Increased choroidal blood flow velocity with regression of unilateral acute idiopathic maculopathy. *Jpn J Ophthalmol.* 2015;59(4): 252–260. https://doi.org/10.1007/s10384-015-0380-6.

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- Pichi F, Aljneibi S, Neri P, Hay S, Dackiw C, Ghazi NG. Association of ocular adverse events with inactivated COVID-19 vaccination in patients in Abu Dhabi. JAMA Ophthalmol. 2021;139(10):1131–1135. https://doi.org/10.1001/ jamaophthalmol.2021.3477.
- Ng XL, Betzler BK, Testi I, et al. Ocular adverse events after COVID-19 vaccination. Ocul Immunol Inflamm. 2021;29(6):1216–1224. https://doi.org/10.1080/ 09273948.2021.1976221.
- Fowler N, Mendez Martinez NR, Pallares BV, Maldonado RS. Acute-onset central serous retinopathy after immunization with COVID-19 mRNA vaccine. *Am J Ophthalmol Case Rep.* 2021;23:101136. https://doi.org/10.1016/j. ajoc.2021.101136.
- Beck AP, Jampol LM, Glaser DA, Pollack JS. Is coxsackievirus the cause of unilateral acute idiopathic maculopathy? *Arch Ophthalmol.* 2004;122(1):121–123. https://doi. org/10.1001/archopht.122.1.121.
- Jung CS, Payne JF, Bergstrom CS, et al. Multimodality diagnostic imaging in unilateral acute idiopathic maculopathy. Arch Ophthalmol. 2012;130(1):50–56. https://doi.org/10.1001/archophthalmol.2011.359.

- Parke 3rd DW, Almeida DR, Albini TA, Ventura CV, Berrocal AM, Mittra RA. Serologically confirmed zika-related unilateral acute maculopathy in an adult. *Ophthalmology*. 2016;123(11):2432–2433. https://doi.org/10.1016/j. ophtha.2016.06.039.
- Dompieri RC, Manzano RPA, Frazão MAM, Kurimori HY, Chao JCT, Lui ACF. Unilateral acute idiopathic maculopathy secondary to yellow fever disease: a case report. Am J Ophthalmol Case Rep. 2019;15:100464. https://doi.org/10.1016/j. ajoc.2019.100464.
- Venkatesh R, Reddy NG, Mishra P, Gupta A, Mahendradas P, Yadav NK. Unilateral acute idiopathic maculopathy following severe acute respiratory syndrome corona virus (SARS-CoV-2) infection. *Ocul Immunol Inflamm*. 2022 Feb 3:1–4. https://doi. org/10.1080/09273948.2022.2028287. Online ahead of print.
- Sahin U, Muik A, Derhovanessian E, et al. COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T cell responses. *Nature*. 2020;586(7830):594–599. https://doi.org/10.1038/s41586-020-2814-7.
- Martin G, Wolf J, Lapp T, et al. Viral S protein histochemistry reveals few potential SARS-CoV-2 entry sites in human ocular tissues. *Sci Rep.* 2021;11(1):19140. https:// doi.org/10.1038/s41598-021-98709-y.