

# New-onset Glaucoma Following Moderna COVID-19 Vaccination

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## ABSTRACT

**Aim:** To report a case of new-onset glaucoma following administration of the Moderna (mRNA-1273) vaccine.

**Background:** Previous studies have reported a low incidence of ocular adverse events induced by the coronavirus disease 2019 (COVID-19) vaccine. The literature on open-angle glaucoma associated with COVID-19 vaccination is limited.

**Case description:** The patient complained of blurred vision 2 days following the administration of the second dose of the Moderna vaccine in July 2021. At presentation, the ophthalmic examination showed elevated intraocular pressure (IOP) of 30 mm Hg in her right eye (OD) and 18 mm Hg in her left eye (OS). There were no signs of intraocular inflammation or glaucomatous optic neuropathy at the initial presentation. She was treated with a topical  $\beta$ -blocker first. In addition, 1 month later, her IOPs were 28 mm Hg OD and 26 mm Hg OS. Although treated with multiple antiglaucoma medications, her optic cup-to-disc ratios were increased in both eyes (OU) compared to May 2019. She developed a glaucomatous visual field (VF) defect OD in October 2021. Optical coherence tomography (OCT) revealed progressive retinal nerve fiber layer (RNFL) thinning in OU.

**Conclusion:** Glaucoma may be a rare but severe ocular adverse event of the Moderna vaccines. The ophthalmologist should pay attention to the risk of increased IOP following COVID-19 vaccination.

**Clinical significance:** We reported a case of new-onset open-angle glaucoma presumably associated with COVID-19 vaccination.

**Keywords:** Adverse event, COVID-19 vaccine, Glaucoma, Moderna.

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## INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been associated with 446 million cases worldwide.<sup>1</sup> Vaccines are the most promising tool to control the epidemic outbreak. Moderna is a nucleoside-modified mRNA-based vaccine that encodes the SARS-CoV-2 spike glycoprotein.<sup>2</sup> It provokes high levels of binding and neutralizing antibodies against S glycoprotein after vaccination. Most adverse events following vaccination are of mild to moderate severity.<sup>3</sup> Ocular complications are infrequent considering the large scale of the vaccination campaign, and the literature on glaucoma associated with coronavirus disease 2019 (COVID-19) vaccination is limited. Over the past 10 years, reactions of the eyelid and conjunctiva have been the most frequent adverse events of all vaccines. In addition, optic neuritis, uveitis, and retinal inflammatory disorders are relatively common potential complications.<sup>4</sup> Singh et al.<sup>5</sup> reported 0.06 cases of glaucoma per million doses for mRNA-1273. However, the study was conducted from the Vaccine Adverse Event Reporting System database and was lack of clinical information on individual patients.

We report a case of new-onset open-angle glaucoma following the administration of the Moderna vaccine. To our best knowledge, this is the first report of open-angle glaucoma presumably associated with the COVID-19 vaccine.

## CASE DESCRIPTION

A 54-year-old woman complained of blurred vision in her right eye (OD) 2 days after receiving the Moderna vaccine's second dose in July 2021. Accompanying symptoms included eye fullness, halos, and photophobia. She had a history of breast cancer and has been

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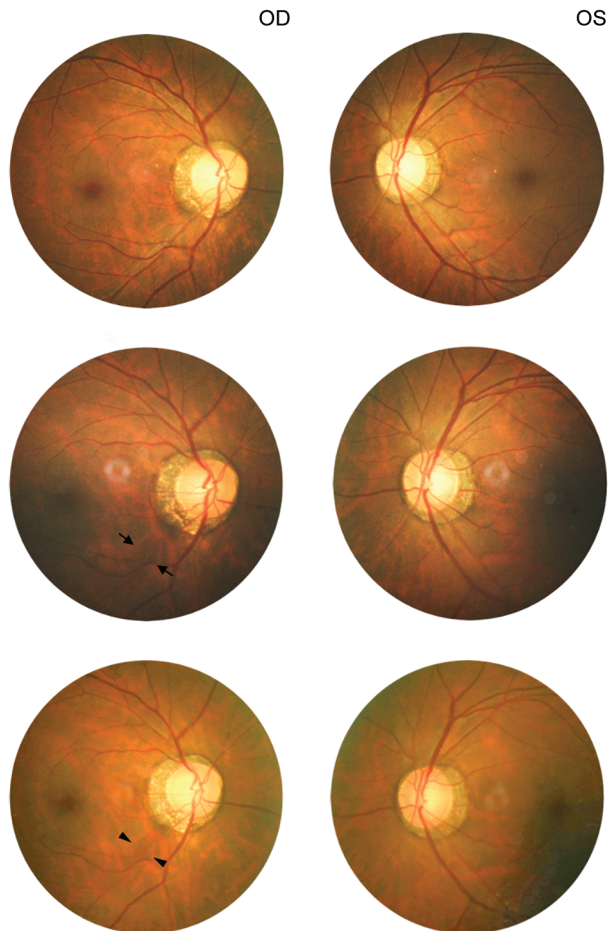
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treated with letrozole. The medical record in 2019 documented that the intraocular pressures (IOP) were 16 mm Hg in both eyes (OU). The fundus examination revealed cup-to-disc ratios of 0.6 × 0.7 OD and 0.4 × 0.5 in her left eye (OS), and there were no signs of glaucoma. She had no family history of glaucoma either.

The best-corrected visual acuity at presentation was 6/7.5 OD and 6/6.7 OS. The noncontact tonometer measured the IOPs as 30 mm Hg OD and 18 mm Hg OS. The central corneal thicknesses were 593  $\mu$ m OD and 594  $\mu$ m OS. The anterior chamber was deep and silent OU. There were no signs of afferent pupillary defect, proptosis, gaze restriction, or intraocular inflammation. Gonioscopy showed grade three open angle without peripheral anterior synechiae OU. No glaucomatous optic neuropathy OU was observed compared to the fundus photos in May 2019. Both the optical coherence tomography (OCT) and 24-2 Humphrey automated perimetry showed normal results. We started with timolol maleate but soon changed to topical latanoprost and oral acetazolamide

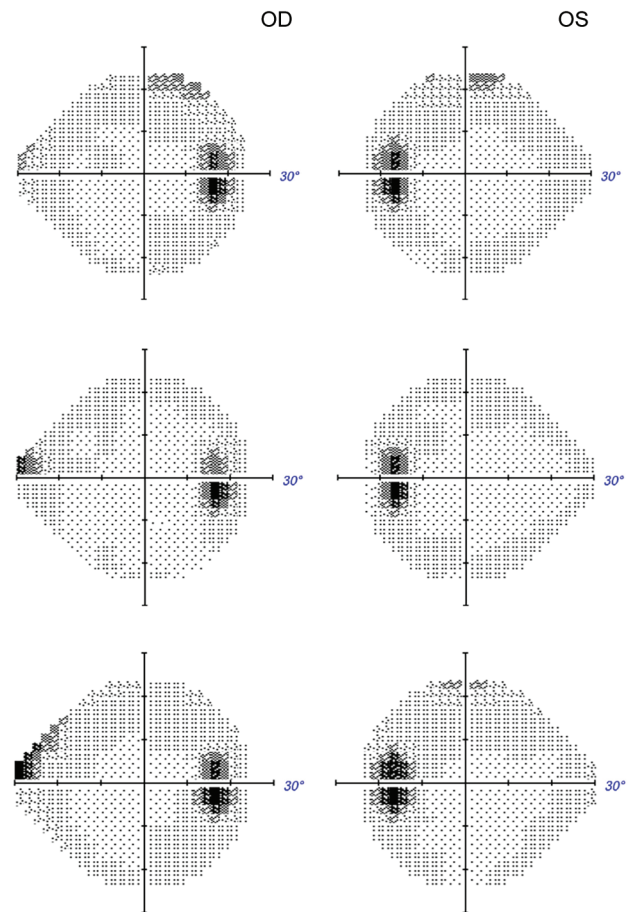


**Fig. 1:** The fundus examination showed no glaucomatous optic neuropathy in OU in May 2019. The fundus in October 2021 showed an increase in cup-to-disc ratio in OU and a RNFL defect (arrow) in the inferotemporal side of the optic disc in the OD, which was more prominent (arrowhead) in January 2022

twice daily due to persistent elevated IOP. Unfortunately, she developed an increased IOP of 26 mm Hg OS in the interim and was treated. However, her IOPs increased to 32 mm Hg OD and 37 mm Hg OS, and more aggressive regimens were prescribed. During the following 3 months, the IOPs were controlled to 18 mm Hg OD and 22 mm Hg OS with topical timolol maleate, brimonidine, brinzolamide, latanoprost, and oral acetazolamide. Nonetheless, the fundus examination in October 2021 showed the cup-to-disc ratio increased from  $0.6 \times 0.7$  to  $0.7 \times 0.8$  OD and  $0.4 \times 0.5$  to  $0.5 \times 0.6$  OS compared to May 2019 (Fig. 1). The fundus also revealed a defect of the retinal nerve fiber layer (RNFL) in the inferotemporal side of optic disc OD, which was more prominent in January 2022. A Humphrey 24-2 perimetry revealed an enlarging superior nasal step OD (Fig. 2). OCT demonstrated progressive RNFL thinning OU and a wedge-shaped RNFL defect in the inferotemporal region OD (Fig. 3). So, 6 months after the initial presentation, her IOPs were controlled to 16 mm Hg OD and 17 mm Hg OS with topical timolol maleate, brimonidine, brinzolamide, and travoprost.

## DISCUSSION

We report a case of new-onset open-angle glaucoma after receiving the Moderna vaccine. The patient suffered from bilateral IOP



**Fig. 2:** Humphrey 24-2 perimetry showed an enlarging superonasal step VF defect in the OD

elevation immediately following the second vaccination dose. Furthermore, she developed a glaucomatous visual field (VF) defect OD and progressive thinning of RNFL thickness OU on OCT 6 months later. We are unaware of the previous report about the relationship between glaucoma and COVID-10 vaccination in the literature review. This is the first report of new-onset open-angle glaucoma presumably associated with COVID-19 vaccination.

As we know, dysfunction of aqueous outflow causes elevated IOP in glaucoma. This may occur due to partial obstruction in the trabecular meshwork, damage to the trabecular endothelial cells, and decreased permeability of endothelium of the Schlemm's canal. Other possible mechanisms involve oxidative stress and dysregulation in the immune, hormone, and sympathetic systems,<sup>6</sup> which may be associated with immunization by vaccines.

Vaccination is a safe and effective way to prevent infectious disease, but the adverse event is inevitable. Ng et al.<sup>7</sup> reviewed the COVID-19 vaccine-induced ocular adverse events, and facial nerve palsy was the most reported. Other complications included cornea graft rejection, uveitis, superior ophthalmic vein thrombosis, and acute macular neuroretinopathy in 89 subjects. Recently Singh et al.<sup>5</sup> reported 0.06 cases of glaucoma per million doses for mRNA-1273. Most glaucoma cases were reported within the 1st week following vaccination. They also found the older age-groups (60s–70s) had a high frequency of glaucoma after receiving the Moderna vaccine.

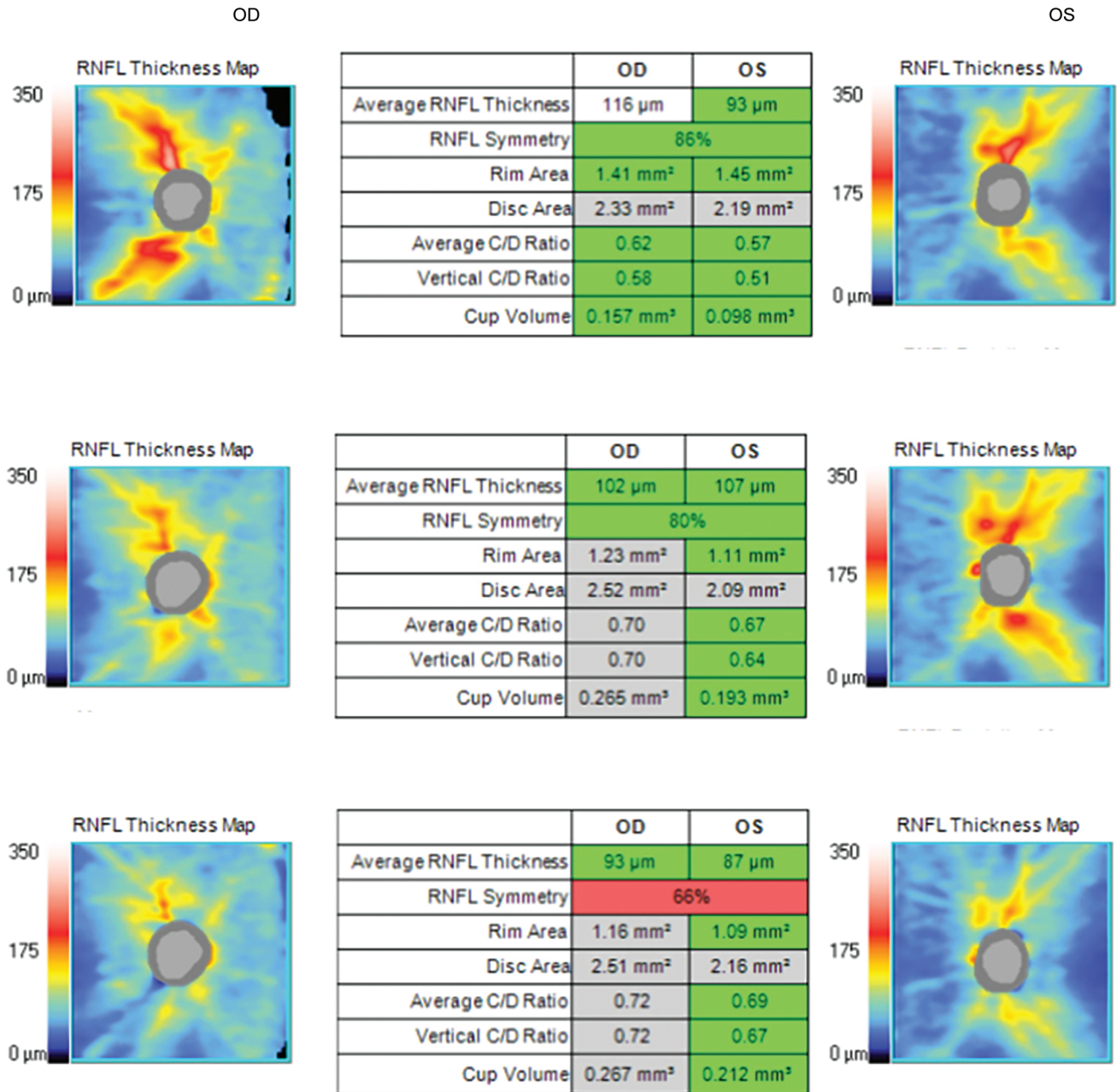


Fig. 3: OCT showed normal results at the initial presentation in July 2021. Then, progressive thinning of RNFL thickness in OU was noted in January 2022

COVID-19 infection was known to have ocular manifestations. Previous studies have shown that the virus can invade the ocular surface and inner ocular tissue. The nucleocapsid protein antigen was isolated in the conjunctiva, iris, and trabecula of the COVID-19 patient.<sup>8,9</sup> Besides, COVID-19 infection was reported associated with new-onset glaucoma in a 66-year-old female, and the viral RNA was identified in her aqueous humor.<sup>10</sup> The SARS-CoV-2 spike glycoproteins share the antigenic mimicry with human proteins. In light of the cross-reactivity of the SARS-CoV-2 proteins with human tissues, viral proteins may induce autoimmunity, or exacerbate underlying conditions. The proinflammation caused by COVID-19 infection also imposes the body in an oxidative stress environment.<sup>11</sup>

Several possible pathophysiologic mechanisms were proposed: ocular inflammation, oxidative stress, and increased serum glucocorticoid. COVID-19 mRNA vaccines may activate humoral and cell-mediated immunity and produce antibodies against SARS-CoV-2 spike glycoprotein. Expressed spike protein in the circulation after vaccination can dysregulate immunity and cause a pro-inflammatory response. Molecular mimicry between vaccines and ocular tissue can trigger an immune response to self-antigens. Vaccine adjuvants are also associated with triggering inflammatory disorders.<sup>12,13</sup> The inflammation and autoimmune dysregulation may cause low-grade, chronic trabecular inflammation, which plays a role in the development of glaucoma.<sup>14</sup> In addition, inflammation induces imbalanced oxidative stress. The reactive

oxygen species and free radicals cause structural and functional damage to the trabecular meshwork. The spike protein could interact with angiotensin-converting enzyme 2 receptors and cause angiotensin II overactivity and less generation of angiotensin 1–7, in which condition can possibly increase the IOP.<sup>15</sup> Last, the mRNA vaccines were hypothesized to provoke endogenous corticosteroid production.<sup>16</sup> The increased serum glucocorticoid can cause changes to the microstructure of trabecular meshwork. Besides, the retinal inflammation related to vaccines can also accelerate the degeneration of retinal ganglion cells coupled with glaucoma.

Glaucoma in association with COVID-19 vaccination is extremely rare. Our case did not have glaucomatous signs in the previous document and there was a temporal relationship between vaccination and the occurrence of glaucoma. Though the causality was presumed and the pathogenesis needs to be verified, open-angle glaucoma may be a rare but severe ocular adverse event after COVID-19 vaccination.

## CONCLUSION AND CLINICAL SIGNIFICANCE

This is the first case report of open-angle glaucoma presumably associated with COVID-19 vaccination. Though the low incidence of COVID-19 vaccine-induced ocular adverse events, glaucoma may be one of the ocular complications. The ophthalmologist should pay attention to the risk of increased IOP following COVID-19 vaccination.

## ACKNOWLEDGMENTS

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