

# Acute Corneal Graft Rejection Following COVID-19 Vaccination

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## Case Report

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# Abstract

## Purpose

To describe a case of acute corneal endothelial rejection as early as 3 days following the second dose of the Moderna messenger RNA-1273 corona virus-19 (COVID-19) vaccine.

## Observations:

An 81-year-old patient who had a penetrating keratoplasty 1 month earlier for a pseudophakic bullous keratopathy developed acute corneal graft rejection 3 days after the second dose of COVID-19 vaccine. Despite 4 weeks after intensive treatment, the corneal graft eventually failed.

## Conclusions and Importance

: Although a direct causative effect is difficult to establish, the timeline of events beginning after the COVID-19 vaccination supports that it might have triggered the rejection episode. Consistent advice must be given to corneal transplant surgeons and patients regarding such possibility and the importance of the follow up after having the vaccination.

## Introduction

Vaccination against severe acute respiratory failure coronavirus 2 (SARS-CoV-2) has been a primary public health focus in mitigating the COVID-19 pandemic. A natural question which has emerged in the wake of these vaccination efforts has been about the existence of possible adverse ocular complications following vaccination. Many of the reported adverse effects of other vaccines exist on a continuum including immunologic and hematologic adverse effects which naturally effect the eye.

To date, a number of adverse ocular events have been reported following COVID-19 vaccination.<sup>1-4</sup> These events have included orbital,<sup>5,6</sup> corneal,<sup>7-9</sup> uveitic,<sup>10,11</sup> neuro-ophthalmologic,<sup>12</sup> retinal,<sup>13-15</sup> and thrombotic<sup>16</sup> events. Some events have been more common than others. In particular, the most common events include uveitis flares, corneal graft rejection, acute macular neuroretinopathy, and various thrombotic events. In this report, we present a case of corneal graft rejection following the Moderna mRNA-1273 COVID-19 vaccine (Moderna, Inc.).

## Case Report

In December 2021, an 81-year-old man presented to the cornea service at the Egyptian Eye Academy, Egypt, with a one-day history of right painful pink eye and rapid decline in vision uneventful penetrating keratoplasty (PK) 6 weeks earlier for a pseudophakic bullous keratopathy (Fig. 1). Three days before

presentation, he received his second dose of the Moderna mRNA – 1273 COVID-19 vaccination (Moderna, Inc.). He experienced mild flu-like illness one day later, followed by his ocular symptoms on the third day. He denied any history of trauma. Post-surgery, he was maintained on topical prednisone acetate 1% 4 times a day and artificial tear drops.

At presentation three days after the second dose of the vaccine, his right eye visual acuity was hand motion. Slit-lamp examination revealed acute corneal endothelial graft rejection evidenced by diffuse corneal punctate staining, diffuse severe corneal graft edema, Descemet's folds, scattered keratic precipitates (KPs), total corneal epithelial defect, loose stitches with inferior graft dehiscence and anterior chamber (AC) activity (Fig. 2). There were no loose sutures, neovascularization, iris synechiae, or any other stimuli for rejection. The left eye examination was unremarkable.

We increased the patient topical steroids to hourly and added tacrolimus 0.03% eye ointment twice daily. We also prescribed a two-week course of oral acyclovir 400 mg 5x/day to cover for any potential underlying herpetic eye disease. He was prescribed systemic prednisone 1 mg/kg/day for 1 week with gradual tapering over 3 weeks. A bandage contact lens was inserted to cover the epithelial defect. Graft failure was noted by the third week post-treatment (Fig. 3).

## Discussion

Adverse corneal events following vaccination to COVID-19 have been increasingly well-documented in the literature during the preceding year. These manifestations have been in the form of acute graft rejection following PK, Descemet's membrane endothelial keratoplasty (DMEK) or Descemet stripping automated endothelial keratoplasty (DSAEK).<sup>7,8,17-23</sup> While less common, corneal melting has also been reported in the literature.<sup>24</sup> The typical presentation of graft rejection events is a patient with acute visual loss days to weeks following COVID-19 vaccine, followed by ophthalmologic examination which most commonly presents with corneal edema with possible conjunctival injection, AC inflammation, and KPs. Our patient was thus similar in presentation and examination compared to previous cases. Our case is unique in that, it is only the third report of Moderna COVID-19 vaccine-related corneal graft rejection after PK. A report of acute unilateral graft rejection after living relative conjunctival limbal allograft following the Moderna COVID-19 vaccine was demonstrated by de la Presa et al.<sup>19</sup>

Shah et al. recently reported on four cases of corneal graft rejection after vaccination with the Moderna COVID-19 vaccine.<sup>25</sup> The cases were in a 74-year-old man after DMEK, a 61-year-old woman and 77-year-old man after PK, and a 69-year-old woman after DSAEK. One case was after the first dose, and the other three (including both PK patients) were after the second dose of the vaccine. All four patients presented with corneal edema and three of the four presented with KPs. Three patients were successfully treated with topical prednisolone acetate 1% and one was treated with topical difluprednate 0.05%.

Balidis et al reported two other cases of corneal graft rejection after the Moderna COVID-19 vaccine.<sup>18</sup> They described a 77-year-old woman who developed acute graft rejection one week after her first dose of

the vaccine and 20 months after DMEK. The patient was unresponsive to subconjunctival dexamethasone and topical corticosteroids but improved with intravenous dexamethasone. In another case, they reported on a 64-year-old woman who developed vision loss in the right eye one week after the second dose of the Moderna COVID-19 vaccine and two years after PKP. The patient presented with diffuse corneal edema and a central corneal thickness (CCT) of 585  $\mu\text{m}$  at the apex of the graft (680  $\mu\text{m}$  nasally) from a baseline of 470  $\mu\text{m}$ . In this case, hourly dexamethasone drops and intracameral fortecortin injections were ineffective, and corneal edema persisted four weeks after beginning therapy. Similarly, our patient had a corneal graft failure despite the anti-rejection measures applied for 4 weeks.

Several other cases have been reported with other vaccines. Phylactou et al. reported 2 cases in women aged 66 and 83, both after DMEK transplants for Fuchs endothelial corneal dystrophy and vaccination with the BNT162b2 vaccine (Pfizer-BioNTech).<sup>8</sup> Both patients presented with KPs and increased CCT, and one had diffuse corneal edema. Both patients were successfully treated with topical steroids. Abousy et al. reported *bilateral* rejection after DSEK in a 73-year-old woman two weeks after receiving the BNT162b2 vaccine.<sup>17</sup> Treatment with prednisolone acetate 1% four times daily in both eyes was initially ineffective over four weeks, but an increase in steroid drop frequency led to resolution of symptoms. Several other similar reports have been made, with the common unifying features being vision loss in an elderly patient within approximately one week of vaccination and presentation with corneal edema, KPs, and assorted features of inflammation.<sup>7, 20–23, 26</sup>

Several possible mechanisms underlying corneal graft rejection following vaccination have been proposed previously. There is a pre-existing precedent for corneal graft rejection after vaccination against influenza, hepatitis B, tetanus, and yellow fever vaccinations<sup>27–30</sup>. Steinemann et al. previously hypothesized that there is a transient state of elevated vascular permeability following vaccination which exposes the cornea to immunologic insults from which it is normally spared. Shah et al. also endorsed a hypothesis centering on compromise of immunologic privilege in their recent report on corneal graft rejection following COVID-19 vaccination.<sup>25</sup> Elsewhere, in their report of graft rejection, Abousy et al. mentioned that SARS-CoV-2 RNA is present in the aqueous humor of patients with COVID-19 infection.<sup>17</sup> Likewise, other reports have found SARS-CoV-2 RNA is present in the corneas of postmortem COVID-19 patients.<sup>31</sup> Taken together, these findings raise the possibility of an immune response taking place in the cornea in patients with previous or current asymptomatic COVID-19 infection at the time of COVID-19 vaccination.

In conclusion, we believe that previous corneal transplantation is not, by itself, a contraindication to vaccination against COVID-19. We propose that ophthalmologists and primary care physicians should make it clear to patients with corneal grafts that there is a possibility of disruption of graft viability, and that patients experiencing vision changes after vaccination should promptly see their ophthalmologist. We propose also that patients who have recently undergone transplantation in the preceding three months undergo close follow-up to assess for graft integrity prior to undergoing vaccination. This report

adds to the growing understanding surrounding corneal transplantation and COVID-19 vaccination and we hope to develop better treatment guidelines as our understanding of this subject further develops.

## Declarations

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**Conflicts of interest:** None

**Patient consent:** Consent was not needed as no identifying information was published.

**A statement on participant consent:** the patient permission was obtained to take and use his eye photos for printed and online publicity.

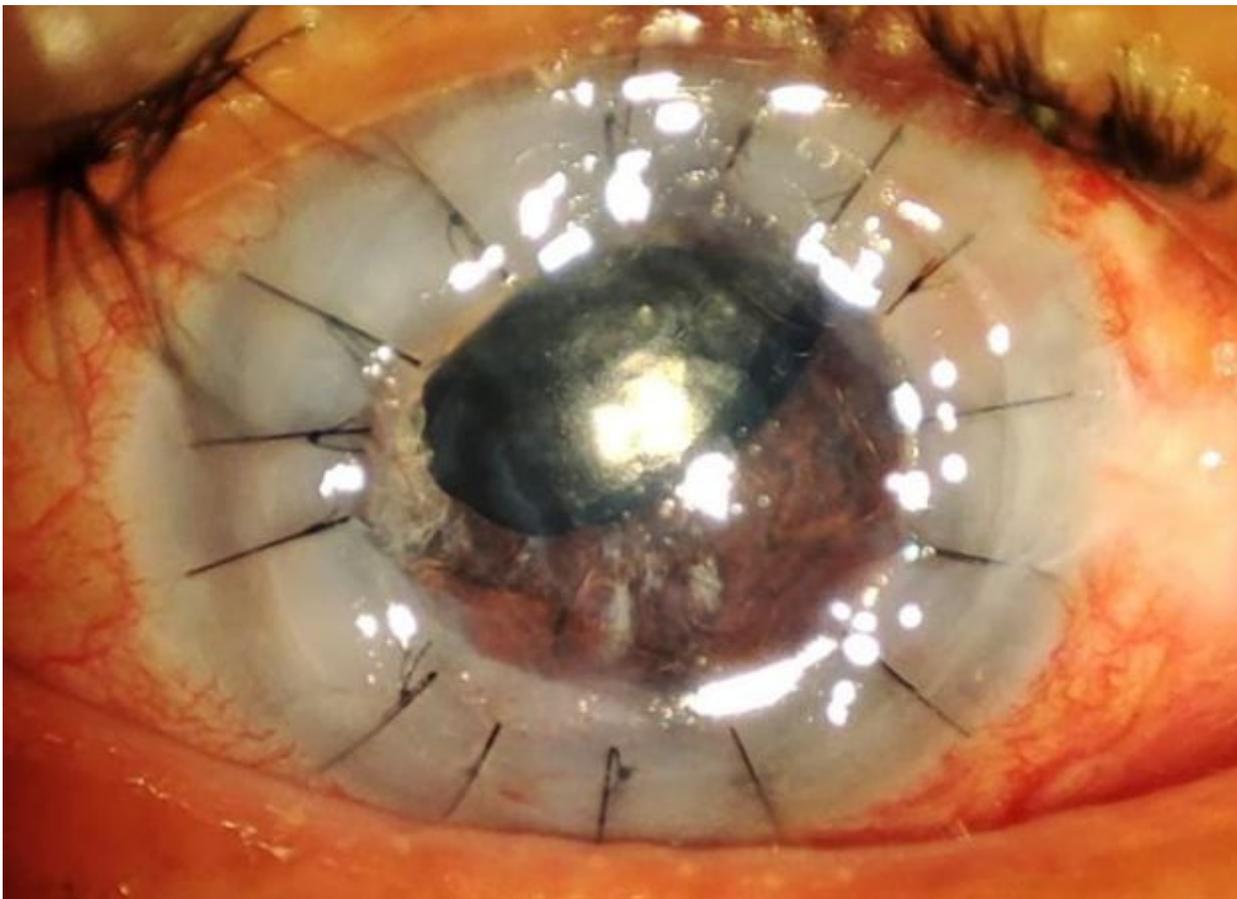
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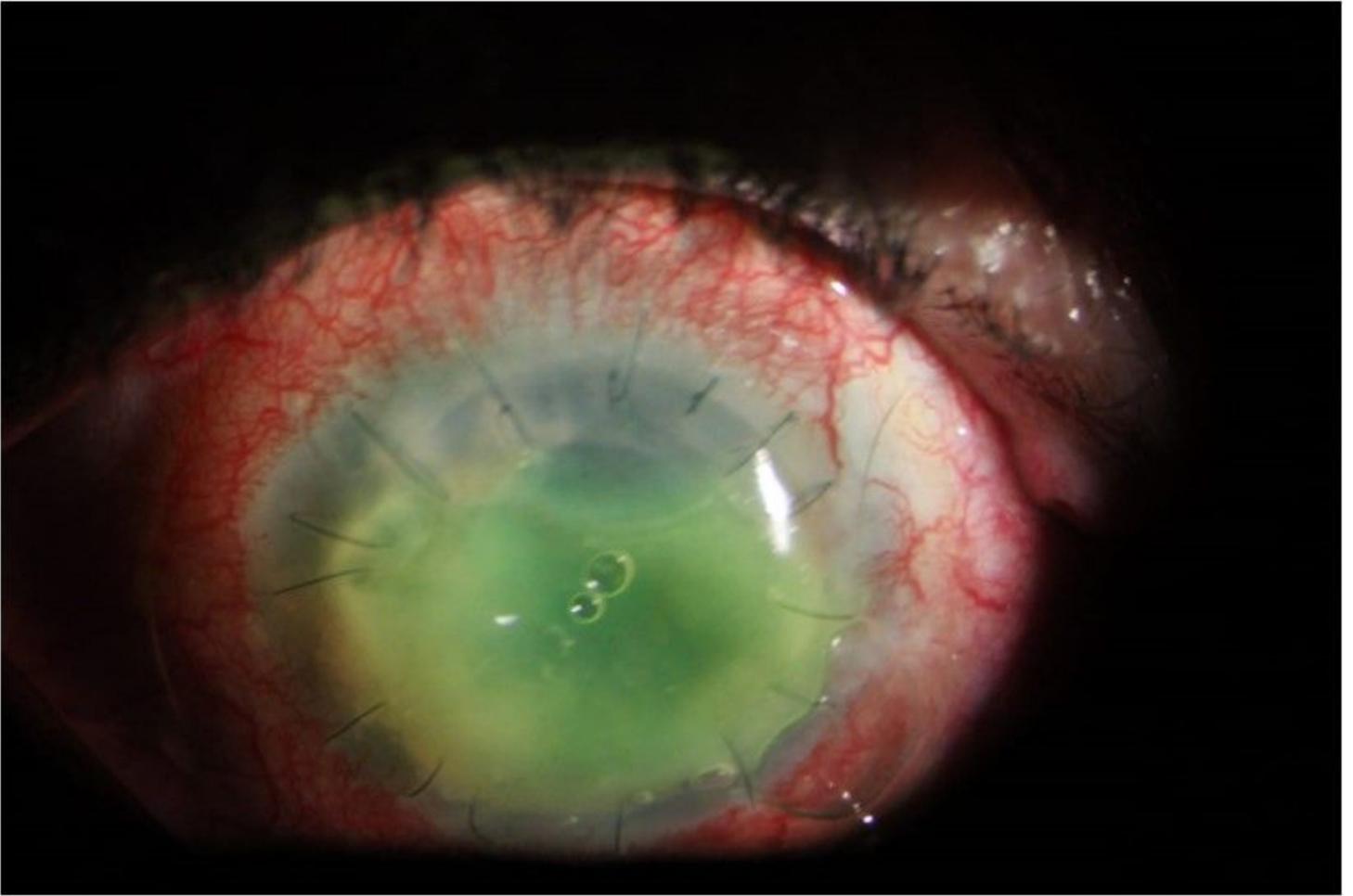
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## Figures



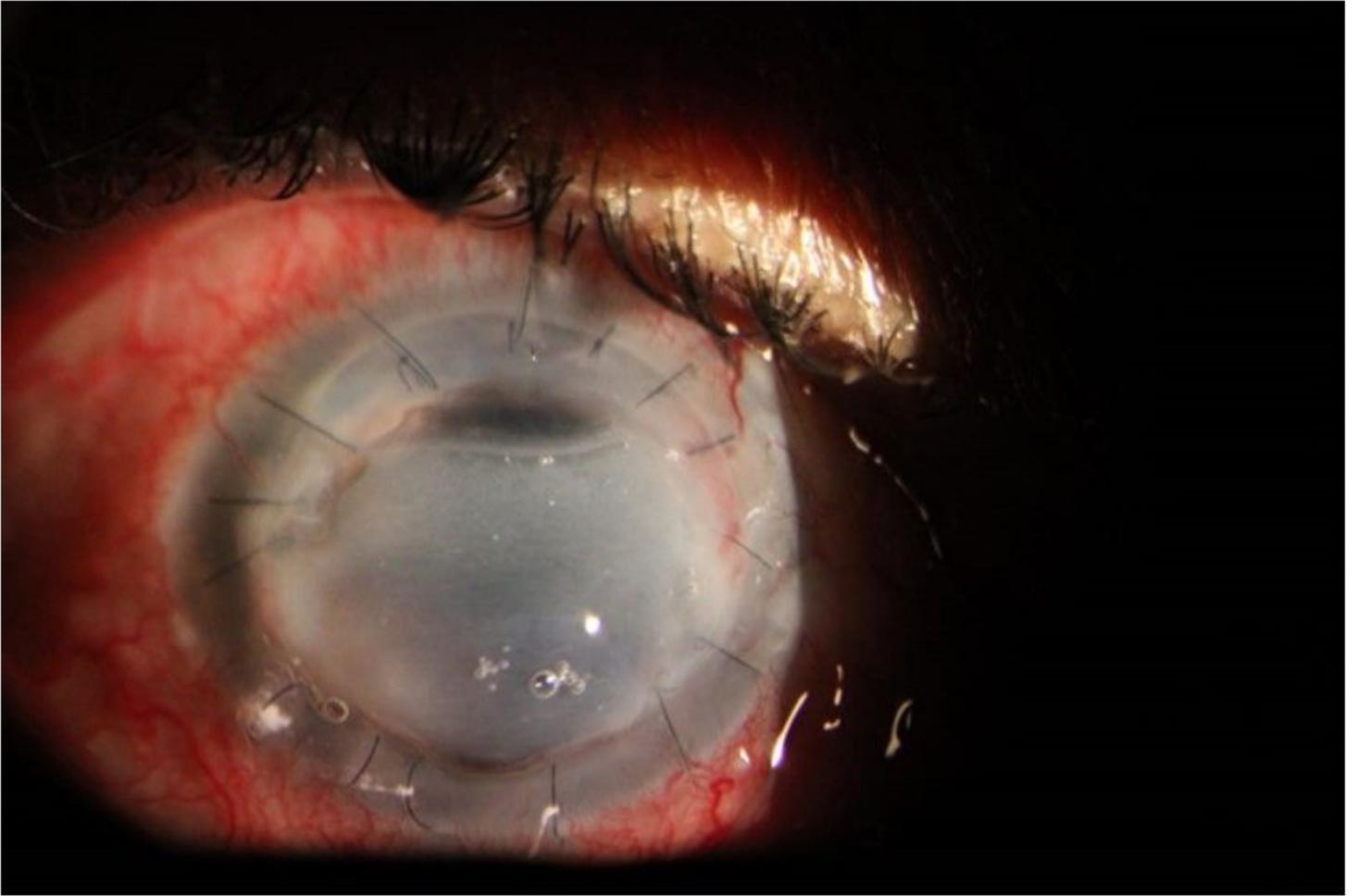
**Figure 1**

A slit-lamp photography of the right eye 4 weeks after penetrating keratoplasty showing a clear graft and intact sutures.



**Figure 2**

Slit-lamp photography demonstrating conjunctival injection, corneal graft edema, Descemet's folds, and loose stitches inferiorly. A diffuse distribution of fluorescein staining over the corneal graft was observed. A bandage contact lens was inserted to cover the epithelial defect. The central corneal thickness (CCT) was 890  $\mu\text{m}$ .



**Figure 3**

At 4-week post treatment, corneal graft failure secondary to the rejection episode was noted. The central corneal thickness was 974  $\mu\text{m}$ .