

Acute Bilateral Descemet Membrane Endothelial Keratoplasty Graft Rejection After the BNT162b2 mRNA COVID-19 Vaccine

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Purpose: We report a case of acute bilateral Descemet membrane endothelial keratoplasty (DMEK) rejection two weeks following BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech), reflecting on possible changes to the management of patients with DMEK scheduled for COVID-19 vaccination.

Patients and Methods: A 94-year-old woman with Fuchs' endothelial dystrophy who underwent DMEK 24 months earlier (right eye) and 20 months earlier (left eye) demonstrated bilateral graft rejection two weeks after the first dose of COVID-19 vaccine. Standard treatment regimen was followed, and clinical status documented with slit-lamp examination and swept-source optical coherence tomography throughout.

Results: Preoperative best corrected visual acuity (BCVA) and corneal thickness (CT) were 0.3 and 679µm right eye and 0.2 and 668µm left eye. Postoperative BCVA and CT were 0.7 and 559µm right eye and 0.4 and 590µm left eye. Standard treatment regimen consisted of dexamethasone/tobramycin and ketorolac, four times daily. At one month, both preparations were discontinued, replaced by dexamethasone 0.1% four times daily. At three months, this was tapered to once daily. Post-rejection, BCVA and CT were 0.2 and 710µm right eye and 0.3 and 710µm left eye. Treatment was with dexamethasone/tobramycin six times daily. Poor response resulted in re-DMEK transplantation, starting in the left eye. At one-month follow-up, BCVA and CT were 0.5 and 538µm right eye and 0.63 and 504µm left eye.

Conclusion: We report the first acute bilateral DMEK graft rejection after a single dose of COVID-19 vaccine. We recommend clinicians exercise vigilance and consider dexamethasone 0.1% during the vaccination period.

Keywords: corneal transplant surgery, vaccination

Introduction

In their 2021 study, Lockington et al found only four articles published in the English language directly associating corneal transplant rejection with recent vaccines.¹ Acute rejection following COVID-19 vaccination has been reported in patients who have undergone corneal transplantation, including Descemet membrane endothelial keratoplasty (DMEK). We wish to report a case of a 94-year-old woman, operated for Fuchs' endothelial corneal dystrophy (FECD) with DMEK in the right eye 20 months previously and in the left eye 24 months previously, who showed acute signs of bilateral graft rejection following routine vaccination with a single dose of BNT162b2 mRNA COVID-19 Vaccine (Pfizer-BioNTech).

Patients and Methods

The patient's past medical history was unremarkable, and her only regular medications were for arterial hypertension. Past ocular history included a cataract operation in the left eye 20 years earlier and in the right eye three years earlier. The

cornea became edematous after the phacoemulsification procedure in the right eye. Best corrected visual acuity (BCVA) expressed as a decimal and corneal thickness (CT) expressed in micrometers (μm) were 0.3 and $679\mu\text{m}$ in the right eye and 0.2 and $668\mu\text{m}$ in the left eye. Three months after cataract surgery, DMEK was performed in the right eye and the patient underwent a re-bubbling procedure due to partial graft detachment one week later. Six months later DMEK was performed in the left eye; however, full detachment of the graft was noted postoperatively, for which the patient underwent successful re-operation after one week. In accordance with hospital guidelines, the patient received the standard post-transplantation treatment regimen: combined dexamethasone/tobramycin and ketorolac, four times daily. After one month, the treatment was changed to one drop dexamethasone 0.1% four times daily and tapered to one drop daily after three months.

Results

Post-operative BCVA and CT were 0.7 and $559\mu\text{m}$ in the right eye and 0.4 and $590\mu\text{m}$ in the left eye after nine and three months, respectively. At two-year DMEK follow-up of the right eye, both corneas were clear, the grafts were described as well-functioning in both eyes and BCVA was 0.4 in the right eye and 0.6 in the left eye. The reduced visual acuity was thought to be due to posterior capsule opacification and the patient underwent posterior capsulotomy with neodymium-doped yttrium aluminum garnet laser (Nd:YAG) in the right eye (Figure 1).

Six months after the posterior capsulotomy, the patient attended two-year follow-up of the left eye complaining of a sudden painless worsening of vision in both eyes. BCVA had reduced to 0.2 in the right eye and to 0.3 in the left eye. Intraocular pressures were normal. Both corneas were increased in thickness, with a CT of $710\mu\text{m}$ in both eyes, and swept-source optical coherence tomography (SS-OCT) showed bilateral Descemet's membrane folds with moderate intraocular reaction, categorized as Standardization of Uveitis Nomenclature (SUN) grade 3 (Figure 1). The patient was diagnosed with bilateral graft rejection. Further enquiry revealed that the visual deterioration started after she had been given her first dose of COVID-19 vaccine two weeks earlier.

The patient was treated with dexamethasone/tobramycin six times a day and with hypertonic saline four times a day in both eyes. In the meantime, she received her second dose of COVID-19 vaccine as planned. The dexamethasone/tobramycin

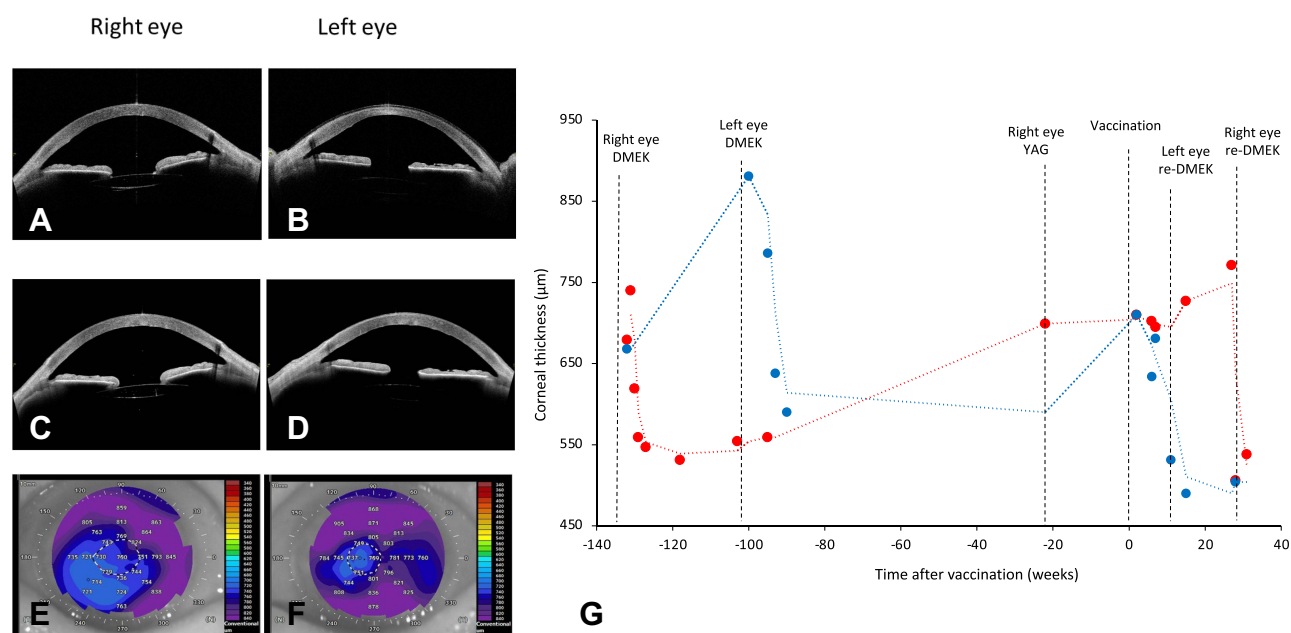


Figure 1 Composite showing: (A) swept-source optical coherence tomography (SS-OCT) of the right eye post-Descemet membrane endothelial keratoplasty (DMEK); (B) SS-OCT of the left eye post-DMEK; (C) SS-OCT of the right eye following DMEK graft rejection; (D) SS-OCT of the left eye following DMEK graft rejection; (E) pachymetry map of the right eye following DMEK graft rejection; (F) pachymetry map of the left eye following DMEK graft rejection; (G) graph demonstrating corneal thickness of the right eye (red) and the left eye (blue) over time after vaccination. The timeline of procedures is shown, including: DMEK, re-DMEK and posterior capsulotomy with neodymium-doped yttrium aluminum garnet laser (YAG).

was tapered to four times daily after one week, but when the corneal edema failed to resolve after one month, the hypertonic saline was discontinued and hourly dexamethasone 0.1% was added, tapering to eight drops daily after five days.

Having failed to respond to medical treatment, the patient was given re-DMEK transplantation first in the left eye and then in the right eye four months later. The right eye required a re-bubbling procedure due to partial graft detachment after one week. The patient received the standard postoperative treatment regimen: dexamethasone/tobramycin and ketorolac four times daily. After one month, both preparations were discontinued, and the patient received dexamethasone 0.1% four times daily. After three months, this was tapered down to one drop daily.

During the recovery period following re-DMEK transplantation, an improvement in overall corneal clarity was noted and the BCVA and CT were 0.5 and 538µm and 0.63 and 504µm in the right eye and the left eye, respectively.

Discussion

DMEK affords smaller rejection rates compared with other types of cornea transplantation. Five-year graft rejection episode rate following DMEK surgery is reported to be 2.6%.² Simultaneous bilateral rejection is rarely seen in clinical practice and may be indicative of an external stimulus.³ A causal relationship between different types of vaccines and corneal graft rejection has long been described in the literature, following influenza vaccination in particular.⁴ Acute rejection following COVID-19 vaccination has been reported in patients who have undergone penetrating keratoplasty as well as other solid organ transplants.⁵ Three other cases of acute DMEK rejection after COVID-19 vaccination have been reported.^{3,6} Of these, one patient was identified as having a bilateral DMEK rejection.³ The clinical picture surrounding this case is similar to ours in that it involved an 83-year-old female who had been operated for FECD with DMEK in the right eye six years earlier and in the left eye three years earlier. However, the onset of symptoms in this patient occurred only after the second dose of the vaccine had been given: full two months after the initial dose of BNT162b2 mRNA COVID-19 Vaccine (Pfizer-BioNTech).

It has already been proposed that changes in the antibody-mediated immune response resulting from COVID-19 vaccination can lead to DMEK graft rejection.³ The rarity of simultaneous bilateral graft rejection after DMEK and the chronology of events may be highly suggestive of causation in this case. Should our findings correlate with other reports, we advise that the cornea community exercise extra vigilance over recently vaccinated graft recipients. Furthermore, it may be prudent to avoid scheduling transplantations on or around the day of vaccination. Preventative steroid therapy in patients with a cornea graft that are due to be vaccinated may also be of benefit.

Conclusion

To our knowledge, this is the first reported case of bilateral acute DMEK rejection after an initial dose of COVID-19 vaccine. This shows that unwilling immune reactions can also appear after a single dose, a finding that is highly relevant to future scenarios in which booster doses may become the norm. Finally, we wish to propose the administration of steroid eye drops during the vaccination period: dexamethasone 0.1% 2–4 times daily starting the week before the first dose, continuing until one month after the second dose of vaccine.

Consent

The authors confirm that the patient has given their informed written consent for publication. Institutional approval for the publication of case details was not required.

Disclosure

The authors report no conflicts of interest in this work.

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