

# Stromal rejection in penetrating keratoplasty following COVID-19 vector vaccine (Covishield) – A case report and review of literature

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Endothelial rejection has been described following both m-RNA and vector-based vaccines for COVID-19. There is one case report of a stromal rejection described following influenza vaccination. We report a case of stromal rejection following vector-based COVID-19 vaccination, which might be the first case reported so far.

**Key words:** COVID-19 vaccine, penetrating keratoplasty, stromal rejection

Corneal graft endothelial rejection following vaccination is rare and has been described most commonly following influenza vaccination besides tetanus toxoid, hepatitis B, yellow fever, and herpes zoster.<sup>[1-5]</sup> Recently, endothelial rejection has been reported in keratoplasties following both mRNA and vector-based vaccines for SARS-CoV-2 coronavirus.<sup>[6-11]</sup> There is only one case report of a stromal rejection following influenza vaccination at 3 weeks in a deep anterior lamellar keratoplasty.<sup>[12]</sup> We report a case of a stromal rejection that occurred at 6 weeks following the second dose of COVID-19 vector vaccine (*ChAdOx1 nCoV-19 CoronaVirus Vaccine (Recombinant) COVISHIELD*) following penetrating keratoplasty, which may be the first case reported in literature so far.

## Case Report

A 79-year-old single eyed patient presented with diminution of vision of one-week duration in the left eye. He had taken his second shot of COVID-19 vector vaccine (*COVISHIELD*) 6 weeks ago prior to the onset of symptoms. The right eye was eviscerated in 2008 following endophthalmitis. In the left eye, the patient underwent Descemet's stripping endothelial keratoplasty in 2012 for pseudophakic bullous keratopathy

followed by penetrating keratoplasty in 2017 for a failed graft. He was treated for Hodgkin's lymphoma in 2016 for a period of 6 months. Both systemic and ocular evaluation 4 months prior to presentation was unremarkable. At presentation, his best-corrected visual acuity (BCVA) was 20/120. The graft had a localized central stromal edema suggestive of a stromal

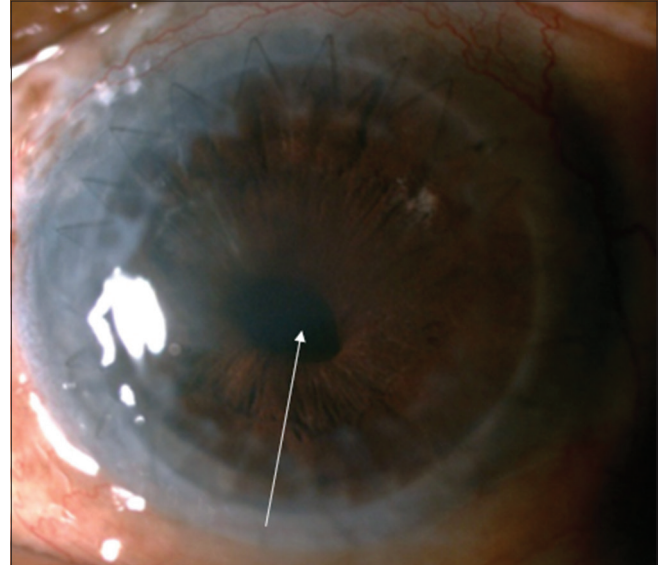


Figure 1: Localized stromal edema

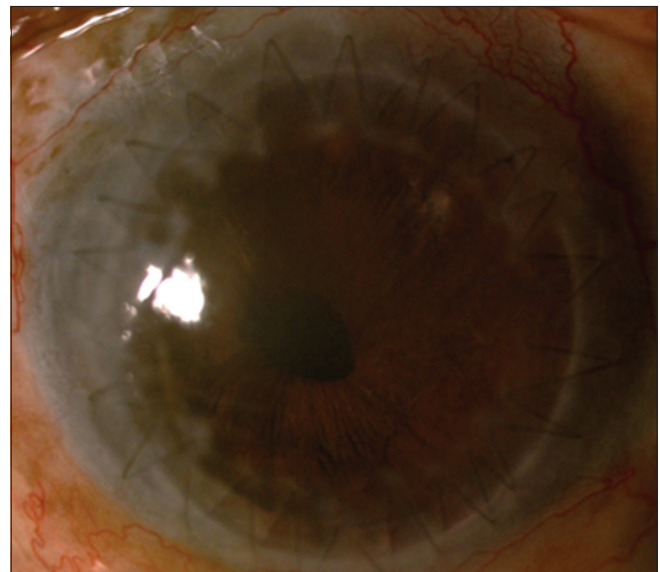


Figure 2: Faint corneal haze 2 months review

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**Table 1: Literature review of corneal graft rejection following COVID-19 vaccination**

Author	Type of COVID-19 vaccine	Details of surgery	Type and time of rejection
Crnej A <i>et al.</i>	BNT162b2 mRNA SARS-CoV-2 vaccine	DMEK	Endothelial rejection 7 days after the first dose
Phylactou M <i>et al.</i>	BNT162b2 mRNA SARS-CoV-2 vaccine	Case 1 - DMEK	Endothelial rejection
		Case 2 - bilateral DMEK	Case 1-7 days after the first dose
			Case 2 - bilateral rejection, 3 weeks after the second dose
Rallis <i>et al.</i>	BNT162b2 mRNA SARS-CoV-2 vaccine	DSAEK followed by PK	Endothelial rejection 3 days after the first dose
Wasser LM <i>et al.</i>	BNT162b2 mRNA SARS-CoV-2 vaccine	Case 1 - PK followed by re-PK	Endothelial rejection
		Case 2 - OU PK, OD RE - PK	Case 1-13 days after the first dose
			Case 2 - OD - 14 days after the first dose
Abousy M <i>et al.</i>	BNT162b2 mRNA SARS-CoV-2 vaccine	Bilateral DSEK	Endothelial rejection Bilateral rejection - 2 weeks after the second dose
Ravichandran <i>et al.</i>	ChAdOx1 nCoV-19 Corona Virus Vaccine Recombinant COVISHIELD	PK	Endothelial rejection 3 weeks after the first dose
Our case	ChAdOx1 nCoV-19 Corona Virus Vaccine Recombinant COVISHIELD	PK	Stromal rejection 6 weeks after the second dose

DMEK: Descemet's membrane endothelial keratoplasty, DSAEK: Descemet's stripping automated endothelial keratoplasty, PK: Penetrating keratoplasty

rejection. The surface was stable, sutures were intact, and there were no keratic precipitates [Fig. 1]. The eye was quiet and patient did not have symptoms of pain or photophobia. There was no past history of viral keratitis. Considering his single-eyed status, he was started on hourly topical steroids along with oral steroids, which were tapered gradually. At 2 months review, BCVA maintained at 20/120, edema resolved with a mild residual stromal haze [Fig. 2].

## Discussion

Corneal transplantation compared to other solid organ transplantation is well tolerated due to immune privilege of the cornea and the absence of major histocompatibility complex (MHC) class II antigen presenting cells.<sup>[2]</sup> Review of literature shows rare reports of unilateral or bilateral cases of endothelial rejection as early as day 1–8 weeks<sup>[3]</sup> following vaccination most commonly following influenza vaccine. Recently, endothelial rejection following both mRNA and vector-based COVID-19 vaccines has been reported from day 1–3 weeks following vaccination<sup>[6-11]</sup> [Table 1]. Ours is probably the first case of stromal rejection following COVID-19 vaccination. Like in all previous reports, we can only speculate that this is vaccine related as the patient was systemically stable and there were no ocular risk factors. Similar to ours, Phylactou M *et al.*<sup>[7]</sup> and Abousy M *et al.*<sup>[11]</sup> have also reported endothelial rejection following the second dose of COVID-19 vaccination. Every immunization elicits an antigenic response due to activation of Class 2 MHC complex in all corneal layers, which in turn activates the immune status.<sup>[3]</sup> Adenovirus-vectored vaccines are known to induce strong cellular immunity and ChAdOx1nCoV-19 vaccination has been shown to be associated with marked increases in SARS-CoV-2 spike-specific effector T-cell responses as early as day 7, peaking at day 14, and maintained up to day 56.<sup>[13]</sup> However, considering the rare reports of rejections in patients receiving influenza, COVID-19, or other similar vaccines, one can presume that there must be other factors titrating immune responses culminating at times in rejection.

Sometimes, the cause and effect relationship is not obvious and hence this may be underreported.

## Conclusion

Hiking steroids prior to and after vaccination both primary and booster in all patients who have undergone transplantation is recommended. Rallis *et al.*<sup>[8]</sup> have suggested that it is prudent to defer elective corneal transplant by 3–6 months after the second dose of COVID-19 vaccines. Patients should also be counselled about these risks and to report at the earliest in case of symptoms of graft rejection to hasten visual recovery.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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