Acute graft rejection in a high-risk corneal transplant following COVID-19 vaccination: A case report

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As COVID-19 vaccination is being undertaken all over the world, its side effects are materializing slowly. One such emerging side effect is acute graft rejection in corneal transplant (CT) cases post COVID-19 vaccination. We report a case of left eye (LE) repeat penetrating keratoplasty presenting with diminished vision in LE within 2 days of COVID-19 vaccination (ChAdOx1 nCoV-19 Corona Virus Vaccine Recombinant, COVISHIELD™). The patient was diagnosed with acute graft rejection post vaccination and was treated with topical and systemic immunosuppression therapy with successful outcome in terms improvement of visual acuity and corneal graft clarity. Timely presentation, diagnosis, and management may help to survive acute rejection episodes post vaccination.

**Key words:** COVID-19 vaccination, graft rejection, high-risk corneal transplant, repeat penetrating keratoplasty

The COVID-19 pandemic has created a medical crisis worldwide. In India, the systematic state-sponsored vaccination efforts have provided some relief to the population at risk of COVID-19. However, as the COVID-19 vaccines have shown to induce a strong immune response, there remains a hypothetical concern of the risk of corneal transplant (CT) rejection. CT rejection following vaccination has been previously reported.[1-3] However, as COVID-19 vaccination is a recent phenomenon, acute allograft rejection following it has been reported only in a few cases.[4-7] We report the first case of acute allograft rejection in high-risk (HR) CT following the first dose of COVID-19 vaccination from western India, which was successfully managed.

**Case Report**

A 35-year-old Indian male laborer presented with an acute onset of diminished vision in his left eye (LE) since 2 days. He had history of taking the first dose of COVID-19 vector vaccine (ChAdOx1 nCoV-19 Corona Virus Vaccine Recombinant, COVISHIELD™) 4 days prior. He had undergone a repeat penetrating keratoplasty (re-PK, donor cornea size 7.5 mm) in his LE 6 months back after having a failed large graft (size not known) post therapeutic PK 3 years ago at another center. Post-re-PK period was uneventful till 6 months with uncorrected distant vision of 6/36 and compliance to once-a-day prednisolone acetate 1% (PA) and twice-a-day cyclosporine 0.05% (CsA) eyedrops.

On presentation, the patient had a vision of counting fingers at 5 m in the LE. Slit-lamp examination revealed microcystic epithelial and stromal corneal graft edema more marked in the lower half. Sutures were intact with peripheral scarring with limbal vessels owing to previous large failed therapeutic graft. Few fresh endothelial keratic precipitates (KPs) were seen in the edematous area with anterior chamber reaction of grade 3. The pupil was irregular in size and shape with patchy iris inflammatory signs (c), resolution of graft edema (d) post treatment (a-d): On presentation, red congested eye with corneal keratic precipitate (yellow arrow) on endothelium of edematous graft (b), graft edema and Descemet folds in the lower part (black arrow, a), epithelial and stromal corneal graft edema more marked in the lower half.

**Figure 1:** Acute graft rejection post COVID-19 vaccination. Pre and post treatment (a-d): On presentation, red congested eye with corneal graft edema and Descemet folds in the lower part (black arrow, a), keratic precipitate (yellow arrow) on endothelium of edematous graft (b), Post treatment at 3 weeks, improved graft clarity with subsidence of inflammatory signs (c), resolution of graft edema (d)

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pigmentations on the anterior lens capsule due to preexisting posterior synechia of previous pathology post primary CT with the rest of the lens relatively clear [Fig. 1a and b]. Digital tonometry revealed normal intraocular pressure with normal posterior segment on ultrasonography. Patient had no systemic complaints on presentation. The patient was diagnosed as LE acute corneal endothelial rejection post COVID-19 vaccination. The frequency of topical PA eyedrops was increased to 1 hourly with atropine sulphate 1% eyedrops added three times a day. He was investigated to rule out any contraindication for treatment with intravenous methyl-prednisone (MPS). As being in HR category (e.g. relatively young age with re-PK for previous failed large vascularized therapeutic graft) for post rejection failure, he was given 1000 mg intravenous methyl prednisone once a day over 3 hours for 3 days under supervision.[9]

After three doses of therapy, the patient was shifted to oral prednisolone 60 mg in two divided doses (body weight: 57 kg). On follow-up at 3 weeks, graft clarity had improved significantly with a best-corrected vision of 6/9 [Fig. 1c and d]. Considering the HR category of the graft, tapering of topical PA eyedrops and oral steroids was advised slowly.[9] Anticipating the second dose of the COVID-19 vaccine, the patient was advised consultation with an immunologist for systemic nonsteroidal immunosuppression for prophylaxis.

Discussion

The cornea has an immune privilege due to its avascularity and lack of lymph vessels in the host bed and absence of major histocompatibility complex (MHC) class II antigen-presenting cells.[10] Thus, essentially the host can accept the allogenic donor tissue without any complications. However, in some cases, due to increased generalized immunological response after vaccination, an immunological reaction toward the allograft results in its rejection. Vaccination can induce Class II MHC complex antigens in all layers of the CT and can trigger allograft rejection like the influenza vaccine.[2,3]

We report an early onset of acute allograft rejection (within 2 days of the first dose of COVID-19 vaccine) in a relatively young patient (35 years) as compared to other cases reported.[4,5] Both types, penetrating and lamellar keratoplasty, have been observed to develop post COVID-19 vaccine graft rejection.[4,5] Rallis et al. observed a re-PK at higher risk of rejection as seen in one of the eyes of a patient with re-pk who had otherwise bilateral CT with endothelial keratoplasty performed in the other eye.[6]

Our is the only case reported with an acute endothelial rejection post COVID-19 vaccine in an eye with multiple HR categories.[8]

The present case had received COVISFIELD™ similar to the case reported by Ravichandran et al.[5] With this case report, we intend to highlight the potential consequence of immunogenicity of the recombinant vaccine, which may be shared with other types of COVID-19 vaccines. The present case was already on topical steroidal and nonsteroidal immunosuppression for HR transplant. Post-acute rejection episode most corneal surgeons would increase the frequency of topical steroid, but there are no set guidelines for rejection prophylaxis post vaccination.[9] However, authors recommend prophylactically step-up topical steroids before receiving first dose of the COVID-19 vaccine, especially for HR optical CT, and close follow-up post vaccination. Hill et al.[8] noted higher survival rate of graft if presented within 8 days of onset of rejection as in present case compared to when presented later than 8 days.

Conclusion

To conclude, as the COVID-19 pandemic and the COVID-19 vaccination drive are still on, corneal surgeons need to be aware of the possibility of acute graft rejection following vaccination. Patients awaiting optical CT should schedule a timeline of vaccine ahead of transplant surgery. Simultaneously, patients with CT need to be sensitized about post vaccination rejection episodes as timely diagnosis and prompt topical &/or systemic management of an acute graft rejection as observed in present case is important to prevent graft failure especially in HR category.

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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