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Commentary on Corneal Graft Rejection after COVID-19 Vaccination: Our Experience and Concerns

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ABSTRACT

Corneal transplantation is among the most successful organ transplantations in humans due to its immune privilege. This owes to lack of blood and lymph vessels and the absence of major histocompatibility complex antigen presenting cells (MHC-II APCs) in the cornea. However, vaccination may trigger MHC-II response as well as antigenic cross reactivity, resulting in allograft rejection. This has been reported earlier in sporadic cases after influenza and yellow fever vaccines. With the rampant vaccination and booster doses against COVID-19, similar episodes of post-vaccination graft rejection in penetrating and lamellar keratoplasties have been reported. We had reported a case of corneal graft rejection post covid vector vaccine which recovered with steroid medications. Allograft rejection with various subtypes of vaccination opens the door to comprehend immune privilege mechanisms and prophylaxis against organ rejection. Clinicians and patients are advised to be alert to this possibility, for prompt recognition as well as treatment of post-vaccination corneal graft rejection.

INTRODUCTION

Immune privileged organs in the human body are those that tolerate a foreign tissue or graft for an almost indefinite period. This is unlike other parts of the body which incite a severe inflammatory or rejection response to external antigens [1]. The eye, brain, pregnant uterus, and testis are immune privileged sites in the body [2]. Corneal transplantation is among the most successfully-performed organ transplantations, due to this phenomenon of immune privilege. Various mechanisms such as the anatomical barrier, Anterior Chamber Associated Immune Deviation (ACAID) and an immunosuppressive microenvironment have been described to contribute to this immune privilege. The anatomical barrier is due to the absence of blood and lymph vessels in the cornea which aid in longer survival of the graft before gaining access of the donor tissue antigens to the regional lymph nodes. The keratocytes and corneal endothelial cells do not express class II major histocompatibility complexes (MHC-II) which are the main targets of a rejection reaction. Thus, immune response is weaker than other solid tissue transplantations, not warranting routine immunosuppression in case of corneal allografts. ACAID is a phenomenon by which a specific antigen introduced into the anterior chamber induces an antigen specific immunological tolerance. Therefore, antigens from the endothelial cells of the donor graft are conferred tolerance which contribute to prolonged graft survival. Lastly, the milieu in the anterior chamber is of immunosuppressive nature as hypothesized in indispensable organs such as the brain and reproductive organs [3].

Vaccination induces an immune response that incites MHC-II antigen presenting cells (APCs), which can trigger an allograft rejection, exposing previously invisible graft antigens to the immune system. Unlike other solid organ transplants, this process is more evident in corneal transplants since regular immunosuppression is not done, [4]. Post vaccination corneal allograft rejection has been reported with influenza and yellow fever vaccines earlier; although, a temporal association could not be established [5,6,7]. Vaccination could cause graft rejection by either activating an immune response or due to a cross-reactivity of virus antigen-specific T cells with the HLA antigen-disparate corneal allograft [4,8]. Hence, it is important to fathom the possible role of any type of vaccination in graft rejection, following penetrating and lamellar keratoplasties.

The mass administration of COVID-19 vaccines of different types worldwide covering a wide age group of

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individuals has brought to notice multiple reports of corneal graft rejections [8,9,10,11,12]. We have reported a case of corneal graft rejection post-COVID vector vaccine [8] (ChAdOx 1 nCoV-19 Corona Virus Vaccine Recombinant COVISHIELDTM). A 62-year-old man had undergone penetrating keratoplasty for a childhood scar in his right eye 2 years ago. It was his only seeing eye but the aphakic and amblyopic eye had regained a vision of 6/36, N12. Though he was on steroid eye drops once a day topically, he had presented with discomfort and diminution of vision of 5 days duration after 3 weeks of his first COVISHIELD vector vaccine dose. On slit lamp examination his eye was congested with an advancing Khododoust's rejection line and inferior graft edema. However, the superior part of the corneal graft was clear and no other stimulus for graft rejection, such as no loose sutures, neovascularization or iris synechiae. He was treated with topical and oral steroids, following which the graft recovered considerably. This case underscored the possibility of immune mediated corneal allograft rejection after, COVID vaccination.

In addition to highlighting the need for vigilance, our case also raises the predicament of timing the second and the booster doses of vaccination in these patients with rejection. Consequently, it has become common practice to hike up steroids, prior to any type of COVID-19 vaccination [13,14]. It is now recommended to increase topical steroids from 2 days prior to 2 weeks after any type of COVID vaccination [15]. Furthermore, patients should not be discouraged from receiving the vaccine as the disease is not only potentially morbid but on its own might trigger a stronger immune response than the vaccine itself. Elective lamellar and full thickness corneal transplants and related procedures like suture removal may be avoided around the time of vaccination. It is also important to educate the post-keratoplasty patient to report immediately on experiencing symptoms of transplant rejection such as Redness, Sensitivity to light, Vision clouding and Pain, abbreviated as R.S.V.P, for easy recall [15].

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