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Case Series

Presumptive contributors influencing cadaveric limbal stem cell graft rejection in cases of muriatic acid injury: A case series

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ABSTRACT

This study aimed at assessing the relevant risk factors regarding limbal graft rejection among recipients of cadaveric limbal stem cell transplantation in cases of unilateral limbal stem cell deficiency due to muriatic acid injury. After a biweekly follow up for 6 months, ten patients who developed graft rejection were included in the present study. All patients were admitted and rejection episode was managed with topical and systemic steroid. All of the patients were analyzed for presence of risk factors which might be contributing towards onset of graft rejection. Timing of surgery, glycemic status, past history of Covid infection, number & type of covid vaccination were found to be possible risk factors contributing graft rejection.

1. Introduction

Corneal surface is covered with a layer of transparent, non-keratinized stratified squamous epithelium. These cells have a high turnover rate and are continuously replaced by limbal stem cells.[1] Limbal stem cell deficiency (LSCD) is the loss or deficiency of pluripotent stem cells of limbus lead to corneal epithelial dysfunction manifest as progressive corneal vascularization, conjunctivalization leading to scarring. This leads to variable visual impairment. Allogenic limbal stem cell transplant is one of the options for ocular surface following ocular surface burn.[2] Iatrogenic LSCD can be avoided by performing cadaveric LSCT in place of living related donor. In this case series we report various risk factors those might be contributing to the cadaveric limbal graft rejection among recipients of muriatic acid injury.[3]

2. Methods

After getting permission from Institutional ethical committee and after obtaining written informed consent from the patients, we had included ten consecutive cases of unilateral acquired limbal stem cell deficiency of varying grade due to muriatic acid injury (Figure 1 A, B). All the recruited patients underwent cadaveric limbal stem cell graft (3mm x 2mm), obtained from the Institutional eye bank, by a single surgeon using standard protocol. Before transplanting the cadaveric donor lenticule (only the fresh tissues with death to transplantation interval of less than forty-eight hours were used), the hyperemic and chemosed conjunctiva and tenon adjacent to the zone of limbal ischemia was excised. The donor limbal lenticule is sutured with 2 to 3 interrupted sutures (10-0 monofilament nylon) except on the corneal site. A large diameter bandage contact lens was applied at the end of the procedure. All the patients received pre operative systemic prednisolone which was continued after surgery (dose; 1mg/kg body weight) with gradual taper over 2 months. Locally they received

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topical 1% Prednisolone acetate (hourly dose gradually tapered to once a day over 3 months) along with topical lubricants eyedrop. After 3 months the potent steroid was replaced by topical Loteprednol etabonate 0.5% once a day for another 3 months various factors that might be contributing to graft rejection among such recipients were analyzed and presented.

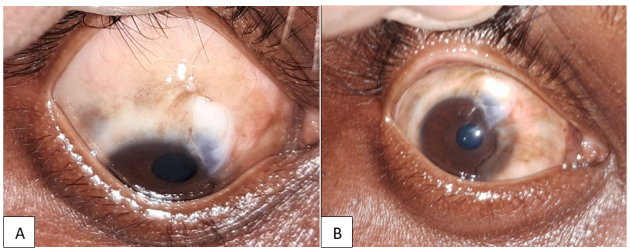

Figure 1: A): Preoperative picture of LSCD due to muriatic acid injury; **B)**: Preoperative picture of LSCD due to muriatic acid injury

3. Case Details

We present ten cases of cadaveric limbal stem cell transplant recipients who developed unilateral limbal stem cell deficiency due to Muriatic acid injury (Figure 1 A, B). As none of the patients were willing for auto- transplantation and no suitable living related donor was available, we opted for cadaveric limbal stem cell transplantation. Standard protocol was followed during transplantation. Only fresh tissue (death to transplantation interval less than forty-eight hours) obtained from Institutional Eye Bank was utilized in each case. After resection of fibro-vascular pannus, donor lenticule was sutured with multiple interrupted 10:0 monofilament nylon sutures except on the corneal side. Mean age of participating patient was 48.3 years with a range from 42 to 63 years. The mean interval between the insult and procedure was 50.1 days with a range of 23 to 90 days. Out of these ten cases six had Roper Hall classification grade 2 and remaining four had grade 3. Presenting visual acuity ranged from 6/18to 1/60. All patients received complete dose of Covid vaccination including booster dose (Covishield was received by six and four received Covaccine). Out of ten cases there was history of moderate Covid infection among four and severe Covid infection was reported in remaining six.

4. Discussion

Out of ten recruited cases five patients have already been suffering from uncontrolled DM (mean pre procedure HbA1c level 8.5) at the time of procedure. Thomas et al had mentioned that exposure of allograft tissue to hyperglycemia could influence the risk of rejection.[4] Out of ten recruited patients; six of them had a history of severe covid infection during the pandemic. Out of six such cases, four were admitted and were treated with systemic steroid with oxygen therapy. The remaining four had a moderate covid infection not requiring any hospitalization. Immune response regarding rejection cascade following Covid infection might be contributing towards allograft rejection in our ten cases. Six recipients of cadaveric allograft completed full course of recombinant Covishield vaccine and remaining four received full course of Covaccine. There had been previous reports of allograft rejection among patients of penetrating keratoplasty 10 days after BNTI62b2 mRNA vaccination against Covid infection.[5] Vaccine associated corneal graft rejection has been previously reported following Influenza, Hepatitis-B, Tetanus toxoid and Yellow fever immunization.[6] Although extensive literature search could not reveal any presumptive causal association between the regime and nature of covid vaccination and cadaveric allograft rejection, there is an ample scope for further research looking into the association. One patient was found to be suffering from active Ankylosing spondylitis during treatment. Ciszek M et al mentioned increased incidence of renal transplant rejection among rheumatological recipients.[7] Three out of ten cases presented with cadaveric allograft rejection within the first month of surgery (Figure 2A, B). Rate of acute onset rejection (rejection episode within first one month of acid insult) is 30%. Inflamed host bed might be a contributing factor for acute rejection in this subset of cases. Nine cases had heightened Mantoux reaction but subsequent CBNAAT has not revealed any Tubercular infection. Although the frequency of Tuberculosis among solid organ transplant recipient is 1.2%-15%, considering wide spread BCG vaccination among Indian cohort, the exact role of strong Mantoux positivity among transplant recipients in our series need further research.[8] Altered immune response among Mantoux positive cases, ankylosing spondylosis and DM cases might be responsible for increase in rejection.

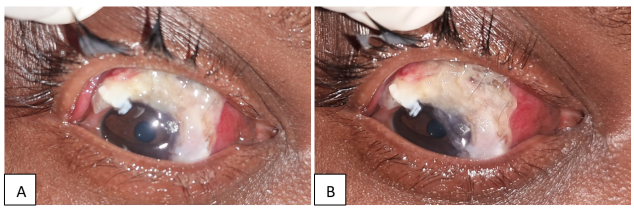

Figure 2: Postoperative picture showing graft rejection

5. Conclusion

Our study highlights the presumptive risk factors of allograft (cadaveric LSCT) rejection in patients with unilateral LSCD secondary to muriatic-acid injury. Uncontrolled Diabetes, COVID-19 infection, Covid vaccination, Hansen disease,

Table 1: Presentation of cases with LSCD due to muriatic acid injury

Variable				
Age (years)	40-45 =4 cases	46-50 =2 cases	51-55 = 3 cases	56-63 =1 case
Interval between insult and surgery (days)	21-35 =3 cases	36-48 = 2 cases	49-65 = 3 cases	66-90 = 2 cases
RH classification at presentation	Grade I = 0 case	Grade II = 06 cases	Grade III = 04 cases	Grade IV = 0 case
V/A at presentation	6/18- 6/36 = 02	6/60- 3/60 = 07	3/60 – 1/60 =01	< 1/60 = 0
Interval between surgery and rejection	0-4 weeks = 03 cases	5- 7 weeks = 02 cases	8-13 weeks = 5 cases	

Table 2: Presumptive risk factors contributing cadaveric graft rejection

Comorbidities	**Type I DM = 01 case Type II DM = 04 cases**	**Hansen disease = 01 case**	**Seronegative arthritis-RA= 02 cases AS= 01 case**	**Mantoux test positive = 09 cases**
Mean Mantoux induration	6-8 mm= 03 cases	8-10 mm = 05 cases	>10 mm = 01 case	
History of Covid-19 infection	Mild Covid = 0 case	Moderate Covid = 04 cases	Severe Covid = 06 cases	
Covid vaccination status	Covishield = 06 cases	Covaccine = 04 cases		

Rheumatoid arthritis Ankylosing spondylitis were found possible contributing risk factors regarding graft rejection. Moving forward further researches are warranted regarding assessment of the allograft rejection factors.

6. Souce of Funding

None.

7. Conflict of Interest

None.

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