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End Stage Stevens Johnson Syndrome: Can We Do Something ???

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Stevens-Johnson syndrome is a rare, acute, blistering disease affecting the skin and at least two mucous membranes. SJS is defined when the denuded cutaneous surface is less than 10% of the body surface area

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End stage ocular sequelae of Stevens Johnson Syndrome (SJS) is characterised by corneal scaring and opacity in a setting of a very severe dry eye. The options of visual rehabilitation in such a clinical setting are limited. We present a novel technique of management of such a case. To the best of our knowledge, this is the first such case performed in this region.

I. CASE

History: A 21 year young male non-hypertensive, non- diabetic male presented with severe dry eyes and decreased vision in the left eye since past 15 years. He gave a history of sudden damage to both eyes in childhood about 15 years back after a severe allergic reaction to the body 15 days after fever. The allergic reaction was severe enough to cause multiple blisters on the whole body including the mouth. As per history while the blisters healed in next 5-6 months, the eye condition continued to worsen after that. The right eye was lost then. He look treatment from his local doctors for the left eye for the next 3 years. He has sufficient vision then to perform his daily chores. Subsequently the vision had been stable for next 5 years after which it gradually deteriorated. Presently, he was unable to perform his daily activities and was dependent on another person to even take him to the bathroom. He had been on various combinations of lubricating eye drops in the past. He also gave the history of multiple consultations for this problem wherein he was told that this disease was un-treatable.

Clinical Presentation: At presentation, he had no perception of light in his right eye and accurate projection of rays in the left eye. On examination, right eye was phthisical (Figure 1A). The patient had difficulty in opening the left eye due to severe photophobia (Figure 1B). Left eye showed lower lid entropion, minimal lid margin keratinization, vascularised pannus and a corneal scar over a bone dry, dermalized ocular surface. Anterior chamber details were haze and the patient had a total cataract (Figure 1C). Intraocular pressure appeared to be normal on digital palpation. B scan ultrasound of the posterior segment was normal. Considering the history of a severe drug reaction in the past with blister formation and the presentation of a very severe dry eye, a diagnosis of Stevens Johnson Syndrome with its consequent ocular sequelae was made.

Management: The ocular surface lubricants were continues and measures to maintain lid hygiene were also initiated. As the patient had a bone severe dry ocular surface, the options of keratoplasty and stem cell transplantation were done away with. We chose to perform a new keratoprosthesis- LVP Keratoprosthesis for the patient. The surgery was planned to perform in two stages. While the first surgery would involve resection of pannus over the cornea covering the ocular surface with a oral buccal mucosal graft, keratoprosthesis proper was supposed to be implanted at the second step 2 months later.

Surgery: Stage 1

Pannus Resection: The patient was advised to perform betadine gargles after every meal for 3 days prior to the surgery. The surgery was performed under local anesthesia. A gauge piece soaked in lignocaine 2% jelly was put in the sub-labial area of the oral cavity 30 minutes prior to the surgery. This was done to anesthetise the area of the graft harvesting (Figure 2A). The eye was painted and draped (Figure 2B). Conjuncival peritomy was performed all around and the tenon's was also

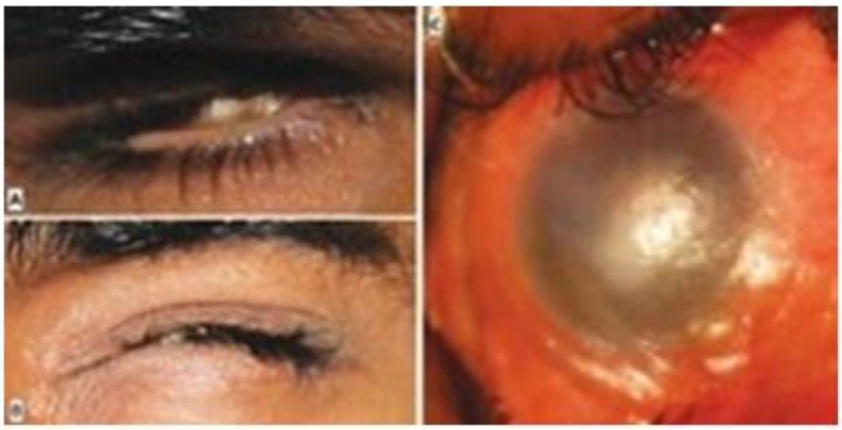

FIGURE 1(A): *Clinical examination revealed a phthisical right eye;* ***1(B):*** *Left eye was severely photophobic* ***1(C):*** *and showed lower lid entropion, minimal lid margin keratinization, vascularised pannus and a corneal scar over a bone dry, dermalized ocular surface.*

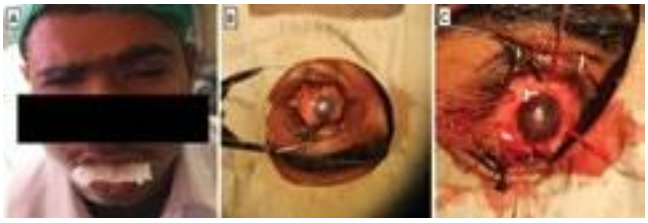

FIGURE 2(A): *Pannus Resection: Gauge piece soaked in lignocaine 2% jelly was placed in the area of the potential graft;* ***2(B):*** *Eye was painted and draped;* ***2(C):*** *Conjuncival peritomy and Tenon's dissection, recti muscles were tagged, pannus over the cornea was resected. A clear cornea with total cataract was observed underneath.*

FIGURE 3(A): *Harvesting Oral Mucosal Graft: sub-labial area was exposed and cleaned with betadine 10% solution;* ***3(B):*** *30 x 25 mm area was marked with gentian violet,* ***3(C):*** *Sub-mucosal lignocaine with adrenaline (1:1,600,000) injected* ***3(D):*** *and blanching was noted* ***3(E,F):*** *Marked area was dissected.*

FIGURE 4(A,B): *Transplantation of Mucous Membrane Graft on ocular surface: harvested graft was sutured on ocular surface using 8-0 vicryl sutures to recti muscles and intervening tenons capsule.* ***4(C):*** *Pink, vascularised graft was seen after 7 weeks.*

ocular surface using 8-0 vicryl sutures. Attachments were made with the four recti muscles and intervening tenons (Figure 4A&B).

Post-operatively the patient was advised betadine gargles after every meal. Systemic antibiotics, corticosteroids and anti-inflammatory drugs were prescribed for the next 2 weeks. A pink, vascularised graft was seen after 7 weeks after the first surgery (Figure 4C).

Surgery: Stage 2

An aphakic keratoprosthesis of standard axial length was ordered. The surgery was again done in local anesthesia.

The oral mucous graft was incised in the centre and lifted from the ocular surface (Figure 5A). The cornea was trephined (Figure 5B) in central 8.5 mm and the cataract was removed. LVP kpro was assembled in the centre of a 9 mm donor graft. This was then secured with 16 interrupted monofilament sutures (Figure 5C). The mucous membrane graft was then sutured back with it surroundings with 8-0 vicryl sutures. Finally, a central 3-4 mm opening was made in the graft and the keratoprosthesis cylinder was exposed (Figure 5D). The cut ends of the graft were tucked in under the 1mm peripheral plate of the keratoprosthesis. A lateral paramedian tarsorrhaphy was done in the end.

Outcome: The patient was stable separated. The four recti muscles were tagged. The pannus over the cornea was resected. A clear cornea with total cataract was observed underneath (Figure 2C) Attention was now diverted to the oral area.

Harvesting Oral Mucosal Graft: The sub-labial area was exposed using 4-0 silk sutures (Figure 3A) and cleaned with betadine 10% solution. A 30 x 25 mm area was marked with gentian violet (Figure 3B) and sub-mucosal lignocaine with adrenaline (1:1,600,000) was injected to separate the planes and achieve hemostasis (Figure 3C). Considerable blanching was seen Within 2 minutes (Figure 3d). The marked area was dissected and a full thickness mucosal graft was harvested using a 15 blade on Bard Parker handle, mono-polar cautery and conjunctival scissors (Figure 3e&f) An adequate graft is thin and without sub-mucosal fat and button- holes. Utmost care was taken to avoid damage to the underlying muscle fibres, nerves and vessels. The harvested graft was kept immersed in 5% povidone iodine until used. The sub-labial area was left bare to heal with secondary intention. Transplantation of Mucous Membrane Graft on ocular surface: The graft was taken and sutured on the and complained of pain in the graft side on post-operative day 1. The edema at the graft-site and at the ocular surface gradually decreased. He had a best corrected visual acuity of 6/12 at 1 month. The graft was vascularised and the patient was happy (Figure6).

II. Discussion

Stevens-Johnson syndrome (SJS) is a rare, acute, blistering disease affecting the skin and at least two mucous membranes[1]. SJS is defined when the denuded cutaneous surface is less than 10% of the body surface area (BSA). It is termed as overlapping SJS-TEN when the detachment involves 10- 30% of BSA and TEN when over 30% of the body surface area is denuded2. The etiology of SJS/TEN is immune mediated triggered by drugs and less commonly by systemic viral or Mycoplasma pneumonia infections3-7. The most common drugs found to be associated are sulphonamide antibiotics, allopurinol, carbamazapine, phenobarbital, phenytoin, and oxicam-NSAIDs8. Patel et al reported that antimicrobials (37.27%), anti-epileptics (35.73%) and non-steroidal anti- inflammatory drugs (15.93%) were the most common culprits in the

Indian population9. The reported incidence varies from 1.2 to 6 per million patient-years for SJS. The incidence rises with increasing age and is strikingly greater in the presence of HIV infection[10-13]. The pathobiological mechanisms underlying the onset of SJS/TEN complex have yet to be fully elucidated. It has both an immunological and a genetic basis.

The acute stage of SJS is characterised by inflammation at least two mucous membranes of the body. The most common ocular condition seen at this stage is bilateral conjunctivitis which occurs in 15-75% of patients[14,15]. However, most patients come to the eye clinic after having recovered sufficiently from the acute state to leave the hospital. They typically complain of a progressively worsening red eye. Persistent inflammation and ulceration of the ocular surface along with cicatricial complications of the lids amount to chronic ocular sequelae occurring in up to 35%

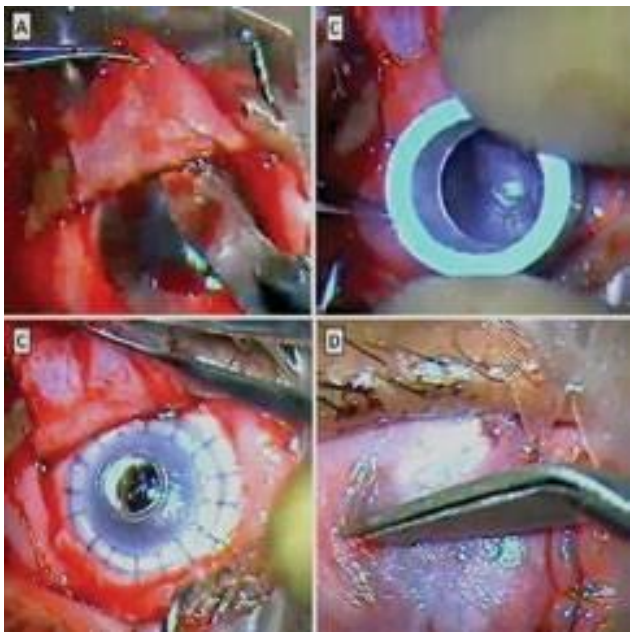

FIGURE 5: *Surgery: Stage 2* ***5(A):*** *Mucous graft was centrally incised and lifted;* ***5(B):*** *Cornea was trephined in central 8.5 mm and the cataract was removed;* ***5(C):*** *LVP kpro assembly was secured with 16 interrupted monofilament sutures;* ***5(D):*** *Central 3-4 mm opening was made in the graft and keratoprosthesis cylinder was exposed [Photo courtesy – Dr Swapnil Bhalekar].*

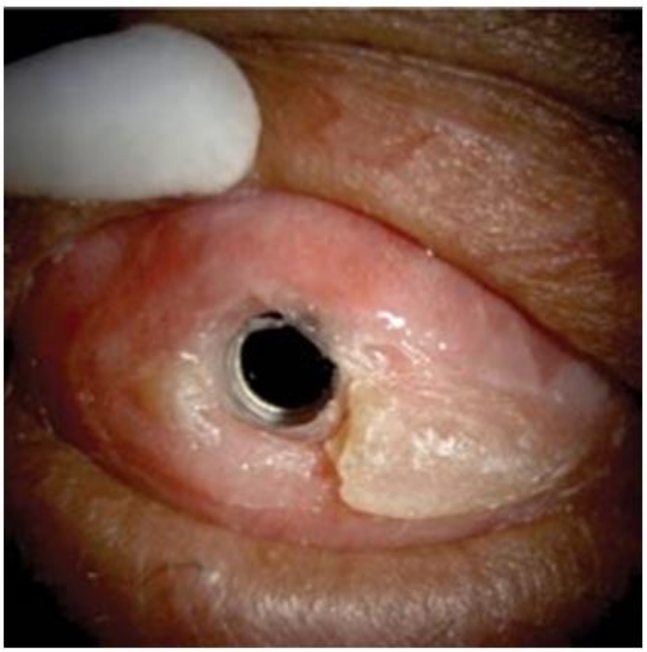

FIGURE 6: *Post-operative 1 month with a healthy and vascularised graft and a Kpro exposed in centre.*

Epithelial transplantation (COMET). These proceures are often complicated by prolonged inflammation, persistent epithelial defects, corneal melting, perforation and eventual graft failure[20-22]. Such eyes are suitable for keratoprosthesis. The commonly used Kpro today are Boston Kpro (Dohlman, USA) and OOKP (Falcinelli, Italy).

In completely dry eyes, the popular Boston type 1 keratoprosthesis cannot be implanted in the standard way as the carrier corneal graft is vulnerable to surface breakdown and melting. The Boston type 2 kpro is specially designed for such eyes[23]. The longer optical cylinder of the type 2 kpro can be exposed through an opening in the lids, which are sutured together. The lid skin acts as a stable epithelial cover over the donor corneal graft preventing exposure. The anatomical survival and visual outcomes of the Boston type

2 kpro are fair to moderate with almost 60% retention over 108 person years and improvement of vision to more than 20/200 in 70% of cases[23]. These outcomes fare well in comparison with the modified osteo-odonto keratoprosthesis (MOOKP) when used in similar indications[24,25]. Alternatives to using type 1 designs by modifying the surgical technique to enhance survival in completely dry eyes have now been described[26]. The first variation is the use of a type 1 design under the cover of a previously transplanted oral mucosal graft covering the of patients[16]. Lid margin inflammation targets the meibomian glands in particular, and causes widespread destruction of the glands and their orifices, and distichiasis. Contracture of the palpebral conjunctiva leads to cicatricial entropion and trichiasis[17,18]. These changes, along with a chronic dry eye due to loss of lacrimal gland function, contribute to corneal damage later via repeated blink-related microtrauma to the corneal epithelium on a compromised ocular surface[19]. Long term, destruction of the corneal limbal stem cells is the most common cause of vision loss in these patients. End-stage disease is characterized by a dry, keratinized ocular surface which further limits any future corneal or limbal cell transplantation[17,18]. Patients with end stage corneal blindness in a setting of a severe dry eye cannot be visually rehabilitated by penetrating keratoplasty, limbal stem cell transplantation or cultivated oral mucosal bulbar surface (Figure 7A). This is a two- staged procedure and requires repeated mucosal trimming subsequently to create adequate exposure of the optical cylinder. Retraction of the mucosal cover with exposure of the underlying corneal graft is also a possibility. Another modification of the type 1 design is the "LVP Kpro", in which the front-plate is modified to project 1 mm above the carrier corneal graft allowing the mucosal graft to be tucked under it thus preventing mucosal

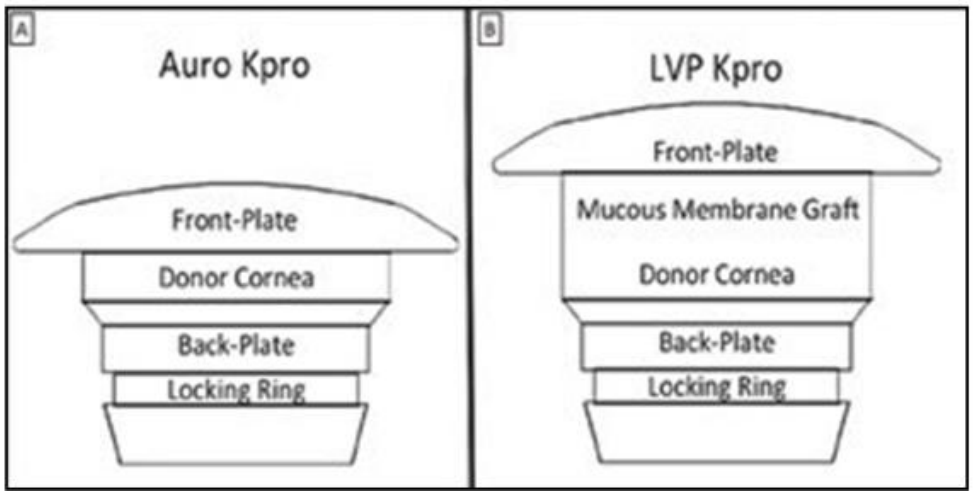

*Figure **7(A):** Variations in LVP Kpro Design: type 1 design under the cover of a previously transplanted oral mucosal graft; **7(B):** "LVP Kpro", in which the front-plate is modified to project 1 mm above the carrier corneal graft allowing the mucosal graft to be tucked under it thus preventing mucosal overgrowth. [reproduced from BMJ Case Rep 2014; Mar 24;2014].*

overgrowth[11] (Figure 7B). However, the reported outcomes of modified type 1 designs and of the type 2 design in completely dry eyes are limited.

Though long-term outcomes are awaited, patients with end stage ocular sequelae of SJS are now treatable with a potential of very good vision and a restricted visual field. Proper patient selection and appropriate surgical planning is essential. The role of pschycological councelling of the patients and the relatives is however paramount.

References

[1]. French LE. Toxic epidermal necrolysis and Stevens Johnson syndrome: our current understanding. Allergol Int 2006;55:9-16.
[2]. Bastuji-Garin S, Rzany B, Stern RS et al. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. Arch Dermatol 1993;129:92-6.
[3]. Borrelli M, Schroder C, Dart JK et al. Long-term follow-up after submandibular gland transplantation in severe dry eyes secondary to cicatrizing conjunctivitis. Am J Ophthalmol 2010;150:894-904.
[4]. McCormack JG. Mycoplasma pneumoniae and the erythema multiforme--Stevens Johnson syndrome. J Infect 1981;3:32-6.
[5]. Revuz J, Roujeau JC, Guillaume JC et al. Treatment of toxic epidermal necrolysis. Creteil's experience. Arch Dermatol 1987;123:1156-8.
[6]. Roujeau JC, Chosidow O, Saiag P, Guillaume JC. Toxic epidermal necrolysis (Lyell syndrome). J Am Acad Dermatol 1990;23:1039-58.
[7]. Sontheimer RD, Garibaldi RA, Krueger Stevens-Johnson GG associated with Mycoplasma pneumoniae infections. Arch Dermatol 1978;114:241-4.
[8]. Mockenhaupt M, Viboud C, Dunant A et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EuroSCAR-study. J Invest Dermatol 2008;128:35-44.
[9]. Patel TK, Barvaliya MJ, Sharma D, Tripathi C. A systematic review of the drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in Indian population. Indian J Dermatol Venereol Leprol 2013;79:389-98.
[10]. Correia O, Chosidow O, Saiag P et al. Evolving pattern of drug- induced toxic epidermal necrolysis. Dermatology 1993;186:32-7.
[11]. Mockenhaupt M, Rzany B. The epidemiology of serious cutaneous drug reaction. In: Williams HC, ed. The Challenge of Dermato Epidemiology. Boca Raton/New York: CRC Press, 1997:329-42.
[12]. Pitche P, Padonou CS, Kombate K et al. [Stevens-Johnson syndrome and toxic epidermal necrolysis in Lome (Togo). Evolutional and etiological profiles of 40 cases]. Ann Dermatol Venereol 2005;132:531-4.
[13]. Wolkenstein P, Revuz J. Drug-induced severe skin reactions. Incidence, management and prevention. Drug Saf 1995;13:56-68.
[14]. Howard GM. The Stevens-Johnson syndrome. Ocular prognosis and treatment. Am J Ophthalmol 1963;55:893-900.
[15]. Patz A. Ocular involvement in erythema multiforme. Arch Ophthal 1950;43:244-56.
[16]. Arstikaitis MJ. Ocular aftermath of Stevens-Johnson syndrome. Arch Ophthalmol 1973;90:376-9.
[17]. De Rojas MV, Dart JK, Saw VP. The natural history of Stevens Johnson syndrome: patterns of chronic ocular disease and the role of systemic immunosuppressive therapy. Br J Ophthalmol 2007;91:1048-53.
[18]. Di Pascuale MA, Espana EM, Liu DT et al. Correlation of corneal complications with eyelid cicatricial pathologies in patients with Stevens- Johnson syndrome and toxic epidermal necrolysis syndrome. Ophthalmology 2005;112:904-12.
[19]. Cher I. Blink-related microtrauma: when the ocular surface harms itself. Clin Experiment Ophthalmol 2003;31:183-90.
[20]. Tugal-Tutkun I, Akova YA, Foster CS. Penetrating keratoplasty in cicatrizing conjunctival diseases. Ophthalmology 1995;102:576-85.
[21]. Solomon A, Ellies P, Anderson DF et al. Long-term outcome of keratolimbal allograft with or without penetrating keratoplasty for total limbal stem cell deficiency. Ophthalmology 2002;109:1159-66.
[22]. Shimazaki J, Higa K, Morito F et al. Factors influencing outcomes in cultivated limbal epithelial transplantation for chronic cicatricial ocular surface disorders. Am J Ophthalmol 2007;143:945-53.
[23]. Pujari S, Siddique SS, Dohlman CH, Chodosh J. The Boston keratoprosthesis type II: the Massachusetts Eye and Ear Infirmary experience. Cornea 2011;30:1298- 303.
[24]. Basu S, Pillai VS, Sangwan VS. Mucosal complications of modified osteo-odonto keratoprosthesis in chronic Stevens-Johnson syndrome. Am J Ophthalmol 2013;156:867-73.
[25]. Iyer G, Pillai VS, Srinivasan B et al. Mucous membrane grafting for lid margin keratinization in Stevens- Johnson syndrome: results. Cornea 2010;29:146-51.
[26]. Basu S, Sureka S, Shukla R, Sangwan V. Boston type 1 based keratoprosthesis (Auro Kpro) and its modification (LVP Kpro) in chronic Stevens Johnson syndrome. BMJ Case Rep 2014; Mar 24;2014.

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