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# Efficacy of a Timely Amniotic Membrane Grafting in a Case of Steven Johnson Syndrome

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**Abstract:** ***Steven Johnson Syndrome A fatal drug reaction which though rare, has a high morbidity and mortality. 48yr male came with sudden onset redness & pain in eyes, fever and rashes on legs & ulceration in oral cavity (developed over few hours)with a 3 day history of intake of Norfloxacin & Carbamazepine for fever and UTI. Systemically- hyperpyrexia, target lesions over lower limb, & ulcerative tender lesions on lips, oral mucosa, tongue & palate. Ocular examination - VA 6/6, lid oedema with ulceration, congestion & extensive forniceal pseudomembranes & a clear cornea. Was diagnosed as SJS and started on iv antibiotics, topical lubricants, steroids &antibiotics. Both eyes underwent AMG within the 1st week with good outcome at 4wk follow up. SJS is an acute inflammatory polymorphic disease affecting skin, mucous membranes & eye. Ophthalmic involvement ranges from mild mucopurulent conjunctivitis to severe perforating corneal ulcers in 50% of patients. If untreated in a timely fashion, morbidity occurs with late corneal complications - opacities, vascularization, perforation & ocular surface abnormalities like symblepharon, occasionally leading to blindness. With early presentation and prompt treatment these dreaded complications were prevented & good results achieved.***

**Keywords:** Steven Johnson Syndrome, Amniotic Membrane Grafting (AMG)

## 1. Introduction

Although drug therapy has come a long way, with very rare adverse effects, they still remain a persistent threat to patient welfare. Steven Johnson Syndrome is one such fatal drug reaction which despite being as rare as 0.05-2 persons per million population per year, has a high morbidity and mortality.

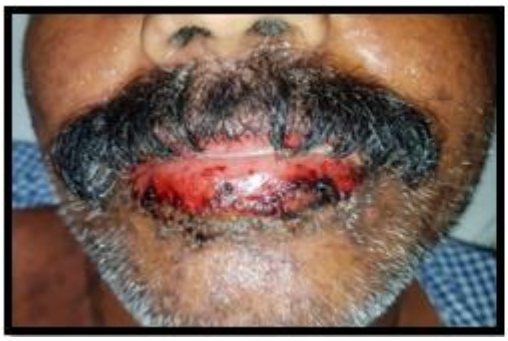
SJS is an immune complex mediated hypersensitivity reaction which can be precipitated by infections, vaccinations, systemic illnesses, food and drugs.More than 80% of cases are drug related. The drugs causing SJS are the commonly used antibacterials (sulfonamides), anticonvulsants (phenytoin, phenobarbital, carbamazepine), non-steroidal anti-inflammatory drugs (ibuprofen, oxicam derivatives) and oxide inhibitors (allopurinol).

The syndrome initially described in 1922 by Alan Lyell has 3 forms according to severity. The mild form of erythema multiforme (10-30% body surface area involved) and the severe ranging from Steven Johnson to Toxic Epidermal Necrosis (TEN) - > 30% involved [(1)]. There is characteristic skin, mucous membrane and ophthalmic involvement.

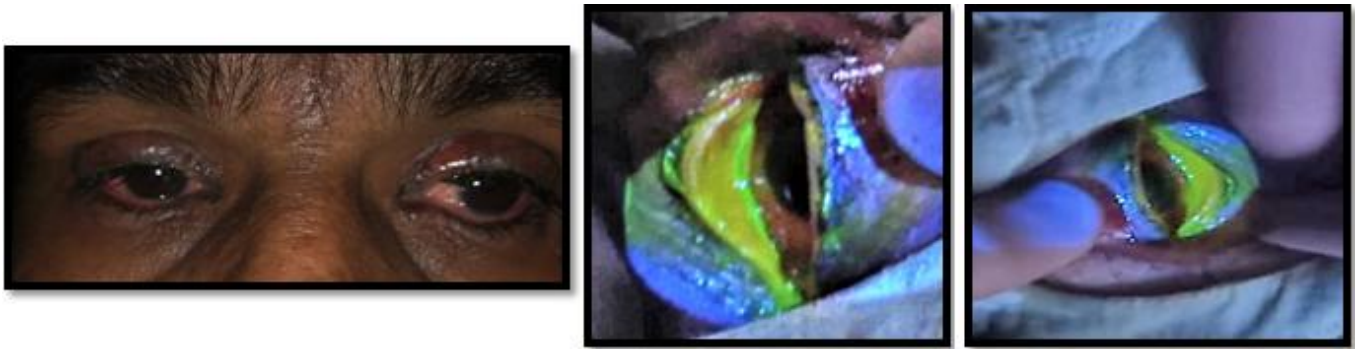
## 2. Case Report

A 48 year old male presented to us with sudden onset redness and pain in both eyes, fever and extensive rashes on the lower limbs and ulceration in the oral cavity which developed over a few hours. There was a three day history of intake of Tablet Norfloxacin and Tablet Carbamazepine as prescribed by a general practitioner for fever and a urinary tract infection after which he developed the reaction.

The patient was well-oriented on examination, had hyperpyrexia, the lower legs had well developed variably sized target like lesions. Intraoral examination revealed ulcerations of the lips and oral mucosa, tongue and palate. The ulcers were hemorrhagic and tender on palpation.

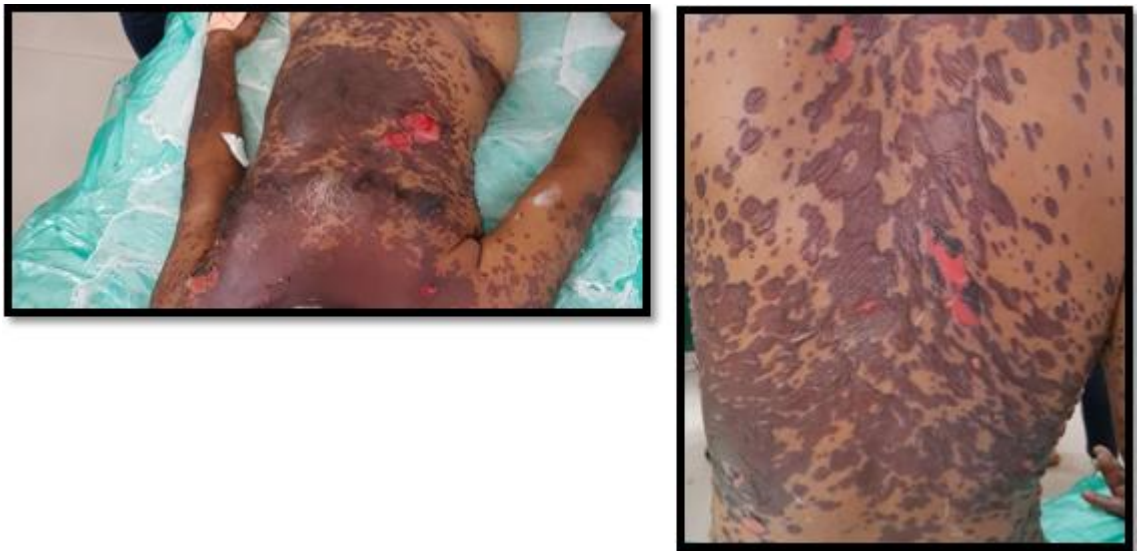


On ophthalmic evaluation, his vision was 6/6. There was severe lid oedema and ulcerations, congestion and chemosis with a mucopurulent discharge. Development of a pseudo membrane was seen on staining in the lower and upper fornices. No involvement of the cornea was noted.

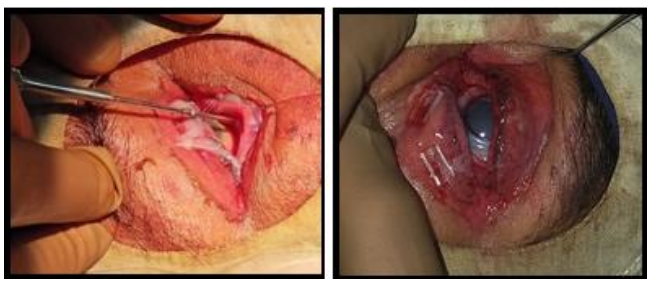


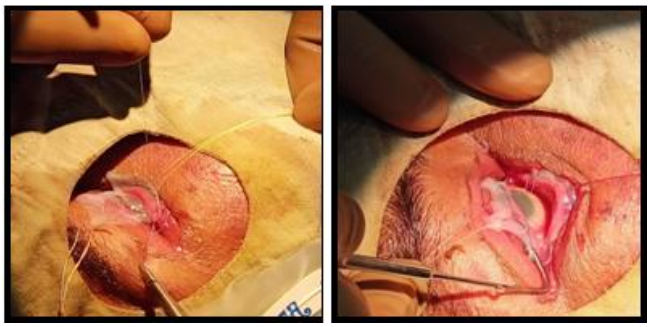
The patient was started on IV Linezolid, and topically on steroids, antibiotics (Tobramycin and Ocupol ointment) and lubricating drops. Local dressing of the lesions was done twice a day.

His vesico-bullous lesions increased to involve the chest, trunk and genital area over the following few days. He was diagnosed with Steven Johnson Syndrome – TEN overlap.

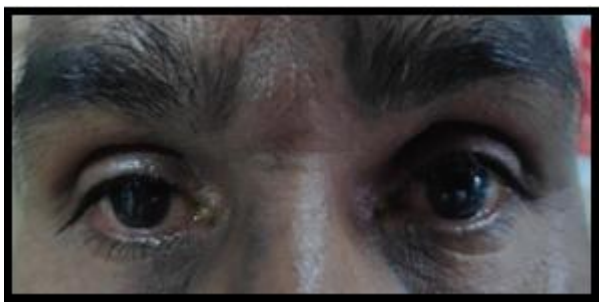


Amniotic Membrane Grafting was done for both the eyes within a week (Day 3 for the Right eye and Day 7 for the Left eye). A 5 x 5 cm graft was placed on both eyes with the epithelial surface upwards. It was tucked and sutured into the fornices using 7-0 proline sutures and covering the lid margins, fixed with 7-0 vicryl sutures. Purse string sutures were taken with 8-0 ethilon around the limbus to cover the cornea.





On removal of the sutures after 2 weeks, the outcome was good with the absence of pseudo membrane formation, corneal involvement or scarring.



At 1 month follow up, the patient had a 6/6 vision with minimal scarring in the upper fornix and no other adverse sequelae of the disease.

## 3. Discussion

Stevens-Johnson syndrome (erythema multiforme) is an acute inflammatory polymorphic disease affecting skin and mucous membranes. All ages may be affected with an equal incidence in both sexes. The incidence of SJS/TEN is low at an estimated 1-7 cases per million per year. It is a severe disease with a 5%–15% mortality rate[8]. Ocular involvement occurs in as many as half of patients and ranges from a mild mucopurulent conjunctivitis to severe perforating corneal ulcers. Blindness occasionally occurs in patients with severe late-phase corneal complications, such as ulceration, vascularization, and perforation [1].

The exact pathogenesis of SJS/TEN is unknown but probably involves cell-mediated keratinocyte apoptosis via the Fas signaling cascade and granulysin release [4]. There is angitis leading to erythematous lesions that become edematous or bullous (Subepidermal) and darken, leaving concentric rings in a target shape.

The syndrome can result from exposure to certain medications, infections, or malignancy, though almost a quarter of cases have no known trigger. Medications are the most frequently implicated inciting factor with antibacterial sulfonamides, such as trimethoprim/sulfamethoxazole, and anticonvulsants, such as phenytoin, carbamazepine and Lamotrigine, Allopurinol and NSAIDS as the leading culprits.[3]. Infections are the next most common cause. There is an especially strong association with Mycoplasma pneumoniae in children, but other infectious causes of SJS/TEN like HIV, HSV and CMV are relatively rare. In addition, it is important to note that HIV patients have up to a hundred-fold increase in susceptibility, due to reduced immunity and intensive drug regimens.

Ocular involvement in SJS begins with edema, erythema, and crusting of the eyelids. The palpebral conjunctiva becomes hyperemic, and distinct vesicles or bullae may occur. A conjunctivitis may appear that is characterized by watery discharge with mucoid strands. Secondary infection, most commonly with Staphylococcus species, can develop. In severe cases, a membranous or pseudomembranous conjunctivitis may result from coalescence of fibrin and necrotic cellular debris Severe pseudomembrane conjunctivitis may lead to symblepharon formation. Primary corneal involvement and iritis are rare ocular manifestations of Stevens-Johnson syndrome[5]. Moderate to severe SJS can lead to corneal opacity, limbal stem cell deficiency. These patients may later require a keratoplasty which has a high rate of rejection because of LSCD and ultimately may need a keratoprosthesis which is a prolonged difficult procedure.

Late ocular complications occur in approximately 20% of patients and include structural anomalies of eyelid position (ectropion and entropion), trichiasis, and symblepharon. Dry eye syndrome may also result from deficiencies in the tear film—either in the aqueous layer, from scarring of lacrimal duct orifices, or, more commonly, in the mucin layer, from destruction of the conjunctival goblet cells. Limbal cell loss may lead to recurrent non healing epithelial defects, pannus formation and extensive opacification and vascularization of the cornea.

Early intervention is important in preventing the late ocular complications of SJS. Use of corticosteroids is controversial. Intravenous immunoglobulin is the upcoming treatment nowadays. Local measures should be instituted early in the course of the disease like regular ocular lubrication with artificial tears and ointments (preferably preservative-free) Daily inspection and debridement of the superior and inferior fornices under topical anesthesia is essential. A glass rod can be used for symblepharon lysis, although this may be ineffective. A symblepharon ring can be useful in severe cases in cooperative patients. Cultures for microbial infection should be taken as needed. Amniotic membrane grafting should be considered in patients with advanced diseasethough its efficacy is doubtful.

The use of amniotic membrane transplantation (AMT) for SJS/TEN was first reported in 2002 with subsequent studies supporting its effectiveness in minimizing long-term visual sequelae[7] . The amniotic membrane (AM) is the innermost layer of the placenta and is comprised of a thick basement membrane with a poorly cellularized stromal matrix. The epithelium consists of a single layer of cuboidal cells with a large number of microvilli on the apical surface. The basement membrane is a thin layer composed of a network of reticular fibers. Histochemically, the basement membrane closely resembles that of the conjunctiva and contributes to the tensile strength of the membrane. The fibroblast layer is the thickest layer of the AM made up of a loose fibroblast network. The outermost layer of the amnion is the spongy layer. The AMG facilitates migration of epithelial cells, the reinforcement of basal cellular adhesion and the encouragement of epithelial differentiation. It reduces inflammation, inhibits neovascularization thus preventing ocular surface scarring.. The amniotic membrane releases a multitude of immunomodulators and growth factors, while simultaneously providing a substrate for epithelial cell growth. It may be used as either a temporary bandage or permanent graft. It has been studied that outcomes are patient-dependent, but a delay in treatment beyond 5 to 10 days after rash onset is associated with decreased visual acuity and increased ocular complications. In addition, AM coverage of the entire conjunctival surface is crucial to maximizing benefit[9].

Not every case of SJS/TEN is suitable for AMT. This technique is generally reserved for patients with moderate or severe conjunctival involvement, as these are the patients at greatest risk of visual loss from ocular surface scarring. Patients with minimal epithelial sloughing may instead be treated medically.

Ocular complications of SJS can be very severe, like forniceal shortening, symblepharon formation, cicatricial entropion, ectropion, trichiasis, ankyloblepharon, keratinization of conjunctiva, keratopathy.

Ocular involvement in SJS, TEN, and Overlap syndrome is common and the ocular manifestations may develop many

months after the initial presentation, mandating the need for long-term follow-up.

In this case, due to early presentation after the reaction and prompt treatment these dreaded complications were prevented and the patient had a good visual outcome.

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