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Research Paper

Ocular Complications of Stevens - Johnson Syndrome And Toxic Epidermal Necrolysis At A Tertiary Hospital In Southern Nigeria

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ABSTRACT
Purpose: *To review the possible aetiological factors of Stevens – Johnson syndrome or toxic epidermal necrolysis, its long term ocular complications and their management in patients seen at a tertiary eye care centre.*
Methods: *We retrospectively reviewed the medical records of patients with Stevens-Johnson syndrome or toxic epidermal necrolysis seen between January 2016 to December 2021 at Department of Ophthalmology University of Calabar Teaching Hospital. Their demographic data and documented clinical evaluation findings were collected and examined to determine possible aetiological factors causing Stevens-Johnson syndrome/Toxic epidermal necrolysis, its ocular complication and treatment given.*
Results.
A total of 10 patients were diagnosed with SJS/TEN during the 6 - year period. There were 4(40%) males and 6 (60%) females. All the patients were adults with mean age of 33.4 years (range 21 to 60). All patients had bilateral involvement and symmetrical in 9 (90%) of the cases.
The duration from initial onset of symptoms to presentation to our centre varied from 16 months to 39 years. No patient presented within one year of onset of symptoms.
Intake of drugs was the identified etiology common to all. On slit lamp and pen light examination complications were seen on the eyelid and conjunctiva of all 10 patients while cornea complication was seen in 9(90%) patients. Seven of the 10 patients received ophthalmic medications which included artificial tears, antibiotics and corticosteroid. Seven patients had surgical intervention and all four patients blind due to keratinized ocular surface were referred for keratoprosthesis.
Conclusion*: Stevens-Johnson syndrome and toxic epidermal necrolysis are complex immunological syndrome that can result in devastating complications of ocular surface scarring and keratinization leading to blindness. Early ophthalmic assessment and management as well as regular follow up care are key factors to recovery and prevention of ocular complications*
Key words: *Stevens-Johnson syndrome, toxic epidermal necrolysis, ocular, complication*

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I. INTRODUCTION

Stevens - Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) represent different ends of the spectrum of the same clinical entity of severe mucocutaneous reactions, usually to drugs, characterized by intraepidermal cell death leading to blistering and epidermal sloughing.

SJS is the milder variant with <10% of total body surface area involvement. TEN is the more severe form with >30% total body surface area involvement. An intermediate classification is the SJS-TEN overlap in which there is 10–30% involvement [1].

SJS/TEN frequently involves the eye and in severe cases can result in blindness. The acute manifestation of the disease on ocular structures (eyelids, conjunctiva and cornea) occur in 60 to 100 percent cases while the late complications have been reported to occur in 20 to 80% of survivors [2, 3].

This retrospective review aims to evaluate the presentation characteristics, possible etiological factors, ocular complications and management of patients presenting with SJS/TEN at our institution.

II. MATERIALS AND METHODS

This was a retrospective study in which the clinical records of all patients diagnosed of SJS/TEN at the Department of Ophthalmology University of Calabar Teaching Hospital (UCTH) over a 6 year period between January 2016 to December 2021 were reviewed. The medical records were reviewed to obtain demographic data. Details of laterality, symmetry, duration of initial insult to time of presentation to the hospital and possible etiological factors were noted. Use of any oral or systemic drug was regarded a possible etiological factor if the drug had been taken within two weeks of onset of prodromal symptoms.

Documented clinical findings on slit lamp and penlight examination of the eyelids, conjunctiva and cornea were noted.

Best corrected visual acuity in the better and worse eye at presentation as well as treatment or any intervention given were also noted.

III. RESULTS

A total of 10 patients were diagnosed with SJS/TEN during the 6 - year period. Patients demographics, clinical features and surgical treatment given are depicted on Table. There were 4 (40%) males and 6 (60%) females. All the patients were adults with mean age of 33.4 years (range 21 to 60). All patients had bilateral involvement and symmetrical in 9 (90%) of the cases.

The duration from initial onset of symptoms to presentation to our centre varied from 16 months to 39 years. No patient presented within one year of onset of symptoms.

Intake of drugs was the identified etiology common to all. Sulfonamide based anti malaria agent under various trade names such as Fansidar and Laridox etc was the most identified drug. In 5 cases the exact drug taken that triggered SJS/TEN was not identified as the patients had taken mixture of several drugs prior to developing the condition.

The Best corrected visual acuity in the better eye was as follows: 3(30%) had an acuity of 6/12 or better; 3 (30%) patients had acuity of 6/18 to 6/60; 4 (40%) patients had only light perception (blind). No patient presented without light perception visual acuity.

On slit lamp and pen light examination complications were seen on the eyelid and conjunctiva of all 10 patients while cornea complication was seen in 9(90%) patients.

The eyelid complications included adhesions, lid margin thickening, blepharitis, trichiasis and distichiasis, entropion, ankyloblepharon, ptosis due to aponeurosis levator aponeurosis dehiscence, punctal occlusion and retention cyst (Figure 1)

Conjunctival complications included chronic congestion, xerosis, symblepharon, forniceal shortening, keratinization, scarring,

Corneal complications included superficial epithelial keratitis, cornea scaring, pannus, keratinization,

7 of the patients received ophthalmic medications which included artificial tears, antibiotics and corticosteroid. Seven patients had surgical intervention and all four patients blind due keratinized ocular surface were referred for keratoprosthesis. Among those that had surgery 3 were entropion surgery, 4 had symblepharon/ankyloblepharon release, one patient had each of marsupializtion of cyst, canaliculotomy, tarsotomy and bilateral levator advancement surgery to correct ptosis. Some patient had more than one surgical procedure (Table 1).

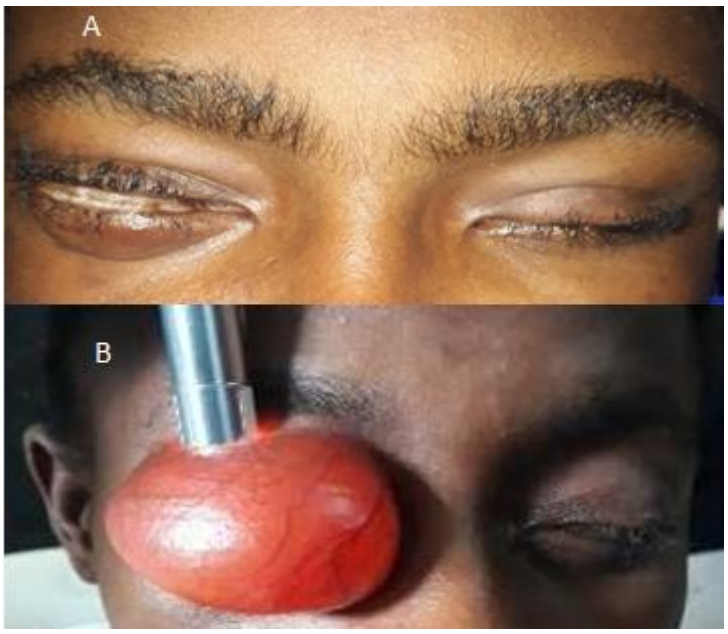

Figure 1 Patients with late complications of SJS/TEN. (A) Patient with bilateral ankylosymblepharon/ocular surface keratinization. (B) Patient with giant upper eyelid retention cyst transilluminated to demonstrate its cystic nature

IV. DISCUSSION

Stevens-Johnson syndrome is a noteworthy cause of ophthalmic morbidity. Most patients who develop SJS/TEN consult a physician or a dermatologist in the acute phase. They consult ophthalmologists only after the resolution of skin lesions and are later referred to tertiary eye-care centers. This explains why non of our patients presented in the acute stage of the disease.

Several studies have shown that drugs are the most common cause of SJS/TEN [1,4,5]. In our study drugs were the cause in all the cases similar to the findings in some studies [4,5] and sulfonamides

Table1: Patient demographics, clinical features and surgical intervention

Case	Age/Sex	VA RE LE	Duration	Causative Agent	Clinical Findings	Symmetry	Surgical Intervention
1	60 M	6/60 6/36	39 years	Drug (sulfonamide)	Distichiasis , trichiasis, symblepharon, pannus Keratitis	Symmetrical	Bilamellar tarsal rotation, tarsotomy Symblepharon release
2	23 F	6/9 6/18	7 years	Drug (sulfonamide)	Punctal stenosis, symblepharon , medial ankyloblepharon, pseudopterygium	Asymmetrical	Symblepharon and ankyloblepharon release with symblepharon ring placement
3	28 F	6/60 6/24	7 years	Drug (Sulfonamide)	Bilateral levator disinsertion , keratitis, chronic inflammation, trichiasis	symmetrical	bilateral levator advancement bilamellar tarsal rotation
4	27 F	LP LP	4 years	Drug	Bilateral ankylosymblepharon Giant eyelid retention cyst	symmetrical	Marsupializtion of cyst Referred for keratoprosthesis
5	51 F	6/18 6/24	5 years	Drug	Trichiasis, Keratitis	symmetrical	Bilamellar tarsal rotation
6	49 F	6/6 6/6	3 years	Drug	Bilateral cannalicular retention cyst Punctal occlusion symblepharon	symmetrical	Cannaliculotomy Symblepharon release
7	21 M	6/6 6/6	16months	Drug (sulfonamide)	Bilateral medial and lateral ankyloblepharon Madarosis of lower lid Bilateral punctal occlusion Paracentral cornea opacity	symmetrical	Ankyloblepharon release
8	28 M	LP LP	5 years	Drug	Bilateral symblepharon with keratinization of conjunctiva and cornea	symmetrical	Referred for keratoprosthesis
9	24 M	LP LP	3 years	Drug (sulfonamide)	Bilateral ankylosymblepharon	symmetrical	Referred for keratoprosthesis
10	23 F	LP LP	15 months	Drug	Bilateral ankyloblepharon , pannus , keratinization of cornea	Symmetrical	Referred for keratoprosthesis

VA = visual acuity, M = male, F= female, LP = light perception, RE = right eye, LE = left eye

based anti malaria drugs was the most common etiological agent. Despite the advent of newer anti-malaria medications which does not contain sulfonamides, patients continue to use sulfonamide based drugs purchased over the counter to treat malaria. This remains a cause of concern. Specific drug cause could not be ascertained in 5 (50%) patients who had taken mixture of several drugs prior to development of SJS/TEN.

The reported ophthalmic manifestation of SJS is broad. The acute phase which usually occur within 2 weeks of onset of symptoms is marked by bilateral conjunctivitis, hyperemia, conjunctival membrane or pseudomembrane formation, meibomitis, symblepharon, conjunctival sloughing and cornea epithelia defects [2, 6].

The sub-acute stage of the disease is described as stage of smoldering chronic conjunctivitis with lid margin changes and trichiasis. At this stage most of the skin lesions are resolved [2]. Ophthalmic findings may include entropion, trichiasis, distichiasis, symblepharon formation, recurrent or persistent corneal epithelial defects, severe dry eye and keratinizaton of the posterior lid margin [6].

The chronic stage of the SJS/TEN is characterized by persistent and prolonged ocular surface inflammation and ulceration. Chronic ocular sequelae with severe visual loss are associated with lid margin abnormality and ocular surface failure [7]. Conjunctival ulcerations or conjunctival membrane formation as well as persistent inflammation can result in permanent symblepharon and ankyloblepharon, which disrupts tear film meniscus and inhibits proper eyelid closure and blinking, and sometimes restrict ocular motility [6]. There may be scarring with contracture of the tarsal conjunctiva causing malpositions of the eyelid and other disorders, including ectropion, entropion, trichiasis, distichiasis, meibomian gland atrophy and inspissation, punctal occlusion, and keratinization of the eyelid margin, tarsal and bulbar conjunctival surfaces, cornea opacification, vascularization or ulceration [2, 6].

Based on severity, the ocular involvement in SJS/ TEN can be classified into mild, moderate, or severe [1]. Mild ocular involvement is characterized by eyelid skin involvement in the form of desquamation and denudation, eyelid edema, mild corneal involvement, mild conjunctival injection, mucous discharge, or chemosis. Moderate cases present with membranous conjunctivitis, epithelial defects with more than 30% healing with medical treatment, corneal ulceration, or corneal infiltrates. Severe manifestations comprise of acquired eyelid malposition, formation of symblepharon, non healing corneal epithelial defects, complete or

partial visual loss, or foreshortening of conjunctival fornix [1]. All our patients presented with severe manifestation. This is contrast with the study by Abrol et al where moderate involvement was seen in most patients (62.9%), followed by mild involvement 25.9% and severe 11.1% [1].

The goal of treatment in SJS/TEN is survival and recovery from the systemic disease as well as the prevention of cicatricial complications in the affected organ systems [2].

The major aim of early ophthalmologic intervention in the acute stage of SJS/TEN is to prevent cicatricial complication and in late stages of the disease is reconstruction of ocular surface to correct the effects chronic inflammation.

The management of late sequelae remains a challenge because of the irreversible alteration in the ocular surface [8]. Most of our patients did not have early ophthalmic intervention. This may account for the severe late complications seen in them.

In the acute stage, liberal use of lubricants (preferably non preserved) is the main stay of care [9]. Prophylactic antibiotic and topical steroids have been reported to improve the outcome of care and have become an acceptable practice. Topical steroid drops plus ointment for the lid margin is recommended only after microbial keratitis has been excluded. A symblepharon ring can be used with copious lubrication to prevent adhesions in the fornix [2, 6].

Various surgical options are available for care of patients with SJS/TEN depending on the nature of ophthalmic complications. Mucus membrane transplantation and amniotic membrane grafting are increasingly being used to mitigate complications and the reconstruction the ocular surface in patients with SJS/TEN. Amniotic membrane tends to reduce ocular surface inflammation, form a scaffold for re-epithelialization, and prevent symblepharon formation, thus mitigating the long term sequelae of the disease [2, 10].

V. CONCLUSION

Stevens-Johnson syndrome and toxic epidermal necrolysis are complex immunological syndrome that can result in devastating complications of ocular surface scarring and keratinization leading to blindness. Early ophthalmic assessment and management as well as regular follow up care are key factors to recovery and prevention of ocular complications.

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