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A case series on Ocular Manifestations in Stevens Johnson Syndrome and Toxic epidermal necrolysis in Acquired immunodeficiency syndrome-Review of literature.

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Abstract:
Aim: *To evaluate the severity of Ocular involvement in patients with Stevens-Johnson Syndrome(SJS),Toxic Epidermal Necrolysis(TEN).*
Study Design*: Retrospective Observational Case Series for a period between january 2013 and october 2015.*
Methods: *Cases of SJS and TEN during a period from 2013-15 were included. Patients with ocular involvement were reviewed for acute ocular complications. 10 patients with diagnosis of SJS, TEN with fever, skin rash, extensive bullae, sloughing of skin, erythematous macules and patches, and other ocular manifestations were studied. Ocular manifestations which include lid edema mild conjunctival injection , chemosis, membranous conjunctivitis, corneal epithelial defects, corneal ulceration,corneal infiltrates, symblepharon formation , nonhealing corneal epithelial defects,visualloss ,conjunctival fornix foreshortening, were classified as mild, moderate or severe. Main outcome measure was severity of ocular involvement with respect to diagnosis.*
Results*: Out of 10 patients, 9 of them were HIV positive. All of them had mucosal involvement and ocular surface involvement. Ocular involvement was moderate in 40% and severe in 60% of the cases. None of the cases examined had mild ocular involvement. Out of 10, 8 patients had SJS, and 2 of them had TEN. One of the patient died from acute complications including severe fluid imbalances, infections, and respiratory failure.*
Conclusion*: Out of 10, 8 patients had SJS, and 2of them had TEN and 9 of them were HIV positive. The above study revealed that HIV patients have an increase in susceptibility, which is likely due to immunologic abnormalities and intensive drug regimens. Of these, 40% had moderate ocular involvement, and 60% had severe ocular involvement. The diagnosis of TEN does not imply a more severe ocular involvement compared with SJS. Care should be taken even in mild cases. Appropriate intervention during acute ocular disease may prevent late complications.*
Keywords: *Ocular manifestations , Stevens- Johnson Syndrome(SJS),Toxic epidermal necrolysis(TEN), Human immunodeficiency virus (HIV) .*

I. Introduction:

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are similar conditions characterized by intraepidermal cell death leading to diffuse vesicobullous eruptions. The differentiating criteria for SJS and TEN is the extent of skin detachment; SJS is defined as <10% total body surface area, and TEN as >30%. Mucosal involvement is common occurring in 90% of patients, and may involve the ocular surface in as many as 80% of patients [1]. The incidence of SJS,TEN is low at an estimated 1-7 cases per million per year [2].

II. Methods:

10 patients with ocular manifestations of stevens-johnson syndrome were studied retrospectively are included in this study. Acute ocular involvement was defined as previously described elsewhere [17]. Briefly, mild ocular involvement comprised lid edema, mild conjunctival injection and chemosis. Moderate involvement comprised membranous conjunctivitis or corneal epithelialdefects or corneal ulceration, corneal infiltrates in which more than 30% are healed with medical treatment. Severe involvement comprised symblepharon formation or nonhealing corneal epithelial defects or visual loss or conjunctival fornix foreshortening.

Inclusion Criteria:

A serious mucocutaneous illness with characteristic target-like lesions **,** bullae and extensive areas of necrosis**,** a prominent acute prodromal period and Involvement of at least two mucosal sites.

Exclusion Criteria: Debilitated patients, Pthysical eyes, intra-ocular malignancies, patients with other associated immunological skin disorders like pemphigus, pemphigoid.

III. Results:

Out of 10 patients, 9 of them were HIV positive. All of them had mucosal involvement and ocular surface involvement. Ocular involvement was moderate in 40% and severe in 60% of the cases. None of the cases examined had mild ocular involvement. Out of 10, 8 patients had SJS, and 2 of them had TEN. One of the patient died from acute complications including severe fluid imbalances, infections, and respiratory failure.

Severity (%)	Mild	Moderate	Severe
SJS	0	4(40%)	4(40%)
TEN	0	0	2(20%)

Table . Severity of acute ocular involvement in Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN)

IV. Discussion

Epidemiology

- Incidence of 2-7 cases per million per year.
- Women more commonly affected than men, 2:1 occurrence ratio.
- Highly associated with certain medications, some association with infections

Pathogenesis and Etiology

The exact pathogenesis of SJS/TEN is unknown but appears to involve cell-mediated keratinocyte apoptosis via the Fas signaling cascade and granulysin release [3] . The syndrome can result from exposure to certain medications, infections or malignancy though almost a quarter of cases have no known trigger [4] Medications are the most frequently implicated inciting factor with antibacterial sulfonamides, such as trimethoprim/sulfamethoxazole, and anticonvulsants, such as phenytoin, as the leading culprits. 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 are relatively rare. In addition, it is important to note that HIV patients have up to a hundred-fold increase in susceptibility, likely due to immunologic abnormalities and intensive drug regimens. Many other medications and infectious agents have been associated with SJS/TEN, but the most common etiologies are listed in[Table 1].

Table 1: Most common causes of SJS/TEN [2]

Pharmacologic	Infectious

• Allopurinol
• Anticonvulsants
  ○ Carbamazepine
  ○ Phenytoin
  ○ Lamotrigine
• Barbituates
• Sulfonamides
• NSAIDs
	• Bacterial
	  ○ Mycoplasma pneumoniae
	  ○ Group A β-hemolytic strep
	• Viral
	  ○ Cytomegalovirus
	  ○ Herpes simplex virus
	  ○ HIV

Consequences

The disease can have severe sequelae. The prognosis varies with severity of disease, but the overall six-week mortality rate for patients on the SJS/TEN spectrum is 23%, arising from acute complications including severe fluid imbalances, infections, and respiratory failure. Mortality remains high even after resolution of the acute phase, with in one-year mortality rate of 34% [5].

Amongst survivors, long-term ocular complications can be serious and are thought to affect approximately 60% of patients [6] . Corneal damage in the form of scarring or limbal stem cell failure is the most severe ocular outcome. Conjunctival scarring can contribute to long-term corneal pathology and subsequent visual impairment. For example, palpebral conjunctival scarring can cause chronic microtrauma with the blink reflex, while symblepharon formation can lead to poor tear film dynamics and predisposition to severe dry eye [7] .

Ocular Examination

Because ocular involvement is common and there is potential for severe visual consequences, all patients with SJS/TEN should be urgently evaluated by an ophthalmologist. Fluorescein staining should be used to evaluate the extent of corneal and conjunctival epithelial defects. Slit lamp examination of the palpebral conjunctiva is a critical component of the examination as it is frequently affected by SJS/TEN.

V. Management

Medical Management

While systemic corticosteroids are frequently used for the management of SJS/TEN, widespread acceptance of this approach has long been controversial. Evidence for its efficacy is lacking and early studies associate systemic steroids with a slight increase in the mortality of pediatric patients [8] Intravenous immunoglobulin (IVIG), administered with the goal of inhibiting the Fas-ligand signaling pathway, has recently gained traction as a possible therapy but studies regarding its efficacy continue to have conflicting findings. Of note, one recent study found improved ocular outcomes associated with IVIG therapy compared to systemic steroids [9]

Ophthalmologic Management

Studies investigating the therapeutic value of topical medications for ocular SJS/TEN are similarly lacking. While there is no standard treatment, a combination of topical corticosteroids and antibiotics are often used in cases of mild ocular involvement, with one retrospective study suggesting that early topical steroids are associated with improved visual outcomes[10]. For more severe ocular involvement, there is evidence that early surgical intervention with amniotic membrane can lead to improved outcomes [7,11,12].

Amniotic Membrane Transplantation

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] . These studies emphasize the importance of early AMT intervention. Outcomes are patient-dependent, but results indicate that delays in treatment beyond 5 to 10 days after rash onset are associated with decreased visual acuity and increased ocular complications [11,12] . In addition, AM coverage of the entire conjunctival surface is crucial to maximizing benefit; patients undergoing AMT only to the bulbar conjunctiva may still develop the chronic sequelae of SJS/TEN [12].

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.

Chronic SJS/TEN Surgical Treatment

Though intervention in the acute stage has the best ocular outcomes, treatments also exist for the chronic sequelae of SJS/TEN. Keratoprosthesis and limbal allografting rarely match the success of early surgical treatment, but these methods can provide some visual recovery despite limbal stem cell loss and corneal conjunctivalization. FIG 1:patient with symblepharon ,corneal epithelial defects

FIG 2:patient with sloughing of skin and erythematous bullae

FIG 1

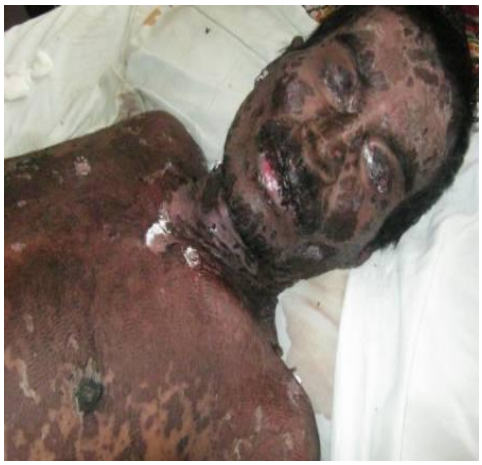
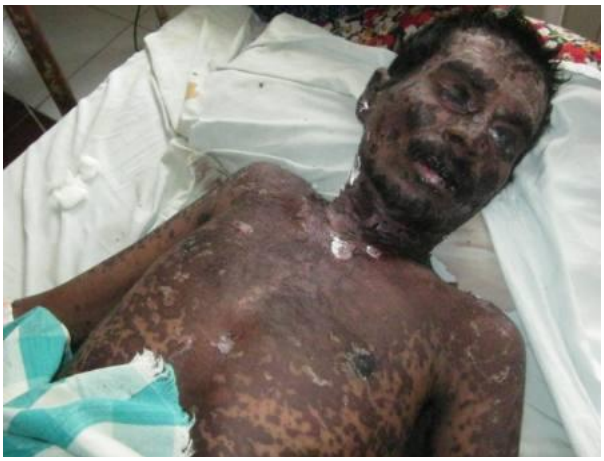

FIG 2

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