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Detailed evaluation of patients with Stevens Johnson syndrome with respect to ocular manifestations.

Ophthalmology

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ABSTRACT

Stevens Johnson syndrome(SJS) is characterised by mucocutaneous affection with associated opthalmic involvement. We prospectively studied 30 patients of SJS with respect to ocular manifestations and visual outcomes over a period extending over 16 months.Ninety percent of patients had bilateral involvement. Common age of presentation for SJS is 18-30 years. All females while 85% of male patients enrolled had ocular involvement. Redness(60%) was the most common presenting symptom followed by diminution of vision(50%). The most common causative agents were Non-steroidal anti-inflammatory drugs (26.66 %) and anticonvulsants (26.66%) . Other features at presentation includes conjunctival congestion (70%), lid edema(50%) and corneal opacity(26.6%). Lid thickening, conjunctival xerosis, symblepharon, superficial punctate keratitis and corneal vascularisation were seen in 23.33%. Only 3.33% patients had corneal thinning. At 6 month follow up,36.66% had corneal opacity as well as lid thickening and 30% had corneal vascularisation. There was increased incidence of dry eyes during follow up. It was observed that patients with good best corrected visual outcome at presentation had better visual outcome.

Conclusion: Ocular manifestations occur in high proportion of patients with SJS. Ophthalmic consultation, evaluation and management should be done at the earliest. Early diagnosis and intervention can prevent sight threatening long term sequelae.

KEYWORDS:

Stevens Johnson syndrome, complications, visual outcomes.

Introduction

SJS is a complex immunological syndrome that is characterised by mucocutaneous blistering of the skin and at least two mucous membranes. A typical lesion has the appearance of a target; this is considered pathognomonic. It is characterized by mucous membrane erosions and blisters on limited areas of the skin (<10% of the total body surface area). Males are affected more than females, and it can occur at any age.The disease is thought to be either a delayed hypersensitivity reaction to certain medications or a response to epithelial cell antigens modified by drug exposure. Genetic predisposition may also play a part due to a genetically determined enzyme deficiency for the metabolites of certain medicines. The incidence of is 1.8 cases per million persons per year between 20-64 years of age .The incidence for patients aged less than 20 years and 65 years and above increased to 7-9 cases per million per year.[1]

Materials and Methods:

This study was conducted in a tertiary care institute, Department of Ophthalmology after approval of ethics committee. It is an observational, population based, cross sectional study of 30 patients diagnosed to have SJS attending our outpatient department and dermatology department.

Inclusive criteria:

1.Patients with a dermatological diagnosis of SJS.
2.Both eyes of patients evaluated, even if there is no clinical evidence of involvement, as it will form part of the statistics.

Exclusion criteria:

1. Patients with eyelid or ocular surface surgery prior to diagnosis of SJS.
2. Age less than 18years.

Study duration

Prospective data collected from August 2015 upto December 2016.

Study Procedure:

Informed written consent was taken.Patients were diagnosed as Steven Johnson syndrome by dermatologists based on Bastuji Garin criteria. Patient's demographic data such as age, sex were recorded. Each patient was enquired about following ocular symptoms: Diminition of vision , redness, discharge, foreign body sensation, watering and history of ocular trauma.

Patients were asked regarding onset ,duration and course of ocular manifestation. Use of any oral or systemic drug was considered a possible etiological factor, if the drug had been taken within four weeks of onset of prodromal symptoms.

All patients were asked to narrate important events that preceded the onset of SJS

Detailed Slit lamp examination included the following:

Lid abnormalities: lid edema , thickening , entropion , Meibomion gland dysfunction , superficial lid erosions.

Conjunctival pathologies: congestion, xerosis, symblepharon , discharge

Corneal abnormalities : superficial punctate keratitis, epithelial defect thinning, opacity and vascularization.

Dry Eyes evaluation : Included schirmer's test , tear break up time .

Best corrected visual acuity was measured.

All patients were treated with topical lubricating eye drops, topical low dose steroids and topical antibiotics as per severity of their manifestations.

Follow up visits were at 1 month, 3 month and 6 month which included evaluation of best corrected visual acuity, slit lamp examination and dry eye evaluation.

Results:

Table 1: AGEWISE DISTRIBUTION AMONG STUDY PATIENTS

Age(years)	No of patients		Percentage of patients	
	With ocular Involvement	Without ocular involvement	With ocular involvement	Without ocular involvement
18-30	14	2	87.5	2.23

31-40	3	0	100	0
41-50	4	1	80	1.23
51-60	4	0	100	0
61-70	2	0	100	0
TOTAL	27	3	90	3.22

Table 2:GENDER DISTRIBUTION

Gender	No of patients (N=30)		Total	Percentage of patients	
	With ocular involvement	Without ocular involvement		With ocular involvement	Without ocular involvement
Male	16	3	19	85	15
Female	11	0	11	100	0

TABLE 3:SYMPTOMS

Symptoms at presentation	No of patients (N=30)	Percentage
Redness	18	60
Diminition of vision	15	50
Foreign body sensation	14	46.66
Watering	11	36.66
Discharge	8	26.66

TABLE4:CAUSE OF STEVEN JOHNSON SYNDROME

CAUSE	NO OF PATIENTS	PERCENTAGE
1)NSAIDS	8	26.66
a)Tab Ibuprofen	4	13.33
b)Tab Nimesulide	4	13.33
2)ANTICONVULSANT	8	26.66
a)Tab Phenytoin	5	16.66
b)Tab Carbamazepine	2	6.66
c)Tab Valproate	1	3.33
3)ANTIBIOTICS	7	23.33
a)Tab Amoxicillin	3	10
b)Tab Ofloxacin/Levofloxacin	3	10
c)Tab Cefexime	1	3.33
5)ANTI KOCHS THERAPY	3	10
6)Tab Chloroquine	2	6.66
7)Ayurvedic therapy (detail unknown)	2	6.66
TOTAL	30	100

(NSAIDS= non-steroidal anti-inflammatory)

The above data shows NSAIDS(26.66 %) and anticonvulsants (26.66%) responsible for majority of cases. Among anticonvulsants, patients on tablet phenytoin had highest incidence of Steven Johnson syndrome (16.66%). Antibiotics were responsible in 23.33% - Anti-Koch's therapy in 10%, Chloroquine in 6.66% and Ayurvedic therapy (detail unknown) in 6.66% .

TABLE5:LATERALITY

LATERALITY	NO OF PATIENTS	PERCENTAGE
UNILATERAL	0	0
BILATERAL	28	90
NO INVOVLEMENT	3	10
TOTAL	30	100

Thus, ocular involvement was bilateral in 90 % patients.

TABLE 6:OCULAR MANIFESTATIONS IN STEVEN JOHNSON SYNDROME

OCULAR MANIFESTATION	No of patients	Percentage	No of patients			Percentage of patients at end of 6 months
	0 DAY	%	1month	3month	6month	%
1)LID						
a)Edema	15	50	2	2	0	0
b)Thickening	7	23.33	8	11	11	36.66
c)Entropion	3	10	3	3	3	10
d)Meibomion glands dysfunction	9	30	15	9	8	26.66
e) lid superficial erosions	11	36.66	3	0	0	0
2)CONJUNCTIVA						
Discharge	11	36.66	0	0	0	0
a)Congestion	21	70	7	8	5	16.66
b)Xerosis	7	23.33	7	7	7	23.33
c)Symblepharon	7	23.33	7	7	7	23.33
3)CORNEA						
a)Superficial punctate keratitis	7	23.33	10	5	3	10
b)Epithelial defect	4	13.33	0	0	0	0
c)Opacity	8	26.66	11	11	11	36.66
d)Vascularisation	7	23.33	8	9	9	30
e)Thinning	1	3.33	1	1	1	3.33

During follow up of 6 months , there was increased in incidence of lid thickening from 23.33% to 36.66%, corneal opacity from 26.66% to 36.66% , and corneal vascularisation from 23.33% to 30% .There was decrease in incidence lid edema, meibomion glands dysfunction, discharge, superficial lid erosions, conjunctival congestion, superficial punctate keratitis and corneal epidefect .

TABLE 8 : DRY EYE EVALUATION

	No of Patients					
	At presentation	Precentage	1 month	3 month	6 month	Percentage of patients at end of 6 months
Schirmer's test						
<10 mm	10	33.32	19	13	14	46.66
>10 mm	20	66.66	11	17	16	53.33
TBUT						
<10	20	66.66	21	21	23	76.66
>10	10	33.33	9	9	7	23.33

(TBUT= tear break up time)

During follow up there was increased incidence of dry eyes inspite of treatment.

Table 9: Visual outcome

	No of patients		No of patients			Percentage of patients at end of 6 months
Visual acuity	At presentation	Percentage	1 month	3 month	6 month	
6/6-6/18	16	53.33	22	22	22	73.33
<6/18-6/60	3	10	2	2	2	6.66
<6/60-3/60	2	6.66	0	1	1	3.33
<3/60 – No PL	9	30	7	5	5	16.66

During follow up there was improvement in visual acuity.

Discussion:

Steven Johnson syndrome is an acute immunological mucocutaneous disorder with high morbidity and mortality. The disease is thought to be either a delayed hypersensitivity reaction to

certain medications or a response to epithelial cell antigens modified by drug exposure. Genetic predisposition may also play a part due to a genetically determined enzyme deficiency for the metabolites of certain medicines.

Approximately 80% of hospitalised patients develop acute ocular complications ,with severe involvement in 25% . Ocular involvement at the onset of disease is frequent, and can range from acute conjunctivitis, eyelid edema, erythema, crusts, and ocular discharge, to conjunctival membrane or pseduomembrane formation or corneal erosion, and, in severe cases, to cicatrizing lesions, symblepharon, fornix foreshortening, and corneal ulceration.[2,3] The severity of acute ocular manifestation is not however predictive of late complications.[4] The major ocular problems occur from the cicatricial stage, after the acute toxic episodes subsides. Conjunctival scarring and symblepharon may occur despite all supportive measures. Destruction of conjunctival goblet cells ,lacrimal gland, and accessory lacrimal gland tissue destruction results in severe dry eye, just as cicatricial pemphigoid.

Entropion, trichiasis and lagophthalmos combined with the dry eye can produce severe corneal problems such as ulceration, vascularization, opacification, limbal stem cell deficiency and eventually perforation. Destruction of the corneal limbal stem cells is perhaps the most dire consequences of the aforementioned pathologies and can lead to vascularization and thickening of the cornea. It creates a poor prognosis for any future corneal transplantation.

Studies have shown that drugs are responsible in upto 60% of cases of Steven Johnson syndrome.[5] In our study drugs were the causative agents in 100% cases , non-steroidal anti-inflammatory drugs and anticonvulsants being the most common. Other uncommon causes are vaccination and exposure to industrial chemicals and fumes , viral infections (*Coxsachie virus, Influenza virus, Epstein Barr virus, herpes virus 6 and 7, Cytomegalovirus, parvovirus*), bacterial agents (*Mycoplasma pneumoniae, Group* A Beta Hemolytic streptococci) and *rickettsia*.[6,7]

The ophthalmologic management of acute Steven Johnson syndrome should focus on infection prophylaxis, adhesion prevention and minimization of destructive inflammation. Studies investigating the therapeutic value of topical medications for ocular Stevens Johnson syndrome 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.[8] For more severe ocular involvement, there is evidence that early surgical intervention with amniotic membrane can lead to improved outcomes.[8,9,10]

Though intervention in the acute stage has the best ocular outcomes, treatment also exist for the chronic sequelae. 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 .[9,10,11] In our study, It was observed that patients with good BCVA at presentation had better visual outcome.

Conclusion:

Ocular manifestations occur in high proportion of patients with SJS. The most frequent causative agents were NSAIDS and anticonvulsants. A careful medications history should be obtained from these patients. Better visual outcomes are seen in patients presenting with good BCVA. Ophthalmic consultation, evaluation and management should be done at earliest. Early diagnosis and intervention can prevent sight threatening long term sequelae.

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