OCULAR INVOLVEMENT IN MUCOCUTANEOUS DISORDERS- A STUDY IN TERTIARY HOSPITAL IN SOUTH ORISSA

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ABSTRACT

BACKGROUND

Diseases of skin, mucous membrane and mucocutaneous junctions may also affect the eyes. Physical findings of dermatological disorders and eyes overlap due to three factors- (i) Genodermatoses often affects both skin and eyes because of origin from embryonic ectodermal layers, (ii) Acquired dermatological disorders may affect the mucocutaneous tissue of periorbital regions, (iii) Systemic diseases can manifest as diseases of skin and periocular mucocutaneous tissue because of their superficial anatomical locations.

The aim of the present study was observation and interpretation of changes in the eye in different mucocutaneous disorders and correlation of the eye changes with severity of the diseases.

MATERIALS AND METHODS

A prospective study was undertaken in the Department of Ophthalmology, M.K.C.G. Medical College and Hospital, Berhampur, South Orissa, during the period of 2014 to 2016 including the referred patients after being diagnosed with mucocutaneous disease from Department of Dermatology, Paediatric and Medicine from the same hospital. A case study of 204 patients (M-164, F-40) was done. All patients underwent detailed ophthalmic examination inclusive of ocular movements, VA, IOP, S/L exam, blood and urine investigation and fundus examination.

RESULTS

Out of 204 patients examined, i.e. 164 males and 40 females, the ocular involvement found was 132, i.e. 64%. Majority of patients having ocular lesions were affected by herpes (72.2%) and leprosy (78.57%). Most common mucocutaneous syndrome in the study was herpes (35.29%) and leprosy (27.45%). Most common ocular lesions in various mucocutaneous ocular syndrome was found to be conjunctivitis (45.4%), blepharitis (34.8%) and periorbital vesicles (30.3%). The least common was found to be trichiasis and conjunctival membrane each 3%. After follow-up of 3 months, the following ocular sequelaes were observed, i.e. dry eye (9%), symblepharon (7.5%), corneal scar (4.5%), corneal vascularisation (3%), trichiasis (3%) and ankyloblepharon (1.5%). Visual acuity analysis was done. We found in 62 cases had vision between 6/18 to 6/6.40 cases had visual acuity between 6/18 to 6/60. 12 cases had total blindness.

CONCLUSION

Recognition of ocular disease progression and prompt access to specialist services may optimise management of these uncommon patterns of ocular disease in mucocutaneous disorders.

KEYWORDS

Mucocutaneous Disorders, Herpes Zoster, Herpes Simplex, Steven-Johnson Syndrome, Leprosy, Tuberculosis (Lupus Vulgaris), Erythema Multiforme, Toxic Epidermal Necrosis, Pemphigus, Xeroderma Pigmentosa, Behcet's Syndrome, Reiter's Syndrome, Acne Rosacea.

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BACKGROUND

Diseases of the skin and mucous membranes having eye involvement is the aim of this study, conventionally various aetiologic factors, e.g. infections, vaccination, drugs, systemic diseases, physical agents, food, idiopathic, toxic and metabolic causes, allergy atonic condition may affect the eyes and mucocutaneous tissue. The commonest type of mucocutaneous disease with ocular involvement are leprosy, herpes, SJS and EM. The varied allied mucocutaneous disorders that occur are toxic epidermal necrosis, pemphigus, tuberculosis, acne rosacea, Behcet's, Reiter's, lupus vulgaris and xeroderma pigmentosa.

Mucocutaneous ocular syndromes with several allied disorders like Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are severe, acute, self-limiting

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inflammatory disorder affecting skin, mucous membranes and eyes, usually attributed to drugs reaction. Ocular manifestations of SJS/TEN are blepharoconjunctivitis, corneal scarring and vascularisation resulting in permanent visual loss. Ocular cicatricial pemphigoid is an autoimmune blistering disease of skin and mucous membranes affecting mainly elderly people. The characteristic ocular findings are cicatricial entropion, trichiasis, conjunctivitis, keratitis, stricture of lacrimal ducts, loss of goblet cells and dry eye, progressive shrinkage of conjunctiva, symblepharon formation. Several dermatitis, i.e. seborrheic dermatitis, allergic contact dermatitis, atopic dermatitis affects periorbital regions and eyes causing madarosis, blepharitis and keratoconjunctivitis, certain infective condition of mucous membranes like herpes simplex, herpes zoster, leprosy and tuberculosis cause blepharoconjunctivitis and keratitis, uveitis, scleritis, etc. Ocular involvement with herpes simplex virus has varied manifestations, which include blepharitis, conjunctivitis, keratitis and iridocyclitis.[1] Leprosy is a major cause of blindness in developing world due to corneal scarring, uveitis, secondary glaucoma and cataract.[2] Inflammatory conditions of skin like Behcet's syndromes, Reiter's syndromes and SLE manifest in eyes as conjunctivitis, keratitis and uveitis. Certain hereditary, HLA related condition also have skin and eyes manifestations. Patients with SJS/TEN genetically are susceptible to specific environmental precipitants. A report from the United States showed an increase of human leukocyte antigen (HLA-B_{12}) (HLA-Bw 44) antigen in white patients with SJS with ocular involvement.

To characterise the patterns of chronic ocular disease in patients with mucocutaneous ocular syndromes after the acute episode included mild, moderate, severe and sequelae as Ocular Surface Failure (OSF), recurrent episodic inflammation (RI), Scleritis (S) and progressive conjunctival cicatrisation resembling Mucous Membrane Pemphigoid (MMP).

MATERIALS AND METHODS

This is a prospective study, which was undertaken in the Department of Ophthalmology, M.K.C.G. Medical College and Hospital, Berhampur (Ganjam), during the period of 2014-2016. This study was made on 204 consecutive patients of mucocutaneous disorders seen in the outdoor and indoor of skin and VD, Eye, Medicine, Paediatric and ID wards. Most of the patients were initially examined in the Department of Dermatology, M.K.C.G Medical College and Hospital. The diagnosis of mucocutaneous disease and type of disease had been established by the dermatologist before the patients were sent to the Department of Ophthalmology for detailed ophthalmic examination. Rest of the patients were clinically diagnosed in ophthalmology OPD as mucocutaneous disease.

Inclusion Criteria

1. All age groups.
2. Getting consent from patients/relatives for examination.
3. Patients having mucocutaneous disorder as per definition or diagnosed by a dermatologist.

Exclusion Criteria

1. Patient with unstable vitals requiring primary systemic stabilisation.
2. Patients having associated systemic diseases where eye involvement is common like diabetics, hypertension, etc.

Examination of Patients

The following examination schedule was followed-

1. General examination of patient was done including pulse and blood pressure measurement by sphygmomanometer.
2. Detailed dermatological examination and mucosal examination specially oral and genital parts was done.
3. Musculoskeletal system examination for presence of arthritis and arthralgia was done.
4. Local examination-
    a. Visual acuity- It was assessed in both eyes separately for distance and near.
    b. Anterior segment was examined by slit-lamp biomicroscopy and any abnormality was noted with special emphasis over corneal sensation, colour pattern of iris, pupillary reaction and lenticular opacity if any.
    c. IOP- Tonometry was done with Schiotz's tonometer.
    d. Ocular movements - Any abnormality was noted.
    e. Fundus examination- Fundus examination was done with direct ophthalmoscopy, indirect ophthalmoscopy and slit-lamp biomicroscopy with +78D and findings were noted.
5. Investigations- Patients underwent following blood and urine investigations.
    a. Blood-
        Fasting blood sugar.
        Hb, DC, TLC, TPC, comment on peripheral smear.
        BT, CT, VDRL, HIV.
        Serum creatinine.
        Blood urea.
        Lipid profile.
    b. Urine- Routine and microscopy.

The patients were primarily treated with topical lubricants, antibiotics, topical low-dose steroids and cycloplegics to avoid scar formation, ciliary spasm and photophobia. In some patients, removal of pseudomembranes and lysis of symblepharon by glass rod was done. In rare cases, surgical intervention was done. They were followed up after three months and complications were noted like dry eye, symblepharon, corneal scar, corneal vascularisation, trichiasis and ankyloblepharon. VA was recorded in all cases and analysis done.

RESULTS

Out of 204 patients examined, i.e. 164 males and 40 females, the ocular involvement found was 132, i.e. 64. Maximum incidence of patient was found in the age group 21-30 years. Male preponderance over female was in the ratio of 4:1. Only 11 patients are below 20 years. Out of them, 6 had ocular manifestations. Majority of patients having ocular lesions were affected by herpes (72.2%) and leprosy (78.57%). Most common mucocutaneous syndrome in the study was herpes (35.29%) and leprosy (27.45%). Rest ocular lesions occurred as follows, i.e. erythema multiforme (25%), Steven-Johnson syndrome (50%), toxic epidermal necrosis (100%), pemphigus (75%), tuberculosis (25%), acne rosacea (66.6%), Behcet's syndrome (100%), Reiter's syndrome (33%) and xeroderma pigmentosa (100%). Most common ocular lesions in various mucocutaneous ocular syndrome was found to be conjunctivitis (45.4%), blepharitis (34.8%) and periorbital vesicles (30.3%). The least common was found to be trichiasis and conjunctival membrane each 3%. After follow-up of 3 months, the following ocular sequelaes were observed, i.e. dry eye (9%), symblepharon (7.5%), corneal scar (4.5%), corneal vascularisation (3%), trichiasis (3%) and ankyloblepharon (1.5%). Visual acuity analysis was done. We found in 62 cases had vision between 6/18 to 6/6, 40 cases had visual acuity between 6/18 to 6/60 and 12 cases had total blindness.

Examined	**204**
Total number of male patients	164
Total number of female patients	40
Total number of patients with ocular involvement	64%

Table 1. Total Number of Patients with Mucocutaneous Disorders

Among the 204 patients, 132 patients had the evidence of the ocular involvement comprising 64% of patients. It points out to the fact that most of the patients develop ocular lesions.

Type	**Total**	**0-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**
Herpes	72	4	4	29	11	16	6	2
Leprosy	56	-	-	4	4	40	4	4
EM	24	-	-	12	12		-	-
SJS	16	-	-	8	6	2	-	-
TEN	3	-	1	2	-	-	-	-
Pemphigus	8	-	-	-			7	1
TB	8	-	-	6	2	-	-	-
Acne rosacea	6	-	0	6	-	-	-	
Behcet's	2	-	-	1	1			
Reiter's	6	-	-	2	4	-	-	-
Xeroderma pigmentosa	3	-	3	-	-	-	-	-

Table 2. Age Incidence in Total Number of Patients

Type	**Number of Patients**	**Percentage**
Herpes	72	35.29
Leprosy	56	27.45
EM	24	11.7
SJS	16	7.8
TEN	3	1.4
Pemphigus	8	3.9
TB	8	3.9
Acne rosacea	6	2.9
Behcet's	2	0.9
Reiter's	6	2.9
Xeroderma pigmentosa	3	1.4

Table 3. Incidence of Mucocutaneous Diseases

Type	**Total**	**0-10**	**11-20**	**21-30**	**31-40**	**41-50**	**51-60**	**61-70**
Herpes	52	0	2	30	8	6	4	2
Leprosy	44	-	-	-	-	30	4	4
EM	6	-	-	4	2	-	-	-
SJS	8	-	0	6	2	-	-	-
TEN	3	-	1	2	-	-	-	-
Pemphigus	6	-	-	-	-	-	2	1
TB	2	-	-	2	-	-	-	-
Acne rosacea	4	-	0	4	-	-	-	-
Behcet's	2	-	-	2	-	-	-	-
Reiter's	2	-	-	-	2	-	-	-
Xeroderma pigmentosa	3	-	3	-	-	-	-	-

Table 4. Age Incidence in Patients Having Ocular Lesions

Infective	Inflammatory	Immune Disorders	Hypersensitivity Reaction
Herpes simplex	Behcet's syndrome	Pemphigus vulgaris	Erythema multiforme
Herpes zoster	Reiter's syndrome	Pemphigoid	Stevens-Johnson's syndrome
Leprosy	Acne rosacea		Toxic epidermal necrolysis
Tuberculosis (lupus vulgaris)			Xeroderma pigmentosa

Table 5. Causes of Mucocutaneous Syndrome

Type	Total	Ocular Lesion	Percentage
Herpes	72	52	72.2%
Leprosy	56	44	78.57%
EM	24	6	25%
SJS	16	8	50%
TEN	3	3	100%
Pemphigus	8	6	75%
TB	8	2	25%
Acne rosacea	6	4	66.66%
Behcet's	2	2	100%
Reiter's	6	2	33%
Xeroderma pigmentosa	3	3	100%

Table 6. Incidence of Ocular Lesion in MCOS

Diseases	Eyebrows	Eyelid	Conjunctiva	Sclera	Cornea	A.C.	Iris	Pupil
Herpes	Periorbital vesicles (40)	Blepharitis (36)	Conjunctivitis (36)		Corneal epithelial defect (22) Keratitis (12)	KP's uveitis (4)		
Leprosy	Madarosis (32)	Trichiasis (2) Lagophthalmos (10)			Keratitis (10)	Uveitis (16)		
EM	-	Blepharitis (2)	Conjunctivitis (4)					
SJS		Blepharitis (2)	Conjunctivitis (4) Conjunctival memb. L					
TEN		Blepharitis (2)	Conjunctivitis (2)		Keratitis (2)	-	-	-
Pemphigus vulgaris	-	Entropion Trichiasis (2)	Conjunctivitis (4)		Keratitis (4)			
Lupus vulgaris		Blepharitis (2) Trichiasis	Conjunctivitis (2)					
Acne rosacea	-	Blepharitis (2)	Conjunctivitis (4)					
Behcet's synd.	-	-	-	-	-	Uveitis (1)		
Reiter's synd.	-	-	Conjunctivitis (2)	-	-	Uveitis (1)		

Table 7. Different Ocular Manifestations in Various MCOS

Ocular Lesions	Numbers	Percentage
Periorbital vesicles	40	30.3%
Madarosis	32	24.2%
Trichiasis	4	3%
Lagophthalmos	10	7.5%
Blepharitis	46	34.8%
Conjunctivitis	60	45.4%
Conjunctival membrane	4	3%
Corneal epithelial defect	22	16.6%
Keratitis	28	21.2%
Uveitis	22	16.6%

Table 8. Incidence of Ocular Lesions in Various MCOS

Ocular Lesions	6/6	6/6 to 6/18	6/18 to 6/60	6/60 to CF3	CF3m to PL+PR+	PL-PR-
Uveal lesions (uveitis)		6	16			
Corneal Lesions						
SPK		22	6			
Epithelial defect		16	6			
Conjunctivalisation						2
Neovascularisation						2
Corneal scars					6	

Conjunctival lesions						
Hyperaemia	40	6	8			
Symblepharon	6	2	2			
Ankyloblepharon						2
Eyelid lesions						
Blepharitis	40	6				
Trichiasis		2				
Lagophthalmos	4	2	2			

Table 9. Ocular Lesions and Visual Acuity

Ocular Lesions	Number of Cases	Percentage
Dry eye	12	9%
Corneal scar	6	4.5%
Corneal vascularisation	4	3%
Trichiasis	4	3%
Symblepharon	10	7.5%
Ankyloblepharon	2	1.5%

Table 10. Ocular Sequelaes

DISCUSSION

Table 2 highlights maximum number of patients belong to age group 21-30 years.

Table 3 shows the most common mucocutaneous syndrome in this study is herpes and leprosy followed by erythema multiforme and Steven-Johnson's syndrome. Herpes incidence (35.29%) and leprosy incidence (27.45%) in our study is almost similar to the study by Soumya Sharat et al.[3]

Most of the patients examined are adults. Only eleven patients are below the age of 20 years. There is no significant difference in the age distribution of patients of mucocutaneous disorders as compared to that of patients with ocular involvement. The only difference is that only six patients below the age of 20 years had ocular manifestations. Similarly, there is no significant variation in the distribution of age in different types of mucocutaneous disorders.

Most of the patients examined are males, who outnumbered females in the ratio of 4:1 approximately with 164 patients being males and only 40 being females. Its significance is of doubtful value because of the smallness of number Table 4.

Mucocutaneous syndromes has been aetiologically, divided into infective causes, inflammatory causes, immune-related disorders and hypersensitivity to certain drugs and in xeroderma pigmentosa hypersensitivity to sunlight Table 5.

In our study, herpes has ocular involvement in 72.2% of cases and ocular involvement in leprosy 78.57% similar to Soumya et al study.[3]

Ocular involvement in erythema multiforme was 22.7% in a study by Fu-Chin Huang et al.[4] In our study, it is 25% correlating with previous studies.

In SJS, 50% cases had ocular involvement in our study, whereas it was 81.3% in previous study (Fu-Chin Huang et al[4]), however, it is seen that the percentages in both studies vary widely in this category (SJS). This could be due to-

i. Early reporting due to better patient awareness in previous study.
ii. Better diagnostic facilities in the former study.
iii. Eye problems might not have been severe enough to warrant consultation even on noticing them in our study.

In our study, rare case of mucocutaneous disorders with ocular lesions, i.e. TEN, xeroderma pigmentosa, Behcet's syndrome put together were only 4% in this total series Table 6.

Ocular Lesion (Adnexa) Involvement

From the present study, it was seen that maximum number of cases had periorbital vesicles (40 cases, i.e. 30.3%).

The present study shows the evidence that loss of eyebrows is present in almost all types of leprosy disease (madarosis, more predominant in lepromatous leprosy, i.e. 24.2%).

Trichiasis is not very common as it is seen in only in 4 cases in our study (3%). Lagophthalmos is seen in 10 cases, i.e. 7.5% in our study.

From the present study, it was seen that maximum number of cases had conjunctivitis (60 cases, i.e. 45.4%).

In the present study, blepharitis features next in frequency to conjunctivitis (46 cases, i.e. 34.8%). It was 51.4% in a previous study (Chie Scotozono et al[5]). Lid and adnexal findings (45.8%) was found in a study by Puri et al[6] to be the most common ocular involvement in herpes zoster ophthalmicus followed by conjunctivitis (41.1%). In a study by Kompella VB et al, eyelid lesions were found in 91.51% patients, conjunctival lesions in 96.84% and corneal complications in 97.89% in patients with SJS.[7]

In the present study, conjunctival membrane has been found in 4 cases.

Cornea Involvement

The corneal lesions are seen in all types of mucocutaneous ocular diseases. The common forms of involvement are superficial punctate keratitis, subepithelial keratitis, stromal keratitis (ant. stromal keratitis, deep stromal keratitis), neurotrophic keratitis, interstitial keratitis, pannus, thickening of corneal nerves and reduced corneal sensation, keratic precipitates and corneal opacities.

Exposure keratitis, perforation of corneal ulcer and iris prolapse was also noticed in some case.

Of all the corneal lesions, punctate keratitis is the commonest corneal involvement. It requires examination with slit lamp using blue filter after fluorescein staining to establish the presence of punctate keratitis. It was found in 22 patients arid accounted for 16% of all cases of all the

types of MCOS. Punctuate keratitis was found to be more common in ocular herpes patients.

Interstitial keratitis, pannus and heated interstitial keratitis leading to corneal opacities are the most important primary corneal lesions, which lead to visual impairment. A total number of 28 cases of keratitis situated in the corneal stromal level was found, which accounted for 21.2% of all cases. Pannus was seen only in 4 cases of lepromatous leprosy. In a study by Salem RA et al,[8] the most common ocular involvement in leprosy was eyelid lesions, where corneal opacity was found to be the major cause of blindness.

Exposure keratitis as a result of lagophthalmos was found in 6 cases out of 10. These findings point out to the fact that patients should be educated to watch for appearance of inadequate closure of eyelids and to report to the ophthalmologist the moment they find it, so that the blinding complication of exposure keratitis can be prevented.

Uveitis was found in 22 patients of all types of mucocutaneous ocular syndrome patients, which was 16.6% of the cases. Acute iridocyclitis was mostly found in ocular herpes. But, chronic anterior uveitis was found mostly in leprosy patients. Other findings were reduced corneal sensation and thickening of corneal nerves, which was seen in leprosy cases. Only 4 cases of scleritis were seen in this study.

Because of the various ocular manifestations of mucocutaneous disease, which can impair vision, an attempt was made to study the same in patients of MCOS in all patients, visual acuity for distance and near was examined after correcting refractive error if any.

When an analysis was made to know the incidence of visual handicap in various types of diseases, some interesting facts came out. The incidence of total blindness was in 12 cases (9%) where visual acuity was less than 6/60. 40 cases (30%) had visual handicap where visual acuity was 6/18 or less than that. Only in 62 cases (47.6%) had vision of 6/18 or more than that. The common causes for visual impairment in all these patients were due to corneal complications.

There is no available literature relating a possible association between visual acuity and ocular lesions in mucocutaneous ocular syndrome.

More severe and prolonged acute ocular inflammation promotes development of late ocular complications like dry eye, corneal scar, corneal vascularisation, trichiasis, symblepharon and ankyloblepharon. Surgical therapy at advanced stage only aims to correct structural defects of lids, conjunctiva and cornea. Corneal transplantation has poor prognosis with cicatricial ocular disorders. Amniotic membrane transplantation for ocular surface reconstruction is done for selected cases of Stevens-Johnson syndrome.[7,9,10]

During 3 months of follow-up in this study, 38 patients (28.5%) of different types of mucocutaneous ocular syndromes developed ocular complications.

A study of the amount of lacrimal secretion is carried out by Schirmer's test. Reading less than 10 mm was considered as hyposecretion or dry eye. It was found that a total of 12 patients (9%) had reduced secretions of tears. The incidence of "dry eye" is maximum in SJS. In a previous study, post syndrome ocular sequelae identified 15% of dry eye in SJS cases within 3 months of follow up (study by Fu-Chin Huang).[4]

Though the exact cause of it is not definite, it may be due to inflammatory reaction involving the ocular surface destroying goblet cells and resulting in decreased secretion of mucin that impairs tear distribution and stability. With healing, cicatrisation may lead to dry eye. Corneal scar was found in 6 cases (4.5%) in our study. Corneal vascularisation was found in only 4 cases of all the types of mucocutaneous ocular syndromes. But, it was more, i.e. 15.9% in a study by Chie Sotozono et al.[5]

Symblepharon in 10 cases (7.5%) and ankyloblepharon only in 2 cases was found in our study.

Surgical treatment required in these cases for example, lysis of symblepharon and conjunctival recession maybe preferred method to reconstruct the conjunctival fornix. However, in patients with cicatricial changes and severe dry eye, the outcomes of many of these surgical interventions are disappointing. Therefore, topical treatment early in the acute stage seems to offer the best hope for reducing the risk of late complications and minimising the morbidity of ocular manifestations in mucocutaneous ocular syndromes.

CONCLUSION

Ocular involvement is found to be very common (64%) and commonest in leprosy and herpes patients. The common lesion of ocular adnexa are periorbital vesicles madarosis, blepharitis and conjunctivitis is also quite common. Corneal involvement is also high. Superficial punctuate keratitis commonest. The corneal complications leading to visual impairment like interstitial keratitis, corneal opacities and corneal ulcers are common. Anterior uveitis and scleritis are also seen in some of the cases.

On the other hand, post mucocutaneous syndrome ocular sequelae like dry eye, corneal scar, corneal perforation and corneal vascularisation, trichiasis, symblepharon and ankyloblepharon may lead to bilateral blindness in these patients.

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