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Review Article

Eye in the skin- A review article

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ABSTRACT

This article emphasizes the interlink between eye and the skin, helping to diagnose systemic diseases based on the ocular manifestations. A complete care of eyes by the ophthalmologist will require simultaneous skin care and treatment of the systemic cause.

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1. Introduction

There is a common embryogenic origin for skin, mucous membranes & corneal epithelium, deriving from surface epithelium. The position between the surface of eye and the eyelids results in "innocent bystander" ocular damage affecting the skin of the eyelids till the eyelid margin.

Cicatricial pemphigoid, xeroderma pigmentosum Vogt-Koyanagi-Harada syndrome & eczema, may result in an autoimmune attack of both conjunctiva & skin. Ocular pathologies associated with skin diseases may involve any part of the eye or its adnexae. Skin diseases which involve the eye can be grouped as (Table 1)

2. Bullous Vesicular Disorders

2.1. Pemphigus

Lids, conjunctiva, cornea, lens & iris are involved rarely.¹

Cnconjunctival bullae & catarrhal or purulent conjunctivitis are seen mostly involving the palpebral conjunctiva² with

edema, purulent discharge, & erythema.^{1,3} In P. foliaceus entropion, trichiasis of both lids leading to corneal damage & in 5% of cases. In few red, nodular iris lesions may be seen.

2.2. Cicatricial pemphigoid

Unilateral as chronic, recurrent catarrhal conjunctivitis, but later becomes bilateral.

Stage 1 – Subepithelial fibrosis

Stage 2 - fornix foreshortening

Stage 3 - symblepharon-hallmark

Stage 4 – ankyloblepharon & surface keratinization.

Obstruction of lacrimal ductules & meibomian gland ducts leading to unstable tear film. Trichiasis, entropion due to subepithelial fibrosis with corneal neovascularization, keratopathy & corneal ulceration & scarring.⁴

2.3. Bullous pemphigoid

Fine striae of tarsal subepithelial fibrosis.

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Table 1: Skin diseases which can involve eye

1) Bullous Vesicular disorders	4) Disorders of skin elasticity
Pemphigus	Ehlers Danlos Syndrome
Cicatricial pemphigoid	Pseudoxanthoma elasticum
Epidermolysis bullosa	
Bullous pemphigoid	
Hydroa vacciniforme	
Dermatitis Herpetiformis	
Acrodermatitis entropathica	
Erythema multiforme	
2) Pigmentary Disorders & Diseases precipitated by light	5) Disorders involving neoplasia
Incontinentia pigmenti	Basal cell nevus syndrome
Xeroderma pigmentosa	Juvenile xanthogranuloma
Chediak-Higashi Syndrome	Hemangioma
Nevus of Ota	
3) Hyperkeratotic diseases:	6) Miscellaneous skin disorders
Ichthyosis	Acne rosacea
Psoriasis	Anidrotic ectodermal dysplasia
	Malignant atrophic papulosis
Atropic dermatitis	Focal dermal hypoplastic syndrome

2.4. Dermatitis herpetiformis

Ocular manifestations are rare. Keratoconjunctivitis sicca, iritis, choroiditis, and papillitis have been noted in few individual patients.

2.5. Erythema multiforme

Ocular involvement occurs in more than half of patients.⁵ Acute manifestations include mucopurulent conjunctivitis, lid scarring, keratoconjunctival sicca, corneal ulceration, neovascularization & scarring. Acute exanthem results in tarsal conjunctival keratinization & chronicity depends on degree of subepithelial fibrosis. Fibrosis of meibomian duct & lacrimal duct obstructions, trichiasis, distichiasis & cicatricial entropion. With every blink there is chronic sandpapering trauma effect on the cornea due to tarsal conjunctival keratinization. Further leading to chronic keratopathy with corneal scarring, neovascularization & ulceration. Other manifestations include recurrent, immunologically mediated conjunctivitis.

2.6. Toxic epidermal necrolysis

Less severe than Steven Johnson syndrome. Manifests as mucopurulent conjunctivitis. Only corneal erosions^{6,7} might be seen.

2.7. Epidermolysis bullosa

Starts as vesicle formation in the conjunctiva, resulting in ulceration & symblepharon. Recurrent corneal erosions causes vascularized scars. In a report by McDonnell, 8 out of 11 patients with the dystrophic form had conjunctival shrinkage, symblepharon & corneal opacities which were slowly progressive and mostly asymptomatic except for patients with recurrent corneal erosions. Aurora and co-workers described a patient exhibiting edema of the trabeculum, iris, ciliary body, lens, and optic nerve histopathologically along with choroidal & retinal focal edema & necrosis.

2.8. Hydroa vacciniforme

Perilimbal chemosis/severe vesicular reaction with conjunctival ulceration/necrosis may result in symblepharon. Vesicular keratitis, may progress to epithelial erosion & scar formation. In a 6-year-old boy with inflammatory kerato-uveitis, the use of UVB filter sun protective glasses prevented new lesions in the eye.⁸ If severe and recurrent facial involvement is present cicatricial ectropion, secondary conjunctival and corneal changes may occur.⁹

2.9. Acrodermatitis enteropathica

Manifests with photophobia, punctal stenosis, conjunctivitis, blepharitis & corneal opacities.¹⁰ In a 7-year-old boy, Warshawsky and co-workers showed bilateral radiating linear superficial opacities in the corneal periphery.¹¹

3. Pigmentary Disorders and Diseases Precipitated by Light

3.1. Incontinentia pigmenti

Ocular involvement is seen in 35% of patients with Bloch-Sulzberger syndrome which include cataracts, optic atrophy, strabismus and nystagmus.^{12,13} 1/3rd of patients, unilateral retro-lenticular mass is present.¹⁴ According to Zweifach, retinal dysplasia with pigment proliferation, along with free pigment epithelial cells within the dysplastic retina is common in incontinentia pigmenti¹⁵ in few cases exudative chorioretinitis and exudative retinal detachment & Pigmentary retinopathy were noted.^{12,16,17} Retinal vascular anomalies like AV anastomoses with preretinal fibrosis upto the equator temporally & beyond which the retina is non-perfused. In one case, Jain and Willetts demonstrated frank proliferative neovascularization which depicts the early formation of the pseudoglioma. Conjunctival pigmentary changes may occur near the limbus- resembling “stellate cluster of nevi”.¹⁷

3.2. Xeroderma pigmentosum

Moderate to severe eye complications are seen in >70% of patients.¹⁸ Earliest manifestation include photophobia, blepharospasm, conjunctival congestion to severe corneal disease with ulceration or perforation.¹⁹ Due to progressive atrophy of lower eyelid, inflammation, symblepharon, corneal ulceration & corneal scarring occurs. Conjunctival congestion with serous/mucopurulent discharge may progress to xerosis, keratinization and shrinkage that may result in ankyloblepharon. Corneal malignancy, usually squamous cell carcinoma is seen in this disease with limbal zone as the commonest site & band-shaped corneal dystrophy in black patients.²⁰⁻²²

3.3. Chédiak-higashi syndrome

Ocular histology in a 5-year-old boy who succumbed to respiratory complications was described by Spencer and Hogan.²³ In the ciliary epithelium, choroid and retina, there was no pigmentation of the iris. The optic nerve and uveal tissue were infiltrated. Leukocytic inclusion bodies were demonstrated in the limbal zone, the iris, and the choroid in a case.²⁴ Decreased pigmentation may be due to abnormal clumping of melanosomes into giant lysosome - organelles.²⁵ The visual acuity is generally normal or only minimally decreased.

3.4. Nevus of OTA

On clinical appearance its difficult to be differentiated from melanosis oculi. The latter may show malignant change in one fourth of patients.²⁶ Scleral pigmentation is the most common ocular finding. Increased pigmentation of all the parts of eye has been reported.²⁷ Malignancy is reported only in white patients.²⁸ Melanomas are reported in the ciliary body, iris, choroid, orbit, brain & skin.²⁸⁻³⁰

4. Hyperkeratotic Disorders

4.1. Ichthyosis

Cicatricial ectropion is the most commonly seen, especially in the lamellar pattern of ichthyosis.³¹⁻³⁴ This may expose conjunctiva and cornea resulting in secondary changes. There is spontaneous resolution in patients with congenital ichthyosis known as collodion baby.^{34,35} Corneal opacities-dot or filament shaped were diffuse and confined to either deep stroma or Descemet's membrane. They are not associated with visual loss & increases with age. It was only noted in female carriers of X-linked ichthyosis.³¹ Conjunctival keratinization, hyperkeratosis, parakeratosis, and papilla formation was reported by Katowitz and his co-workers as characteristic histologic features.³⁵ Choriorretinitis with macular and perimacular pigmentary degeneration seen in 20% - 30% of patients.

4.2. Psoriasis

Ocular signs seen in 10% of cases. They are more frequently involves eyelids & seen more in males & as the only clinical feature of the disease.³⁶ An inflammatory ectropion with trichiasis or madarosis may occur.³⁷ Edema of eyelid margins with erythema and scaly lesions & granulating lesions of conjunctiva and vascular infiltration of the cornea may develop.³⁶ Patients have severe photophobia. Plaque like lesions over the conjunctiva or cornea alone, or along with eyelid lesions. It has a xerotic appearance with dilated vessels in the surrounding. There is minimal parakeratosis and acanthosis in the conjunctiva with no acanthosis on cornea.³⁸ There is significant association between ocular involvement in psoriasis & psoriatic arthritis

4.3. Atopic dermatitis

The ocular manifestations are potentially serious. Hogan emphasized the corneal complications.³⁹ The following are the sequelae of undertreatment or inappropriately treated:-

1. Keratoconus
2. Recurrent herpes simplex keratitis
3. Secondary infection with staphylococcus organisms
4. Superficial punctate keratopathy
5. Nonhealing epithelial defects
6. Corneal stromal ulceration, scarring, and neovascularisation. Patients with atopic keratoconjunctivitis (AKC) also show conjunctival pathology, including subepithelial fibrosis, fornix shortening and frank symblepharon. Steroid induced Glaucoma, retinal detachment and recurrent herpes keratouveitis developed in 4% of cases.

5. Disorders of Skin Elasticity

5.1. Ehlers-danlos syndrome

The most common finding is marked epicanthal folds. Angioid streaks and macular pigmentary degeneration have been reported alone or in combination with pseudoxanthoma elasticum.⁴⁰ Strabismus, blue sclera, microcornea, keratoconus, ectopia lentis, severe myopia, and familial retinal detachment are the other signs.⁴¹ Pemberton described severe myopic staphyloma and retinal detachment in a family with 4 of them having systemic manifestations of the Ehlers-Danlos syndrome.⁴²

5.2. Pseudoxanthoma elasticum

Angioid streaks in the fundi is seen in 85% of patients known as the Grönblad-Strandberg syndrome. They usually occur bilaterally It is complicated by disciform macular degeneration causing central vision loss.⁴³ Diffuse mottling is the earliest fundus change. 6% of pseudoexfoliation patients had optic nerve drusen too.⁴⁴ They may present

with or without angioid streaks.

6. Disorders Involving Neoplasia

6.1. Basal cell nevus syndrome

Orbital involvement by tumors, and strabismus are the common manifestations.⁴⁵ Others are epicanthal fold, hypertelorism, congenital cataract, glaucoma, coloboma of the choroid/optic nerve & retinal atrophy.^{46,47} Multiple tumors on the skin of eyelid have direct extension to the orbit & brain.^{45,48,49}

6.2. Juvenile xanthogranuloma

Ocular involvement often occurs without skin lesions. Ocular involvement may be bilateral & complications are due to iris and ciliary body involvement with the tumor. Choroid & retina are rarely involved.⁵⁰ Iris may present as a solitary nodule, or diffusely thickened and have a muddy coloration. Characteristically, Touton giant cells are present. The histiocytes may collect in iris and then be shed into the aqueous layer.⁵¹ Paracentesis of anterior chamber helps in diagnosing. The highly vascular iris lesions are histologically resemble hemangiomas. Patients with iris & ciliary body involvement presents in one of five ways: spontaneous hyphema, glaucoma, uveitis, heterochromia iritis, or an asymptomatic iris tumor.⁵⁰ Lesions may occur on the eyelids, in the orbit, in epibulbar tissues, and on the cornea. Patients with eyelid lesions do not seem to have concurrent uveal involvement.⁵⁰ Orbital lesions include congenital unilateral proptosis. Intra orbital disease may involve extraocular muscles, resulting in orbital bone destruction.^{52,53}

6.3. Hemangioma

Following a study, Stigmar reported the visual outcome and ocular complications.⁵⁴ 44% were amblyopic, and 34% had strabismus. The severity of amblyopia correlated with the length of time the eyes were totally occluded by eyelids involving with tumor. As little as 1 month of complete eyelid closure resulted in severe amblyopia. Anisometropia in 70% of cases, were more hyperopic. Delayed complications include ptosis, proptosis, paralytic strabismus & optic atrophy.

7. Miscellaneous Skin Disorders

7.1. Acne rosacea

Ocular manifestations include meibomian gland dysfunction, blepharitis, conjunctivitis with small marginal catarrhal corneal ulcers, nodular conjunctivitis, scleritis, and keratitis. Rosacea keratitis being the most severe complication.⁵⁵ It begins as interstitial keratitis. Eyelid trauma produces erosion and scarring of central cornea.⁵⁵

7.2. Anhidrotic ectodermal dysplasia

Various forms of ocular abnormalities include microphthalmos, telecanthus, absence of the meibomian gland openings, absence of brows and eyelashes, entropion, congenital cataract, chorioretinal atrophy, absence of the lacrimal puncta, nasolacrimal atresia, deficient lacrimation, keratoconjunctivitis sicca, corneal pannus, conjunctivitis, and blepharitis.⁵⁶⁻⁵⁹ Granular dystrophy of the cornea has been reported. Ectodermal dysplasia, ectrodactyly, cleft lip & palate has been reported as a syndrome. Corneal changes have been attributed to deficient lacrimation.⁵⁹ The corneal involvement is due to an inherent epithelial defect.⁵⁶

7.3. Malignant atrophic papulosis

Ocular involvement in Degos' syndrome has included atrophic skin lesions of the eyelids, conjunctival microaneurysms and telangiectasias, atrophic, plaque-like lesions of the conjunctiva.⁶⁰ Atrophic chorioretinal scars are also noted. Episcleral, Optic disc, retinal, and choroidal vessels showed thickening of the walls, subendothelial fibrosis & fibrinoid necrosis. Winkelmann and his co-workers reported cerebral involvement in two cases. Cerebral edema was present and the patient had bilateral papilledema.⁶⁰

7.4. Focal dermal hypoplasia syndrome

Photophobia is the most common manifestation.⁶¹ Anophthalmos, enophthalmos, microphthalmos, ectropion, strabismus, nystagmus, coloboma of the iris, choroid, and optic disc, aniridia, subluxation of the lens and retinal pigment epithelial changes may occur. The inheritance pattern is thought to be X-linked or autosomal dominant with variable expression.⁶²

8. Conclusions

Ocular manifestations of skin disorders are important, especially to the Ophthalmologists because if not properly diagnosed and treated, it may result in profound vision loss. Any systemic disorder must have a multidisciplinary approach. The multidisciplinary approach by the Ophthalmologist, Dermatologist, Immunologist/Allergist will provide the best care & complete treatment to the patients with these disorders. This article is written in the hope that it can provide the information to address the most common dermatologic disorders with ocular manifestations, with special emphasis on those diseases which have serious blinding potential.

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None.

10. Conflict of Interest

None.

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