Introduction

Eyelids consist of skin, muscle, and connective tissue. The eyelids protect the eyes and spread tears over the front of the eyes. The inside of the eyelids are lined with the conjunctiva of the eyelid (the palpebral conjunctiva), and the outside of the lids are covered with the body's thinnest skin ***(Lica, 2005).***

Eyelid problems range from benign, self-resolving processes to malignant, possibly metastatic tumors. Inflammation, infection, benign and malignant tumors and structural problems such as ectropion, entropien and blepharoptosis may occur. However, most eyelid disorders are not vision-threatening or life-threatening ***(Carter, 1998).***

Common Dermatoses of the Eyelids:

- Looseness of tissue of the eyelid makes it liable to oedema, dermatomyositis for example causes periorbital oedema ***(Hall et al., 2003).***

- Inflammatory conditions affecting the skin may attack the lid: blepharitis, allergic dermatitis, cosmetics, drugs, bacterial infection, herpes zoster virus ***(Obata et al., 2003),*** and fungal infection ***(Rajalekshmi et al., 2003).***

- Discoid lupus erythromatosis presenting as madarosis, which is a common connective tissue disease ***(Franzco et al., 2003)***.

However, the most serious lesions are the malignant eyelid lesions, basal cell carcinoma is the commenest malignancy of the eyelid ***(Salomon et al., 2004).***

- Endocrinal disease such as hyperthyroidism that help in the diagnosis of this endocrinal abnormality ***(Higuchi et al., 2003).***

- Dermoid cysts are the most common orbital lesions in the childhood ***(Font, 1986).***

- Phakomatous choristoma represents a hamartoma of the lens tissue, most lesions are confined to the eyelid ***(Szyfelbein et al., 2004).***

However, the eyelid is considered as a mirror reflecting clinical pictures of different dermatological diseases.

Aim of the Work

In this work we aim at reviewing that eyelid lesions can provide guide lines in the diagnosis of various skin diseases and also various systemic diseases may reflect a specific picture in the eyelids, which is useful in diagnosis and helpful in the treatment.

The Anatomy of the Eyelid

The purpose of the eyelid is to protect the globe, maintain the tear film on the corneal surface, and serve as the mainstay of the lacrimal pump system. The eyelid extends approximately 30mm in length from the medial canthus, where the medial canthal ligament inserts into the anterior and posterior lacrimal crest, to the lateral canthus, where the lateral canthal ligament inserts into the zygoma. The lateral canthus is typically located 2mm superior to the medial canthus, but may be higher in Asian eyelid ***(Stewart and Carter, 2002).***

Each eyelid is divided by a horizontal furrow, the superior palpebral sulcus, in to an orbital and tarsal part. The sulcus of the upper eyelid is formed by insertion of the aponeurotic fibres of the levator palpebrae superiosis in to the skin. The sulcus of the lower eyelid, which is less obvious, is produced by few connections between the skin and the orbicularis oculi muscles ***(Snell and Lemp, 1989).*** The structure of the eyelid from superficial to deep, each eyelid consists of skin, subcutaneous areolar tissue, striated muscle (Orbicularis oculi), submuscular areolar tissue, smooth muscles and conjunctiva ***(Bron et al., 1997)*** (Figs.1 & 2).

The eyelid skin is the thinnest in the body, allowing substantial swelling to result from the accumulation of small amounts of subcutaneous fluid. An important feature of the eyelid skin is the lid crease. In the upper eyelid, the crease is formed by the superior most anterior projections of fibres from the levator

palpebrae superiosis to the orbicularis oculi and skin. For this reason, the distance from the lid margin to the crease indicate whether a dehiscence of the levator aponeurosis is present. A high or asymetrical crease raises this possibility. In the lower lid, analogous fibres course anteriorly from the capsulopalpebral fascia to the orbicularis and subcutaneous tissue, forming the lower lid crease, the lid crease has less clinical relevance in the lower lid than in the upper ***(Stewart and Carter, 2002).*** The microscopic examination shows a thin epithelium, which has a stratum corneum, stratum granulosum and stratum spongiosum of three or four layers. The basal layer (Stratum germinativum) rests on a basement membrane. The epithelium at the palpebral margin thickens when traced backwards, to contain between seven and ten layers and the dermis become denser, mobile, elastic and folded in to high, and narrow papillae ***(Bron et al., 1997).*** The eyelids margin shows the cilia (lashes), they form several irregular rows and point anteriolry ***(Stewart and Carter, 2002).*** They are short, thick, curved and are more numerous on the upper eyelid (150 in the upper lid and 75 in the lower lid). In the upper lid the lashes curved upward, while in the lower lid they curve downward. They are commonly darker than scalp hair, they do not become grey and are replaced every 100 to 150 days. The sebaceous gland of Zeis open into each hair follicle and between the follicles, there are modified sweat glands. The ciliary's glands of Moll, open into the follicles or onto the eyelid margin. Just infront of the posterior edge of the margin of the lids are the orifices of tarsal glands (Meibomian gland). The tarsal gland can be seen as yellowish lines

on the inner surface of the everted eyelid ***(Snell and lemp., 1989).*** The lacrimal gland is a modified sweat gland, is lodged in a depression at the outer angle of the orbit. Its anterior margin is closely adherent to the posterior part of the upper eyelid. The gland has 6-12 ducts, which open by a serious of minute orifices on the upper and outer half of the palpebral conjunctiva. In addition there are a variable number (4-36) of much smaller accessory lacrimal glands in the upper conjunctiva. The tear film consists of three layers: a superficial lipid layer (from the Meibomian glands) which retards evaporation and prevent spillage from the lid margin; a middle watery layer (from the lacrimal gland), and a posterior layer, which is mucoid, produced by the goblet cells of the conjunctiva. The tears drain into the nose via the lacrimal cannals ***(Burton, 1992).***

The conjunctiva is a mucous membrane covering that is divided into three portions: palpebral or tarsal, bulbar and limbal. The epithelium of the palpebral conjunctiva is a nonkeratinized stratified squamous epithelium. The thickness of which decrease as it proceeds further from the lid margin. The superficial cells become less flattened and eventually contain a more cuboidal or transional shape in the midregion of the palpebral conjunctiva. There are numerous mucin containing goblet cells particularly near the fornix. The underlying stroma is composed of delicate connective tissue and vessels ***(Apple and Rabb, 1985).***

The palpebral blood vessels show that the medial and lateral palpebral arteries are branches of ophthalmic and lacrimal

arteries, respectively. The palpebral veins are larger and more numerous than the arteries, they from a dense plexus near the upper and lower conjunctival fornices some drain into the frontal and temporal veins, other transverse orbicularis to become tributaries of the ophthalmic veins. The lymphatic drainage of lateral side of the eyelid runs to the preauricular and deep parotid nodes and then to the deep cervical chain, while the medial parts of the lids, especially the lower, drain to the submandibular lymph nodes and hence to the deep cervical. Small lymphoid nodules have been described into the palpebral connective tissue ***(Bron et al., 1997).***

The sensory nerve supply to the eyelid is from branches of ophthalmic division of the trigeminal nerve. Orbicularis oculi muscle is innervated by the temporal and zygomatic branches of the facial nerve. The smooth muscles of the eyelids are supplied by sympathetic nerve fibres from the superior cervical sympathetic ganglion ***(Bron et al., 1997).***

Embryology of Eyelids

The eye is formed from both ectoderm and mesenchyme. The ectoderm that is derived from the neural tube gives rise to the retina, the fibres of the optic nerve and the smooth muscles of the iris. The surface ectoderm on the side of the head forms the corneal and conjunctival epithelium, the lens, the lacrimal and tarsal glands. The mesenchyme forms the corneal stroma, the sclera, the coroid, the iris, the ciliary musculature, part of the vitreous body and the cells lining the anterior chamber ***(Snell and Lemp, 1989).***

The eyelid fold forms at 8 weeks of gestation as folds of surface ectoderm above and below the developing cornea. Upper lid forms by fusion of medial and lateral frontonasal processes. Lower lid forms by fusion of lateral maxillary processes and medial nasal processes. As they grow, they become united with each other at 12 weeks of gestation. The lids remain fused until about the 5th month when they start to separate. Separation from the nasal side occurs and is completed by the 7th month. Plica forms at the same time. While the lids are fused, a closed space, the conjunctival sac, exists infront of the cornea. The mesenchymal core of the lids forms the connective tissue and tarsal plates. The orbicularis oculi muscle is formed from the mesenchyme of the second pharyngeal arch, which invades the eyelids and is supplied by the 7th cranial nerve ***(Snell and Lemp, 1989).***

The cilia develop as epithelial buds from the surface ectoderm. They arise first in the upper eyelid and are arranged in two or three rows, one behind the other. The ciliary glands of Moll and Zeis grow out from the ciliary follicles. The tarsal glands (Meibomian glands) develop as columns of ectodermal cells from the lid margins. The lacrimal glands form as a series of ectodermal buds that grow superolaterally from the superior fornix of the conjunctiva into the underlying mesenchyme. These buds later canalize forming the secretory units and the multiple ducts of the glands. The glands become divided into orbital and palpebral parts with the development of the elevator palpabrae superioris. Tears are not produced until the 3rd month after birth ***(Snell and Lemp, 1989).***

Eyelid Dermatoses

Our classification of the eyelid dermatoses will depend on the morphological prsentation of the lesions. It can be classified into the following:

I- Macular and patchy lesions.

II- Papular lesions.

III- Plaque lesions.

IV- Nodular and tumoral lesions.

V- Cystic lesions.

VI- Vesicular and bullous lesions.

VII- Urticarial lesions.

VIII- Telangiectatic lesions.

IX- Skin diseases with more than one morphological presentation.

X- Skin diseases associated with changes in the shape of the eyelids.

XI- Disorders of the eyelid lashes.

XII- Conjunctivitis.

Macular and Patchy Lesions

Genetic and developmental disorders:
Albinism
Naegli-Franceschetti Jadassohn syndrome
Piebaldism
X-linked Anhidrotic/hypohidrotic-ectodermal dysplasia

Benign neoplastic lesions:
Melanocytic lesion
Ephilides or freckles
Lentigo simplex
Nevus of Ota
Solar lentigo

Vascular malformation:
Salmon patch

Pigmentary disorders:

Periorbital hyperpigmentation:
Addisonian hyperpigmentaiton
Chloasma or melasma
Erythema dyschronium perstans
Familila periorbital melanosis
Hemochromatosis
Ochronosis
Orange palpebral spots
Other causes of periorbital hyperpimgneration

Periorbital hypopigmentation:
Vitiligo
Vogt Koyanagi-Harada syndrome

Macular and Patchy Lesions

Genetic and Developmental Disorders:

Albinism:

It is a hereditary derangement in melanin pigment metabolism, characterized by extreme lightness of skin and blondness (including the cilia) ***(Apple and Rabb, 1995)***. Involvement of the eye only is called ocular albinism (OA) ***(Spielvogel and Kantor, 2005)***. The most common form of OA is clinically normal without notable pigmentary dilution. While in autosomal recessive OA, some cases actually represent OCA 1B or OCA2 but with subtle cutaneous finding ***(Ortonne, 2008)***.

On histologic examination, OA1 contains macromelano-somes ***(Ortonne, 2008)***.

Oculocutaneous albinism (OCA) affects both eyes and skin ***(Spielvogel and Kantor, 2005).*** All types of OCA have an autosomal recessive inheritance pattern except for the rare families that have autosomal dominant OCA. Based upon molecular studies, four types of OCA have been defined: OCA type 1 (OCA1) results from reduced (OCA1B) or absent (OCA1A) tyrosinase activity, OCA type 2 results from mutation in the P gene, OCA type 3 results from mutation in the tyrosinase-related protein 1 (TYRP1) gene, and OCA type 4 where the gene involved is MATP (membrane-associated transporter protein), encodes a protein that probably functions as a transporter ***(Ortonne, 2008)*** (Fig.3)***.***

Table (1): Types of oculocutaneous albinism:

Type of oculocutaneous albinism	Clinical picture
OCA1A	White hair, milky white skin, and blue-grey eyes. With age, the skin color remains white, but the hair may develop a slight yellow tint.
OCA1B	Yellow albinism because the enentual color of the patients hair. No or little pigment at birth but they develop some pigmentation of hair and skin during the first and second decades. In temperature sensitive type, the patients are born with white hair and skin and blue eyes. During puberty, scalp and axillary air remain white, but arms hair turn light reddish brown and leg hairs turn dark brown
OCA2	It ranges from minimal to moderate pigmentary dilution of hair, skin and iris. Brown OCA shows light brown hair and skin with grey to tan irides at birth.
OCA3	Rufous OCA has been identified in individuals with type III - IV skin color and the phenotype includes red-bronze skin color, ginger-red hair, and blue or brown irides.
OCA4	Generalized hypopigmentation of skin and hair with ocular abnormalities that fell within the phenotypic range associated with OCA2.

(Ortonne, 2008).

Histopathologically, in OCA there is a reduction in melanin content with normal number of melanocytes present within the epidermis ***(Ortonne, 2008)***. In both OCA1 and OCA2, the skin shows melanocytes as suprabasal clear cells. The use of silver stain does not demonstrate melanin in either types. Electron microscopy may illustrate some melanosomes with melanin in OCA2, where as in OCA1 melanosomes has complete absence of melanin. Normal structure of melanocytes is demonstrated in both types. In addition macromelanosomes have been noticed in OCA2. Stage II malanosome are rarely present in OCA2 ***(Oculicz et al., 2003).***

Syndromic albinism:

There are several syndromes of albinism associated with systemic pathology. They include:

Angelman syndrome (AS):

It is a neurogenic disorder with severe developmental delay, virtual absence of speech, and motor impairment. Behavioural phenotype that includes happy demeanor and distinctive rhythmic electroencephalographic feature, epilepsy is present in 90% of patients ***(Pelc et al., 2008).*** One percent of patients with AS also have OCA2 ***(Ortonne, 2008).***

Chèdiak-Higashi syndrome:

It is a rare autosomal recessive disorder. The clinical phenotype includes OCA with a silvery grey cast of the hair, photophobia, nystagmus and ocular hypopigmentation, bleeding diathesis, progressive neurologic dysfunction and severe immunodeficiency ***(Ortonne, 2008).***

Histologically, there is giant melanosomes within melanocytes, due to the uncontrolled fusion of not only malanosomes but also other lysosome-derived organelles ***(Ortonne, 2008).***

Cross-McKusick-Breen syndrome (CMBS):

It is a syndrome that consists of ocular and cutaneous hypopigmentation, severe mental retardation with spastic tetraplegia, and athetosis. It is also characterized by growth

retardation, dolichocephaly, cataract, high arched palate, small widely spaced teeth, progressive neurological manifestations, hypochromic anemia, generalized osteoporosis, urinary tract abnormality, bilateral inguinal hernia and focal interventricualr septal hypertrophy of the heart ***(Scheinfeld, 2003).***

Elejalde syndrome (ES):

It is a rare autosomal recessive disorder characterized by silvery hair, central nervous system dysfunction and a wide spectrum of ophthalmologic abnormalities ***(Scheinfeld, 2003).*** Silvery eyelashes are present in these patients. Intense long lasting skin tanning after sun exposure occurs ***(Afifi et al., 2007)***.

Histopathological study reveals increased pigment in the basal layer, more clearly seen as irregularly distributed oval clumped melanin in the basal melanocytes ***(Afifi et al., 2007).***

Griscelli syndrome (GS):

It is a rare autosomal recessive disorder that results in pigment dilution of skin and hair (silver hair). Children with GS may develop neurological problems, and may develop an uncontrolled T-lymphocyte and macrophage activation syndrome known as hemophagocytic syndrome or hemophagocytic lymphohistiocytosis ***(Scheinfeld, 2003).***

Histopathologically, there is prominent melanocytes in the basal layer of the epidermis. The malanocytes are large and distended with a large volume of melanin. The adjacent keratinocytes are completely devoid of melanin ***(Patrick et al., 2007).***