

Topical Adjuvant Therapy In The Treatment Of Ocular Surface Tumors

**Essay
Submitted by**

Dalia Mohamed Abu Zeid,

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Under Supervision
of

Prof. Dr. Hamdy Mohamed Esam El Din Hamdy

Professor of Ophthalmology
Faculty of Medicine
Cairo University

Prof. Dr. Esam Abd El Ghaffar Metwaly

Professor of Ophthalmology
Faculty of Medicine
Cairo University

Dr. Ihab Saad Othman, MD, FRCS

Assistant Professor of Ophthalmology
Faculty of Medicine
Cairo University

**Cairo University
Faculty of Medicine
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Table of contents

List of abbreviations	
List of figures	
List of tables	
Introduction	2
Chapter one: Anatomy of the ocular surface	
Conjunctiva	5
Cornea	10
limbus	12
Chapter two: Diagnosis of ocular surface tumors	
Ocular Surface Squamous Neoplasia	16
Melanocytic ocular surface tumors	29
Lymphoid lesions	38
Work up of ocular surface tumors	41
Differential diagnosis of ocular surface tumors	51
Chapter three: Management	
Different modalities of management	54
Chapter four: Topical chemotherapy	
Mitomycin	
Mitomycin background	70
Uses of mitomycin-c in ocular surface tumors	73
Impression cytology following mitomycin C therapy	80
Side effects	81
Interferon-alpha-2b	
Interferon-alpha-2b background	82
Uses of topical Interferon-alpha-2b in ocular surface tumors	83
Side effects & toxicity of topical & intralesional Interferon-alpha-2b	90
Fluorouracil	
5-Fluorouracil background	92
Uses of Fluorouracil in ocular surface tumors	93
Side effects & toxicity	96
Cyclosporine	
Cyclosporine background	97
Uses of Cyclosporine in ocular surface tumors	98
Summary	
References	
Arabic summary	

List of abbreviations:

5-FU	5-fluorouracil
CALT	conjunctiva-associated lymphoid tissue
CCIN	corneal- conjunctival intraepithelial neoplasia
CIN	conjunctival intraepithelial neoplasia
CIS	Carcinoma in situ
CSA	Cyclosporine A
E4P	erythrose-4-phosphate
GI	Gastrointestinal
HLAs	human leukocyte antigens
HPV	human papilloma virus
IC	Impression cytology
IFNα2b	Interferon alpha-2b
MALT	mucosa-associated lymphoid tissue
MM	malignant melanoma
MMC	mitomycin C
OSSN	Ocular surface squamous neoplasia
PAM	Primary acquired melanosis
PEP	phosphoenolpyruvate
SCC	squamous cell carcinoma
SLN	Sentinel lymph node biopsy
UVR	ultraviolet radiation

List of figures

Figure 1-1	Sagittal or vertical section of both eyelids and the eye are shown to the left(Jakobiec., 1982).
Figure 1-2	Lymphatic drainage into the preauricular & submandibular lymph nodes (Snell ., 2003).
Figure 1-3	Microscopic picture of the cornea (Snell ., 2003).
Figure 1-4	The limbus is the corneal-scleral junction(Jakobiec., 1982).
Figure 2-1	Conjunctival intraepithelial neoplasia (CIN;carcinoma- in-situ) with corneal involvement, displaying leukoplakia on both the conjunctiva and cornea(Shields et al., 2004)
Figure 2-2	Invasive squamous cell carcinoma of the conjunctiva(Shields et al., 2004)
Figure 2-3	IC of normal conjunctival epithelium mild ,moderate &severe dysplasia. carcinoma in situ, invasive squamous cell carcinoma (Barros et al 2009)
Figure 2-4	Light photomicrograph of mild ,moderate &severe dysplasia. carcinoma in situ, invasive squamous cell carcinoma (H&E, x 50) (Lee et al 1995).
Figure 2-5	Conjunctival nevus, PAM & vmalignant melanoma of the conjunctiva (Othman., 2009).
Figure 2-6	Left istopathologic section from a patient with PAM with atypia of the conjunctiva shows prominent nests of atypical melanocytes in the junctional region with pagetoid invasion (arrows) of the overlying epithelium H&E Right: Histopathologic section shows epithelioid melanoma cells in the junctional region of the conjunctiva with pagetoid invasion (arrows) of the overlying epithelium (hematoxylin and eosin, × 400) (Jakobiec., 1982).
Figure 2-7	In vivo confocal microscopy of conjunctival papilloma.& conjunctival intraepithelial neoplasia (Messmer et al., 2006).
Figure 2-8	In vivo confocal microscopy of conjunctival nevus & primary acquired melanosis without atypia(Messmer et al., 2006).
Figure 2-9	In vivo confocal microscopy of primary acquired melanosis with atypia & malignant conjunctival melanoma (Messmer et al., 2006).
Figure 3-1	Surgical excision of conjunctival malignancy using the “no touch” technique (Shields& Shields ., 2004).

Figure 4-1	Mitomycin formula (Peters., 1995).
Figure 4-2	Synthesis of the key intermediate, 3-amino-5-hydroxy-benzoic acid (Salmon ., 1995).
Figure 4-3	Formation of mitosane core followed by tailoring specific to Mitomycin C (Salmon ., 1995).
Figure 4-4	Pre&post treatment with MMC of conjunctival tumor(Papandroudis et al., 2002).
Figure 4-5	Pre&post treatment with MMC of conjunctival tumor(Ozcan et al., 2007).
Figure 4-6	Pre&post treatment with MMC of primary acquired melanosis(Demirci et al., 2000).
Figure 4-7	Pre&post treatment with topical interferon alfa-2b in a patient with CCIN (Sturges et al., 2008).
Figure 4-8	Pre&post treatment with topical interferon alfa-2b in a patient with Conjunctival papillomata (Schechter et al., 2002).
Figure 4-9	Pre&post treatment with topical interferon alfa-2b in a patient with conjunctival melanoma (Finger et al., 2008).
Figure 4-10	5-FU formula (Longley et al., 2003).
Figure 4-11	Pre&post treatment with 5-FU of conjunctival tumor (Yamamoto et al., 2002).
Figure 4-12	Cyclosporine formula (Toba et al., 2005).
Figure 4-13	Suggested treatment pathway for corneal or conjunctival tumors (Chalasani et al., 2006).

List of tables

Table 1	Main differences between papillomata affecting children and adults
Table 2	Topical Mitomycin C 0.04% drops for Extensive Recurrent Conjunctival Corneal SCC in Ten Cases
Table 3	Topical MMC for patients with PAM with atypia and/or malignant melanoma
Table 4	Topical and intralesional IFN α 2b for patients with CCIN, conjunctival papilloma
Table 5	Topical interferon alfa-2b for treatment of patients with PAM with atypia & conjunctival malignant melanoma
Table 6	Toxicity of topical& intralesional IFN α 2b
Table 7	Systemic toxicity of intralesional IFN α 2b
Table 8	topical 5-FU for patients with CCIN
Table 9	topical 5-FU for patients with SCC

Aim of the Work:

This essay will involve the reviewing of new modalities used for treating ocular surface tumors such as topical mitomycin c, 5- fluorouracil(5-FU), interferon alpha-2b and other medications used as a primary and adjuvant therapy in the treatment of ocular surface tumors.

The review will include types, conventional treatment of ocular surface tumors also indications, regimens used, efficacy, side effects and complications of topical therapy.

Introduction

Historical background:

Squamous cell carcinoma of the conjunctiva and cornea has been long established in the literature, described as early as 1860 by Von Graefe under the name epithelioma **(Duke-Elder., 1985)**. Nicholls in 1939 reviewed a condition called epithelial plaque. Other names that have been used previously in the literature are tyloma, keratosis and conjunctival callosities. There was no specific reference to dysplasia, but to a so-called "precancerous" condition **(Nicholls ., 1939)**.

In 1942, McGavic described five lesions showing histopathologic changes similar to that of Bowen's disease of the skin, i.e., cellular variation without violation of the basement membrane. McGavic suggested the terms "intraepithelial epithelioma" (Bowen's disease) and "Bowenoid epithelioma" to describe lesions not fully characteristic of Bowen's original description **(McGavic ., 1942)**.

Later that year, Ash and Wilder published a series of 93 epithelial tumors of the limbus, which included so-called epidermalization and dyskeratoses, carcinoma and papilloma. They concluded that epidermalization was an important precursor to development of tumor and that some basic factors such as Vitamin A deficiency, drying, or chronic irritation were responsible for this metaplasia **(Ash et al.,1942)**.

Janert in 1956 differentiated Bowen's disease as epithelial hyperplasia with dyskeratosis as opposed to leukoplakia with hyperkeratosis **(Janert, 1956)**.

Lugossy et al preferred the term "precancerous" epithelioma of the limbus. This was based on the theory that carcinoma develops by gradual thickening and transition in the limbal epithelium **(Lugossy .,1956)**.

One of the largest single series was Irvine's study of 104 dyskeratotic epibulbar tumors. He observed that there was little correlation between the microscopic criteria of degrees of dyskeratosis and clinical behavior and doubted the potential for metastasis **(Irvine., 1963)**. Zimmerman in 1964 stated that leukoplakia should only be used as a clinical descriptive term to describe an opaque white placoid lesion in a mucous membrane. He also stated that Bowen's disease, as a specific histological entity **(Zimmerman.,1964)**.

Carroll and Kuwabara in 1965 differentiated the tumors into four distinct cell types and correlated this with recurrence rate **(Carroll & Kuwabara., 1965)**.

The term conjunctival intraepithelial neoplasia (CIN) was coined by Pizzarello and Jakobiec in 1978, paralleling the gynecological pathology term for cervical intraepithelial neoplasia **(Pizzarello ., 1978)**.

Waring et al extended the term to include the cornea **(Waring ., 1984)**. Erie et al further extended it to include invasive neoplasia **(Erie et al., 1986)**.

Lee et al suggested the use of the "umbrella" term ocular surface epithelial dysplasia (OSD), then in 1995 introduced the term ocular surface squamous neoplasia (OSSN). Ocular surface denotes involvement of the conjunctiva or cornea; squamous epithelium excludes other epithelial cells such as basal cells and melanocytes and neoplasia includes both dysplastic and carcinomatous lesions **(Lee et al., 1995)**.

CHAPTER1:ANATOMY OF THE OCULAR SURFACE

Introduction

The anatomical ocular surface is composed of the mucosa that lines the globe and palpebral surfaces, the corneoscleral limbus, the corneal epithelium, and the tear film. The normal structure of these tissues is described in the following (**Spencer & Zimmerman., 1996**).

Conjunctiva

The conjunctiva is a thin mucous membrane that lines the eyelids and is reflected at the superior and inferior fornices onto the anterior surface of the eyeball. The conjunctival epithelium is continuous with the epidermis of the skin at the lid margin and with the corneal epithelium at the limbus. The conjunctiva thus forms a potential space, the conjunctival sac, which is open at the palpebral fissure(**Spencer & Zimmerman., 1996**).

The lid margin forms a transitional zone between the conjunctiva and the skin of the eyelids, is about 2 mm thick and has a thin gray line separating its anterior and posterior borders. The anterior border has two or three rows of stiff, sensitive cilia. The sharp posterior border, positioned against the globe, contains the orifices for the tarsal glands. The meibomian glands are located within the tarsal plates and secrete lipids for the oily layer. They are not connected to the lash follicles(**Spencer & Zimmerman., 1996**).

General arrangement

The conjunctiva is divided into three regions: 1) the palpebral conjunctiva, 2) the conjunctival fornices and 3) the bulbar conjunctiva.

Palpebral Conjunctiva

This portion lines the eyelids and is reflected at the superior and inferior fornices onto the anterior surface of the eyeball. At the margins of the eyelid, the conjunctiva continues into the skin along the posterior openings of the tarsal glands. A shallow groove on the back of the lid, the sulcus subtarsalis, lies about 2 mm from the posterior edge of the lid margin. The area of the conjunctiva that covers the upper tarsal plate is strongly bound to it in its entire extent. The conjunctiva covering the lower tarsal plate is adherent only to its upper half (**Greiner et al., 1977**).

Conjunctival Fornices

The conjunctiva of the superior and inferior fornices forms a transitional region between the palpebral and bulbar conjunctivae. It is loosely attached to the underlying fascial expansions of the sheaths of the levator and recti muscles .

Bulbar Conjunctiva

This portion lies in contact with the eyeball. It is thin and translucent. It is loosely attached by connective tissue to the sclera and the fascia bulbi. At 3mm from the cornea ,the conjunctiva becomes more closely attached to the sclera and the fascia bulbi. The line along which fusion of the conjunctiva to the cornea occurs is called the conjunctival limbus. It is situated about 1 mm anterior to the edge or limbus of the cornea, that is, the junction between the cornea and the sclera. The bulbar sheath fuses with the sclera about 1.5 mm posterior to the corneal limbus (**Greiner et al., 1977**).

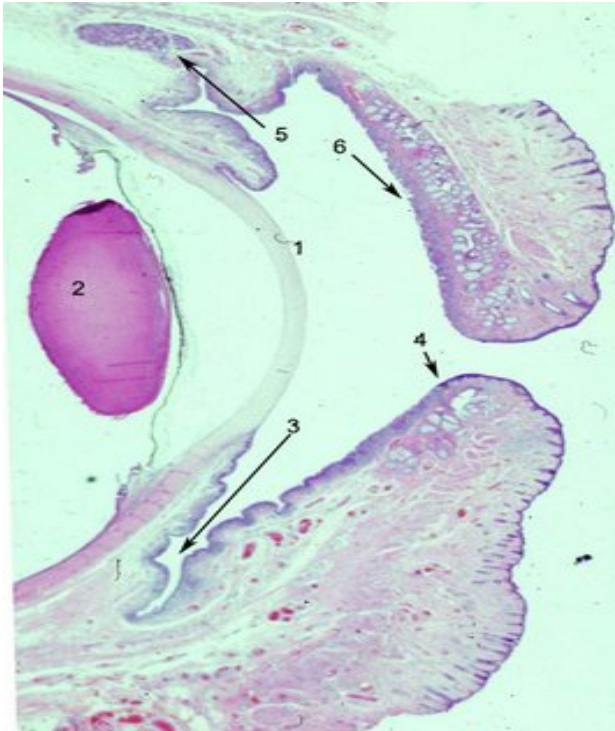


Fig 1-1 sagittal or vertical section of both eyelids and the eye are shown to the left. (1) The cornea (2) The lens 3) The fornix (has more redundant conjunctiva. (4) The marginal conjunctiva (6)The tarsal conjunctiva (5) The palpebral portion of the lacrimal gland is also shown in this photograph (Jakobiec., 1982).

Structure

Histologically, the conjunctiva has an epithelial covering of stratified columnar cells consisting of two to five layers resting on a lamina propria of loose connective tissue. At the limbus there is a change to stratified squamous non keratinized epithelium, which is continuous with the epithelium covering the cornea. On the posterior edge of the lid margin, along the posterior margins of the opening of the tarsal glands, the conjunctiva joins the skin (**Greiner et al., 1977**).

Conjunctival submucosa

This consists of fine delicate connective tissue, which ends at the edges of the cornea. In its superficial part are large collections of lymphocytes, which are present in highest concentration in the fornices and are absent in the marginal